Vitiligo surgical treatment

Vitiligo surgical treatment

DOI: http://dx.doi.org/10.5935/scd1984-8773.20168401

ABSTRACT

The evolution in surgical techniques for treatment of vitiligo has been producing extremely satisfying results in patients with stable vitiligo, without Köebner phenomenon and resistants to other types of treatment. Many techniques are available and should be used accordingly to the patient and to the dermatologist experience to optimize the results.

Keywords: vitiligo, surgery, transplantation, dermatologic surgical procedures

RESUMO

A evolução nas técnicas cirúrgicas do tratamento do vitiligo tem proporcionado resultados extremamente satisfatórios em pacientes com vitiligo estável, sem fenômeno de Köebner e refratários a outros métodos terapêuticos. Diversas técnicas são conhecidas e devem ser adequadas de acordo com o paciente e a experiência do dermatologista para otimizar os resultados obtidos.

Palavras-chave: *vitiligo, cirurgia, transplante, procedimentos cirúrgicos dermatológicos*

INTRODUCTION

Melanocytes transplantation procedures are therapeutic options indicated for patients bearing vitiligo in its stable phase and that has not responded to previous clinical treatments. [1] These techniques can potentially yield excellent results, even in anatomical areas that are traditionally refractory, such as distal extremities, elbows, knees, nipple areolas, eyelids and lips. [2] In recent decades, research on surgical treatment of vitiligo has increased substantially, and autologous melanocytes transplantations have become increasingly accessible to dermatologist physicians.

The disease's stability is the most important prerequisite for a successful surgical procedure. [1,3] Most authors define the stability criterion as the absence of new lesions or enlargement of pre-existing lesions within one year. [1,3,4] In cases of doubtful stability, a test can be carried out with the transplantation of four or five mini-grafts using 1.0 mm to 1.2 mm punches in the area to be treated, evaluating whether after a period of three to four months some repigmentation halo has been formed in the region. [5] Absence of the Köebner's phenomenon in candidates to undergo surgery also is of utmost importance, since the surgical manipulation of donor and receptor

Continuing Medical Education

Authors:
Gerson Dellatorre[1]
Fernando Eibs Cafrune[2]

[1] Dermatologist Physician. Preceptor at the Dermatology Service, Hospital Santa Casa de Curitiba - Curitiba (PR), Brazil.

[2] Dermatologist Physician. Preceptor at the Dermatology Service, Hospital Santa Casa de Misericórdia de Porto Alegre - Porto Alegre (RS), Brazil.

Correspondence:
Gerson Dellatorre
Serviço de Dermatoloia
Pça. Rui Barbosa, 694
Cep 80010-030 - Centro
Curitiba – PR, Brazil
e-mail: dellatorre@gmail.com

Received on: 28/07/2016
Approved on: 26/08/2016

This study was performed at the Hospital Santa Casa de Curitiba - Curitiba (PR), Brazil.

Financial support: None.
Conflict of interests: None

areas can induce new achromatic lesions. [1] Although it is possible to treat all types of vitiligo with good efficacy using this method, segmental vitiligo tends to yield a better response. [6] Therefore, accurate classification of the disease it is crucial, since it may influence the patient's prognosis.

Surgical modalities can to be classified into tissular or cellular techniques, according to the type of graft to be transplanted. [1,4] Most of the techniques require de-epithelization of the receptor area in order it can receive the tissular or cellular graft. This preparation is usually performed applying superficial dermabrasion, which is a simple, widely used and cost effective technique (Figure 1). Other options include the use of carbon dioxide and Er:YAG lasers, suction blisters, curettage and cryotherapy. [7,8]

In general, dressings are applied immediately after autologous transplantation surgery, and are left untouched in the treatment area over a period ranging from 7 to 14 days. Their function is to accelerate the healing of the dermabraded areas, prevent bacterial contamination, and keep transplanted tissues or cells in the receptor area. [8] To this end, it is common to use collagen-based and/or non-adherent dressings.

As a complement to the surgical treatment, phototherapy can be performed aimed at increasing the repigmentation outcome. It has been recently demonstrated that the use of narrow-band UVB phototherapy in the pre and postoperative periods is related to better repigmentation rates. [9]

TISSULAR TECHNIQUES

Punch grafts

Punch grafting (PG) is a simple, low cost, and widely used technique for the surgical treatment of vitiligo. It consists in obtaining multiple circular grafts from the donor area, taken with 3 mm punches, for subsequent transplantation to the receptor area, which in turn is prepared with punches of the same size (or slightly smaller), in a layout whose spacing corresponds to 2,5x the size of the graft (Figures 2 and 3). [10-12] As an adverse effect, the technique can produce undesirable cosmetic effects known as "cobblestone " appearance, meaning that the graft becomes slightly more elevated than the neighboring receptor area. This is mainly observed when grafts with greater diameters are used. This effect can resolve spontaneously or be treated using electrofulguration. [13] Due to the long time needed to obtain grafts, PG is typically reserved for the treatment of small areas. However, the use of devices with motor driven punchs can reduce this time, allowing the treatment of greater areas. [10]

Regarding its effectiveness, a study that included 880 patients showed that 90-100% repigmentation was achieved in 74.55% of patients during a two-year follow-up period. [11]

SUCTION BLISTER BASED EPIDERMAL GRAFTING

This procedure involves the induction of subepidermal suction blisters in the donor area (usually thighs or arms) by prolonged application of vacuum, with the subsequent transplantation of its roof ? to the receptor area. [1] The vacuum is normally applied with the aid of a syringe or a device specifically used for this purpose (Figure 4). This technique has some advantages over PG, since the donor area heals leaving only a minimal post-in-

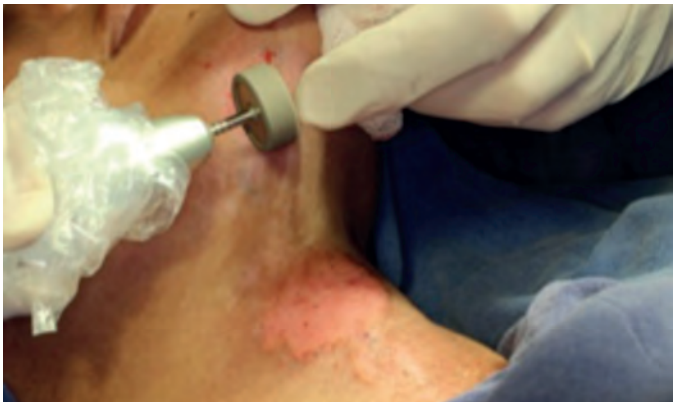


Figure 1: Dermabrasion of the receptor area using motor-driven dermabraser with diamond sandpaper

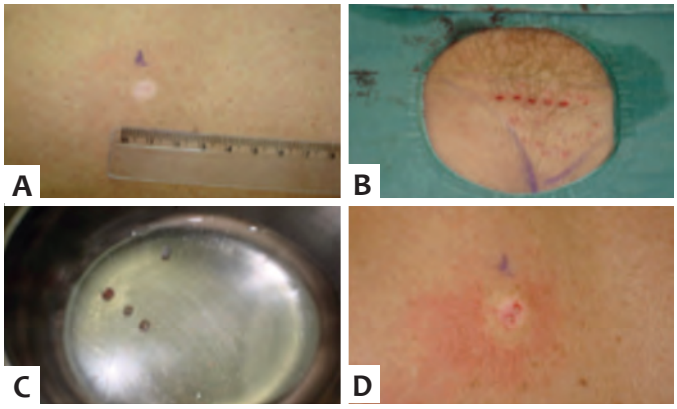


Figure 2: Punch grafting. **A.** Stable and recalcitrant achromic lesion after clinical treatment; **B.** Harvesting of the grafts from the sacral donor area; **C.** Harvested grafts; **D.** Grafting of the receptor area

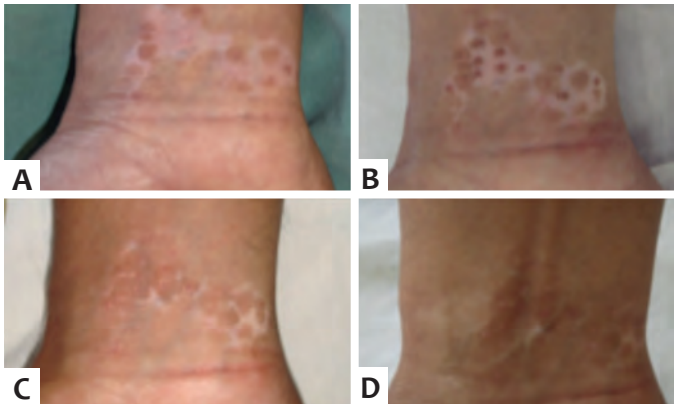


Figure 3: Punch grafting. Six-month development of repigmentation halos, with more than 90% repigmentation. This image was kindly supplied by Dr. Gustavo Braz Tha - Dermatology Service of the Hospital Santa Casa de Curitiba

flammatory hyperpigmentation. [14] Moreover, the "cobblestone" effect described for the previous technique does not occur due to the fact that the graft is purely epidermal. [15]

According to a recent study, suction blister based epidermal grafting (SBEG) can yield results that vary from good to excellent (65-100% repigmentation) in 80% of patients. Although it is cost effective, this method is deemed as protracted, since approximately two hours are necessary to obtain a blister using a 10ml syringe. That time can be shortened using the anesthetic injections in the dermis or applying heat to the donor area before the blister is obtained. [15.16]

PARTIAL THICKNESS SKIN GRAFTING

Partial thickness skin grafts (PSG) have the advantage of treating large areas with good response (90-100% repigmentation) on a single procedure. The graft is obtained with the assistance of a dermatome, meaning the surgeon must have the proper expertise and experience to conduct the procedure. [17] Furthermore, color incompatibility in the receptor area and the potential for unaesthetic healing in the donor area are possible side effects of this technique. [4]

TISSUE FRAGMENTATION TECHNIQUES: EPIDERMAL CURETTAGE AND TISSULAR MACERATION

Different melanocyte transplantation techniques have been described using tissue fragmentation. A common characteristic to these techniques is the fact that the harvesting process of the tissue from the donor area leaves the skin macerated into small fragments to be grafted in the receptor area. In general, they are rapid and technically easy to perform methods, and can be carried out in simple and inexpensive surgical settings. They are capable of re-pigmenting areas that are four to ten times larger than the donor area. [18.19]

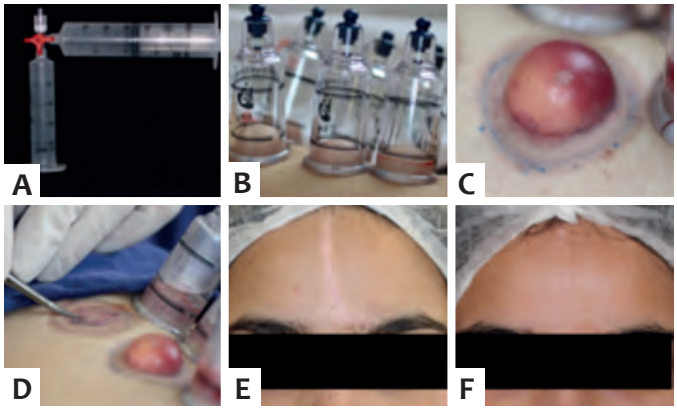


Figure 4: Suction blister epidermal grafting. **A.** Suction device using conventional syringes and a three-way tap; **B.** Differentiated suction equipment, with one-way valve; **C.** Sub-epidermal blister formed after prolonged suction; **D.** Incision of the blisters' periphery for subsequent transfer to the dermabraded area to be treated; **E.** Segmental vitiligo linear lesion in the forehead. Pretreatment; **F.** Six-month postoperative, with greater than 90% repigmentation of the lesion

The epidermal curettage (EC) technique is performed after asepsis and demarcation of the donor area (usually thigh or sacral region), where topical or injectable anesthesia is performed. With a sterile curette, the tissue is removed up until the pinpoint bleeding is visualized. The removed material is placed in a jar with saline solution, and may undergo further maceration up until a paste consistency is obtained. After dermabrasion of the receptor area, the macerated tissue is put in place observing a homogeneous distribution. Next, the area is covered with non-adherent dressing. The dressing should be kept in place with restriction of movement for one week. [18] This method leads to rapid re-epithelialization, usually without residual scarring in the donor area.

In the tissular maceration (TM) method, a thin layer of skin (with little dermis) is removed from the donor area with the aid of a flexible blade. The tissue is placed in saline solution and shredded with the aid of a delicate scissors up until the fragments are substantially reduced in size. Once the material has been prepared, it is placed on the dermabraded area, followed by a dressing, just as described in the previous method. [19,20] Absence of scars in the donor area and intense repigmentation (over 90%) were observed in a study. [19]

CELLULAR TECHNIQUES

Suspension of non-cultured epidermal cells

In the non-cultured epidermal cells suspension (NECS), a thin partial thickness graft is obtained from the donor area with the aid of a razor blade or a dermatome (Figures 5A and 5B). Then the tissue fragment is incubated at 37°C in a solution of trypsin with ethylene dinitrilotetrascetic acid (EDTA), which separates the epidermis from the dermis and ungroups the epidermal cells. After centrifugation of the solution, a concentrated suspension of melanocytes and keratinocytes is obtained, re-suspended in a small volume, and transferred to the dermabraded receptor area (Figures 5C, 5D and 6).

This method has the advantage of the possibility of expanding the ration between the donor and receptor areas from five to ten times, meaning it is capable of treating large areas with satisfactory results. [1.4] Good to excellent results (75-100% repigmentation) can be achieved in 89% of patients. [21] Among this technique's disadvantages is the need for expertise and experience for obtaining the donor tissue fragment, in addition to requiring specific laboratory equipment for the trypsinization phase. [1]

Suspension of non-cultured cells from the external follicular sheath

In this procedure, a cellular suspension is obtained from hair follicles obtained using a follicle unit extraction method assisted by small punches – similar to how hairs are obtained in the hair transplant technique (Figure 7). Approximately 15 to 25 follicles are extracted per patient, depending on the area to be transplanted. Once extracted, the hair follicles are subjected to a trypsinization process similar to that of NECS, aiming at obtaining the cellular suspension. [22.23]

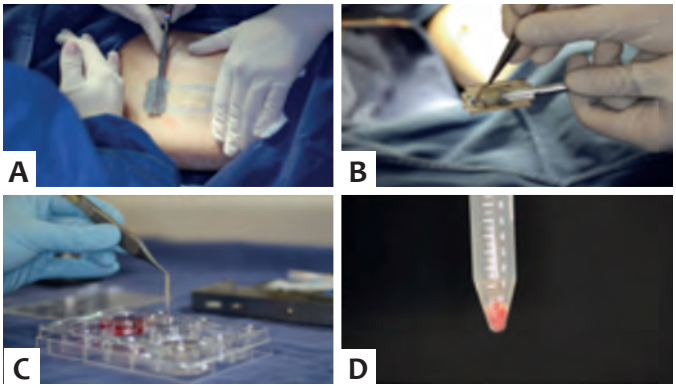


Figure 5: NECS. **A.** Preparation of the skin graft with the aid of a shaving blade, **B.** A thin graft is obtained; **C.** Graft's epidermal cells detachment phase after trypsinization; **D.** Cell pellet consisting of keratinocytes and melanocytes in the lower portion of the tube after centrifugation

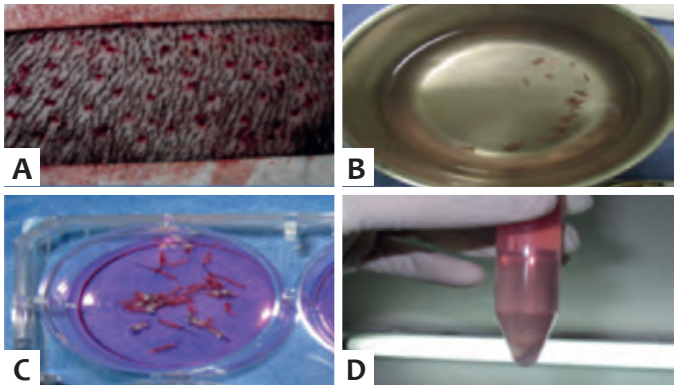


Figure 7: NECS. **A.** Preparation of the receptor area; **B.** Application of the cell suspension on the prepared area; **C.** Receptor area pre-treatment (above the dashed line); **D.** Receptor area post-treatment (above the dashed line)

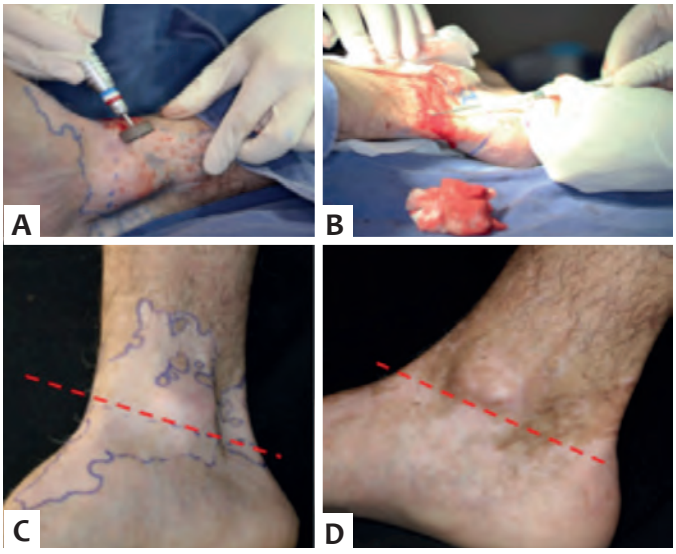


Figure 6: Figure 6: NECS. **A.** Preparation of the receptor area; **B.** Application of the cell suspension on the prepared area; **C.** Receptor area pre-treatment (above the dashed line); **D.** Receptor area post-treatment (above the dashed line)

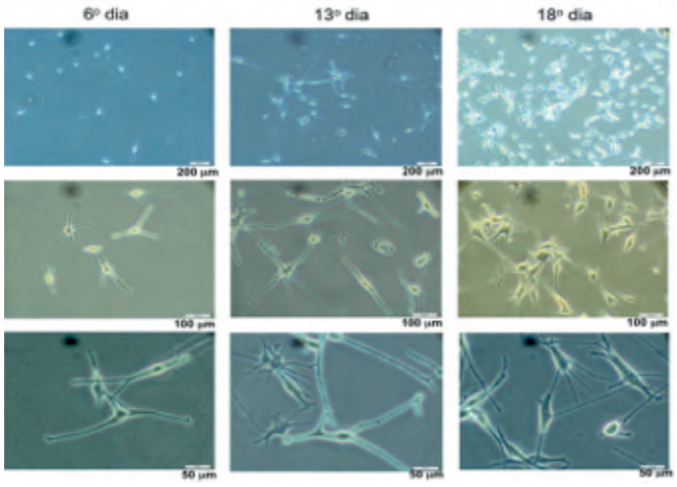


Figure 8: Optical micrographs of cultured human primary melanocytes isolated from skin specimens (4x, 10x and 20x magnification, top to bottom). Cells were previously treated with geneticin for eliminating the fibroblasts and keratinocytes. After treatment with geneticin, melanocytes were cultured for 18 days in medium supplemented with growth factors (bFGF and HGF), which allowed the maintenance and proliferation of cells. Image kindly provided by: Dr. Renata Helena Monteiro Sindeaux and Mariana Kraft Soares, Núcleo de Investigação Molecular Avançada (Advanced Molecular Research Nucleus) - NIMA, Pontifícia Universidade Católica do Paraná - PUC-PR.
6° dia = 6th day; 13° dia = 13th day; 18° dia = 18th day

Obtaining cells originated from hair follicles has some advantages. In addition to being considered an important reservoir region of melanocytes and their precursors, the scars resulting from follicular extraction are virtually invisible. [22] In a comparative and randomized study contrasting NECS and the suspension of non-cultured cells from the external follicular sheath (SNCEFS) conducted with 30 patients, repigmentation of 92% and 78% of the lesions were obtained, respectively. However the difference was not statistically significant. [24]

Suspension of cultured cells

The *in vitro* culture of melanocytes (Figure 8), combined or not with keratinocytes, can dramatically increase the number of transplanted cells. One of the greatest advantages of this technique dwells in the fact that, from a small skin fragment, it is possible to obtain sufficient cells to treat large areas. [25] This method can lead to even greater repigmentation rates when compared to techniques without culture of cells. [25,26] In a recent study, the suspension of cultured cells (SCC) was able to produce more than 90% of re-pigmentation in up to 81.3% of patients. [9]

Despite these advantages, the high cost, the dependence on a specialized team and on laboratory cell culture equipment are important disadvantages of the method. [1] Moreover, since the culture media contain mitogenic factors, prolonged follow-up of patients is recommended due to the theoretical potential post-transplantation malignant transformation. [26] Although in some countries this risk is still considered an ethic barrier for the use of the technique for therapeutic purposes, there are an increasing number of studies in the medical literature with absence of adverse events. [9,25]

REFERENCES

1. Gupta S, Olsson MJ, Kanwar AJ, Ortonne JP, editors. Surgical management of vitiligo. Oxford: Blackwell Publishing; 2007.
2. Mulekar SV, Al Issa A, Al Eisa A. Treatment of vitiligo on difficult-to-treat sites using autologous noncultured cellular grafting. Dermatol Surg. 2009;35(1):66-71.
3. Sahni K, Parsad D. Stability in Vitiligo: Is there a Perfect Way to Predict it? J Cutan Aesthet Surg. 2013;6(2):75-82.
4. Parsad D, Gupta S, IADVL Dermatosurgery Task Force. Standard guidelines of care for vitiligo surgery. Indian J Dermatol Venereol Leprol. 2008; Suppl 74:S37-45.
5. Falabella R, Arrunategui A, Barona MI, Alzate A. The minigrafting test for vitiligo: detection of stable lesions for melanocyte transplantation. J Am Acad of Dermatol. 1995;32(2 Pt 1):228-32.
6. Falabella R. The minigrafting test for vitiligo: Validation of a predicting tool. J Am Acad of Dermatol. 2004;51(4):672-3.
7. Silpa-Archa N, Griffith JL, Williams M, Lim HW, Hamzavi IH. Prospective comparison of recipient-site preparation with fractional carbon dioxide laser vs. dermabrasion and recipient-site dressing composition in melanocyte-keratinocyte transplantation procedure in vitiligo: a preliminary study. B J Dermatol. 2016;174(4):895-7.
8. Al-Hadidi N, Griffith JL, Al-Jamal MS, Hamzavi I. Role of recipient-site preparation techniques and post-operative wound dressing in the surgical management of vitiligo. J of Cutaneous Aesthetic Surg. 2015;8(2):79-87.
9. Zhang DM, Hong WS, Fu LF, Wei XD, Xu AE. A randomized controlled study of the effects of different modalities of narrow-band ultraviolet B therapy on the outcome of cultured autologous melanocytes transplantation in treating vitiligo. Dermatol Surg. 2014;40(4):420-6.
10. Chandrashekar B, Madura C, Varsha D. Autologous mini punch grafting: an experience of using motorized power punch in 10 patients. J Cutan Aesthet Surgery. 2014;7(1):42-5.
11. Malakar S, Dhar S. Treatment of stable and recalcitrant vitiligo by autologous miniature punch grafting: a prospective study of 1,000 patients. Dermatology. 1999;198(2):133-9.
12. Saldanha KD, Machado Filho CD, Paschoal FM. Action of topical mometasone on the pigmented halos of micrografting in patients with vitiligo. An Bras Dermatol. 2012;87(5):685-90.
13. Falabella R. Surgical treatment of vitiligo: why, when and how. J Eur Acad Dermatol Venereol. 2003;17(5):518-20.
14. Ashique KT, Kaliyadan F. Long-Term Follow-up and Donor Site Changes Evaluation in Suction Blister Epidermal Grafting Done for Stable Vitiligo: A Retrospective Study. Indian J Dermatol. 2015;60(4):369-72.
15. Gou D, Currimbhoy S, Pandya AG. Suction blister grafting for vitiligo: efficacy and clinical predictive factors. Dermatol Surg. 2015;41(5):633-9.
16. Kim T, Roh HJ, Kim JY, Noh S, Oh SH. Rapid formation of suction blister through intradermal injection of local anesthetics in epidermal graft for vitiligo. Dermatol Surgery. 2010;36(10):1642-3.
17. Agrawal K, Agrawal A. Vitiligo: repigmentation with dermabrasion and thin split-thickness skin graft. Dermatol Surg. 1995;21(4):295-300.
18. Machado Filho CD, Timoner FR. Epidermal curettage technique (ECT) for tissue harvest from the donor area for melanocyte autologous grafting in cases of vitiligo. An Bras de Dermatol. 2014;89(4):681-3.
19. Krishnan A, Kar S. Smashed skin grafting or smash grafting - a novel method of vitiligo surgery. Int J Dermatol. 2012;51(10):1242-7.
20. 20. Pahwa M, Gupta S, Khunger N. Multimodal single-step vitiligo surgery: a novel approach. Dermatol Surg. 2010;36(10):1627-31.
21. Budania A, Parsad D, Kanwar AJ, Dogra S. Comparison between autologous noncultured epidermal cell suspension and suction blister epidermal grafting in stable vitiligo: a randomized study. B J Dermatol. 2012;167(6):1295-301.
22. Vinay K, Dogra S, Parsad D, Kanwar AJ, Kumar R, Minz RW, et al. Clinical and treatment characteristics determining therapeutic outcome in patients undergoing autologous non-cultured outer root sheath hair follicle cell suspension for treatment of stable vitiligo. J Eur Acad of Dermatol Venereol. 2015;29(1):31-7.
23. Kumar A, Mohanty S, Sahni K, Kumar R, Gupta S. Extracted hair follicle outer root sheath cell suspension for pigment cell restoration in vitiligo. J Cutan Aesthet Surg. 2013;6(2):121-5.
24. Singh C, Parsad D, Kanwar AJ, Dogra S, Kumar R. Comparison between autologous noncultured extracted hair follicle outer root sheath cell suspension and autologous noncultured epidermal cell suspension in the treatment of stable vitiligo: a randomized study. B J Dermatol. 2013;169(2):287-93.
25. Chen YF, Yang PY, Hu DN, Kuo FS, Hung CS, Hung CM. Treatment of vitiligo by transplantation of cultured pure melanocyte suspension: analysis of 120 cases. J Am Acad Dermatol. 2004;51(1):68-74.
26. Verma G, Varkhande SR, Kar HK, Rani R. Evaluation of repigmentation with cultured melanocyte transplantation (CMT) compared with non-cultured epidermal cell transplantation in vitiligo at 12th week reveals better repigmentation with CMT. J Invest Dermatol. 2015;135(10):2533-5.

Questions for Continuing Medical Education – CME

1) **Regarding the indication for surgical treatment of vitiligo, which of the below is not true?**
   - **a.** Surgical treatment is indicated for stable cases.
   - **b.** The presence of the Köebner phenomenon is a formal contraindication for these methods.
   - **c.** In general, the surgical treatment is today considered a first line treatment for vitiligo.
   - **d.** Anatomical regions normally resistant to clinical treatment can be treated with these techniques.
   - **e.** Although all types of vitiligo can be treated surgically with good results, segmental vitiligo tends yield better therapeutic response.

2. **Regarding the stability of vitiligo, the more widely currently accepted clinical criterion is defined as:**
   - **a.** Absence of new lesions or enlargement of old lesions in the lapse of one year.
   - **b.** Absence of new lesions for one year, with or without enlargement of old lesions.
   - **c.** Absence of new lesions or of enlargement of old lesions for two years.
   - **d.** Absence of new lesions for two years, with or without enlargement of old lesions.
   - **e.** Absence of new lesions or of enlargement of old lesions for three years.

3. **Regarding the surgical modalities in the treatment of vitiligo, it is possible to state that:**
   - **a.** Among tissular techniques are the suspension of non-cultured epidermal cells suspension (NECS) and the suspension of non-cultured cells from the external follicular sheath (SNCEFS).
   - **b.** Cellular techniques have the potential to expand the area to be treated using in general a smaller portion of the donor area.
   - **c.** Tissular techniques such as the partial thickness skin graft require little surgical skillfulness, based on the fact that it is easy to obtain the grafts.
   - **d.** Punch grafting (PG) and tissular fragmentation techniques are considered cellular techniques based on the fact that their grafts are constituted of small fragments.
   - **e.** Cellular techniques usually require less laboratory equipment.

4. **Regarding the suction blister based epidermal grafting (SBEG), which of the below is deemed as false?**
   - **a.** During the suction blisters formation process, the separation of the skin takes place at the dermoepidermal junction level.
   - **b.** The time for obtaining grafts using the suction technique is usually long, though the process can currently be accelerated with the implementation of some changes.
   - **c.** The donor area / receptor area ratio is generally 1: 1.
   - **d.** It is a tissular technique.
   - **e.** The residual scars in the donor area have great probability of becoming hypertrophic scars.

5. **Regarding the non-cultured epidermal cells suspension (NECS), which of the below can be considered true?**
   - **a.** It can be used for treating large areas.
   - **b.** The ratio donor area's size/receptor area's size can reach 1:10.
   - **c.** The necessity of laboratory equipment and supplies is a disadvantage.
   - **d.** Involves the use of mitogenic factors in the laboratory preparation of the suspension.
   - **e.** a, b and c above are true.

6. **The following techniques are preparation methods of the receptor area, except for:**
   - **a.** Cryotherapy.
   - **b.** Fractional laser.
   - **c.** Dermabrasion.
   - **d.** Shaving.
   - **e.** Suction blisters.

7. **Below are factors that increase the expectation for the repigmentation of the treated area, except for:**
   - **a.** Pre and post operative phototherapy.
   - **b.** Keep the receptor area with restricted motion.
   - **c.** The use of antioxidants.
   - **d.** In vitro trypsinization of the donor tissue.
   - **e.** Use of non-adherent dressings.

8. **Which of the below statements is correct?**
   - **a.** The suction blister based epidermal grafting (SBEG) has limited use due to the necessity of a laboratory support team so that it can be performed.
   - **b.** The tissue maceration (TM) and non-cultured epidermal cells suspension (NECS) techniques are similar regarding the removal of tissue from the donor area.
   - **c.** Epidermal curettage (EC) usually leaves an unsightly scar in the donor area.
   - **d.** Cellular techniques lead to faster repigmentation than the so called tissular techniques.
   - **e.** The suspension of non-cultured cells from the external follicular sheath (SNCEFS) has higher repigmentation rates than those of other cellular techniques.

9. **Regarding the punch grafting technique (PG):**

   I. It is indicated for the treatment of small areas.
   II. It can be performed in places with limited resources, at low cost.
   III. It might lead to unsightly scarring of the area treated, known as " cobblestone" appearance.

   Which are correct:
   - **a.** Only I.
   - **b.** Only II.
   - **c.** Only III.
   - **d.** I and III.
   - **e.** All statements are correct.

10. **The surgical treatment of vitiligo:**
    - **a.** makes repigmentation possible even in vitiligo refractory to other treatments.
    - **b.** can be used in any patient with segmental vitiligo.
    - **c.** is the treatment of choice for young patients.
    - **d.** should not be performed in patients being treated with phototherapy.
    - **e.** always leaves scars in the donor area.

Key:

Laser assisted drug delivery 2016;8(3):193-204.

1B, 2C, 3C, 4C, 5D, 6E, 7B, 8C, 9D, 10A

Answers must be submitted online using the website www.surgicalcosmetic.org.br. The deadline for submitting answers will be available on the journal's website.

Original Articles

Primary axillary hyperhidrosis treatment: a prospective and comparative study between liposuction and laserlipolysis

Tratamento da hiper-hidrose axilar primária: estudo prospectivo e comparativo entre lipoaspiração e laserlipólise

Authors:
Guilherme Bueno de Oliveira[1]
Natália Cristina Pires Rossi [2]
Gustavo Bueno de Oliveira [3]

[1] Dermatologist Physician. Member of the Brazilian Dermatology Society and the Brazilian Society of Dermatologic Surgery. Micrographic Mohs surgeon, Dermatology and Dermatologic Surgery Instructor at Faculdade de Medicina Estadual de São José do Rio Preto (Famerp) – Rio Preto (SP), Brazil.

[2] Dermatologist Physician. Member of the Brazilian Dermatology Society and the Brazilian Society of Dermatologic Surgery.

[3] Medicine student, Universidade São Francisco – Bragança Paulista (SP), Brazil.

Correspondence:
Guilherme Bueno de Oliveira
Rua Dr. Presciliano Pinto, 2928
Jardim Santos Dumont
Cep 15020-000 – São José do Rio Preto (SP), Brazil

Received on: 25/06/2016
Approved on: 14/08/2016

This study was performed at a private practice in São José do Rio Preto (SP), Brazil

Financial support: None
Conflict of interests: None

DOI: http://dx.doi.org/10.5935/scd1984-8773.201684850

ABSTRACT

Introduction: Hyperhidrosis is a common disease characterized by excessive sweating. Several treatment options are described as axillary liposuction and laserlipolysis.

Objective: To compare the effectiveness of two treatment methods for axillary hyperhidrosis – one exclusively surgical (liposuction) and the other employing invasive laser therapy (laserlipolysis) – using a prospective, comparative study with a one-year follow up.

Methods: Liposuction was carried out in the right axilla, while laser lipolysis was performed in the left axilla. The evaluation was conducted using the starch-iodine test, comparative histological analysis and patient self-assessment questionnaires.

Results: Twelve patients took part in the study. The starch-iodine test indicated decreased sweating in all patients within one year after the procedures, while the histological analyses showed absence or reduction of the secreting ducts and acini on both sides and in all cases. After one year of follow-up, the patient's satisfaction index measured by the questionnaires remained positive in all cases, with 75% asserting maximum satisfaction, and 25% reporting difference between the sides (better results were described in the right hand side axilla).

Conclusions: Both techniques showed similar effectiveness after one year of follow-up. Laserlipolysis had a lower frequency of postoperative complications.

Keywords: lasers; laser therapy; dermatology; dermatologic surgical procedures

RESUMO

Introdução: *A hiper-hidrose é condição comum caracterizada por sudorese excessiva. Diversas opções terapêuticas são descritas, entre outras a lipoaspiração axilar e a laserlipólise.*

Objetivo*: comparar a eficácia de dois métodos de tratamento para hiper-hidrose axilar: um exclusivamente cirúrgico (lipoaspiração) e outro com laserterapia invasiva (laserlipólise), mediante estudo prospectivo, comparativo, com seguimento de um ano.*

Métodos*: na axila direita foi realizada lipoaspiração, e, na esquerda, laserlipólise. A avaliação foi feita pelo teste do amido-iodo, por estudo histológico comparativo e questionários de autoavaliação dos pacientes.*

Resultados*: 12 pacientes participaram do estudo. O teste do amido-iodo demonstrou diminuição da sudorese em todos os pacientes até um ano após os procedimentos, e o estudo histológico mostrou ausência ou diminuição dos ductos e ácinos secretores nos dois lados também em todos os casos. O índice de satisfação dos pacientes detectado pelo questionário permaneceu positivo em todos os pacientes, sendo que, após um ano de seguimento, 75% deles declararam satisfação máxima, e 25% relataram diferença entre os lados, tendo o direito apresentado resultados melhores.*

Conclusões*: As duas técnicas mostraram igual eficácia após um ano de seguimento. A laserlipólise apresentou menor frequência de intercorrências no pós-operatório*

Palavras-chave: *lasers; terapia a laser; dermatologia; procedimentos cirúrgicos dermatológicos*

INTRODUCTION

Hyperhidrosis is a common condition characterized by excessive sweating. It can manifest in one or more areas: axillae, palms, face, scalp, soles, and groin. [1] Excessive production of sweat – more than necessary to regulate the body's temperature – can significantly influence the affected patients' quality of life, possibly leading to depression or social isolation. Hyperhidrosis can be classified as primary, secondary, generalized (whole body) or focal (specific body sites). [1,2]

Primary axillary hyperhidrosis (PAH) is idiopathic and focal. In addition to affecting the patients' quality of life, it can also lead to a variety of complications, such as bacterial or fungi overgrowth, muscle cramps, eczematous dermatitis, and other dermatological conditions. [3] Secondary hyperhidrosis can be generalized or focal, and results from some triggering event, such as endocrinopathies, neuropathies, infections etc. [1-3] Several treatment options are available for the treatment of axillary hyperhidrosis: topical antiperspirants, systemic medications, iontophoresis, botulinum toxin type A, eccrine glands curettage, axillary liposuction, laserlipolysis, radiofrequency, [3,4] and microwave. [5] Cases should be evaluated on an individual basis in light of the severity, the picture's extension, and advantages and disadvantages of each method. Conservative treatments should be given priority. [1]

The liposuction of eccrine glands is a procedure aimed at aspirating the axillary region's glands, and is performed under local tumescent anesthesia. Laserlipolysis is based on the emission of 915nm wavelength diode laser beams, which stimulate heat in the axillary region, leading to the destruction of sweat glands, in turn interrupting its production at once and definitively. [1-4]

The present paper describes a prospective, comparative and monocentric study aimed at comparing the effectiveness of two approaches for treating axillary hyperhidrosis: an exclusively surgical method (liposuction) and another based on invasive laser therapy (laserlipolysis).

METHODOLOGY

Patient selection

Twelve patients bearing primary axillary hyperhidrosis who underwent prior treatment with topical antiperspirant and botulinum toxin type A injections were selected. Only patients who had similar intensity of hyperhidrosis in both axillae (verified by the starch-iodine test) were included. The study complied with the Declaration of Helsinki's ethical principles.

The group's epidemiological analysis was conducted based on the following factors: age, gender, and complications during and after surgery.

Exclusion criteria

Patients with conditions that could stimulate hyperhidrosis, those who used drugs that stimulated sweating, or who had undergone thoracic sympathectomy or another surgical method to treat hyperhidrosis were excluded.

EVALUATION METHODS

1.Hyperhidrosis quantification test

The starch-iodine test comprises the application of iodine solution in the sweating area, followed by drying and subsequent spraying of starch on the same zone. The combination of starch and iodine with sweat lends a dark blue color to the region. This test was performed before, 30 days after, and one year after the procedure. The difference between the sides received the following classification:

No = It has neither improved nor worsened
In case of improvement:
Similar = Similar sweating on both sides
Right = Less sweating on the right
Left = Less sweating on the left

2. Histological analysis

Histology was performed on both axillae after biopsy with 5mm punch in the axillary cavities (intersection of the horizontal and vertical middle axillary lines) before the procedure and 30 days later. The objective was to identify the area with the greatest number of glands (acini and ducts) in a fixed observation field.

3. Satisfaction questionnaires

The patients answered a questionnaire about their degree of satisfaction with the procedures 1 week, 30 days and 1 year after the procedures were performed, using the ratings below:

-2 = My sweating has worsened and I would not undergo the procedure again

-1 = My sweating has worsened, but I would like to undergo the procedure again

0 = My sweating has not changed

+ 1 = My sweating has improved, but I would like to sweat any less

+2 = I am completely satisfied

4. Questions about the difference in the results obtained for each side

The patients answered a second questionnaire 1 week, 30 days and 1 year after the procedure, aimed at subjectively quantifying the difference between the sides, using the following ratings:

No = It has neither improved nor worsened
In case of improvement:
Similar = Similar results on both sides
Right = Better results in the right axilla
Left = Better results in the left axilla

Statistical analysis for the assessment of the difference in outcomes using diverse techniques

The statistical analysis of this correlated paired sample was performed based on the results obtained with starch-iodine test, using Microsoft Excel's McNemar test with continuity correction, and a 5% significance level (alpha = 0.05 for the rejection of the null hypothesis) and with degree of freedom = 1. According to the formula below, the number of failures is "a" – which denotes the failure in transitioning from the absen-

ce of difference in the intensities of sweating between the two sides, into the presence of difference in the intensity of sweating between the two sides – and the number of successes is "d" – which denotes the absence of asymmetry in the intensity of sweating between the sides, meaning the sweating in the two sides are equal:

$$Q^2 = (|a-d| \ 1)^2 / a+d$$

The analysis was performed aiming at comparing the statistical evidence – if they existed at all – for the difference in the ratings attributed to the intensity of sweating between the sides after 1 year of follow-up. The study's null hypothesis (Ho) was "both procedures lead to the same outcome".

Description of the procedures

Right axilla: Liposuction

- Tumescent solution anesthesia is performed with the injection of 250ml 9% saline solution, 10 mL 1% lidocaine injectable solution without vasoconstrictor, 2.5ml 8.4% sodium bicarbonate, and 0.25 ml 1:1000 adrenalin.
- Liposuction is performed with a 2.5mm gauge, two-hole cannula, with the lumen facing up.

Left axilla: Laserlipolysis

- Tumescent solution anesthesia is carried out with the injection of 250ml 9% saline solution, 10 mL 1% lidocaine injectable solution without vasoconstrictor, 2.5ml 8.4% sodium bicarbonate, and 0.25 ml 1:1000 adrenalin.
- Laserlipolysis is performed with the Delight® device (Industra Technologies, São Paulo, Brasil), with 6,000 J of accumulated energy, set on continuous mode, potency at 6W, using the 915nm wavelength. Aspiration was not performed after the laser was applied .

RESULTS

Twelve patients (8 men, 4 women) with primary axillary hyperhidrosis who underwent previous treatment with antiperspirants or topical botulinum toxin type A injection were selected. The mean age was 24 years (min = 17, max = 39) with a mean of 22 years.

The indices of patient satisfaction with the outcomes of the procedures carried out can be seen in Table 1. Seven days after the procedure, 41.6% of the patients described absence of change in the amount of sweating, while 58.4% reported some degree of improvement. Thirty days after all patients described some degree improvement, with 83.3% reporting being completely satisfied. At the end of 1 year of follow-up, the satisfaction index remained positive in all patients, with 75% reporting maximum satisfaction.

An individual patient self-assessment questionnaire and the starch-iodine test were applied, aimed at studying the differences between the outcomes obtained with each of the procedures performed. The self-assessment results are shown in Table 2. After 1 week, 66.6% described the presence of differences between the sides, with 62.5% reporting a greater decrease in sweating on the left. After 30 days, 91.6% of the study patients reported a similar decrease in sweating in the two sides. After 1 year of follow up, 25% reported the presence of differences between the sides, with the right presenting the best results.

The starch-iodine test evidenced a decrease in sweating in all cases, both at 30 days and after 1 year of follow-up (Table 3). At 30 days, only one case presented differences between the sides, with the right showing a greater decrease in sweating. At 1 year, three patients showed differences between the sides, with the right presenting greater decrease in sweating. The McNemar

Table 1: Index of patient satisfaction with the procedure

PATIENT	SATISFACTION 1 Week	SATISFACTION 30 Days	SATISFACTION 1 Year
Patient 1	1+	2+	2+
Patient 2	2+	2+	2+
Patient 3	1+	2+	2+
Patient 4	0	2+	1+
Patient 5	0	2+	2+
Patient 6	0	2+	2+
Patient 7	1+	2+	2+
Patient 8	0	1+	1+
Patient 9	2+	2+	2+
Patient 10	1+	2+	2+
Patient 11	0	2+	2+
Patient 12	1+	1+	1+

Note: -2 = My sweating has worsened and I would not undergo the procedure again; -1 = My sweating has worsened, but I would like to undergo the procedure again; 0 = My sweating has not changed; + 1 = My sweating has improved, but I would like to sweat any less; +2 = I am completely satisfied.

Table 2: Self-assessment of the difference of outcomes between the right and left axillae

PATIENT	WEEK 1	30 DAYS	1 YEAR
Patient 1	Similar	Similar	Similar
Patient 2	Right	Similar	Similar
Patient 3	Left	Similar	Similar
Patient 4	Left	Similar	Similar
Patient 5	Right	Similar	Similar
Patient 6	Similar	Similar	Similar
Patient 7	Left	Similar	Similar
Patient 8	Similar	direita	Right
Patient 9	Left	Similar	Right
Patient 10	Right	Similar	Left
Patient 11	Similar	Similar	Similar
Patient 12	Left	Similar	Similar

Note: No = It has neither improved nor worsened; Similar = Similar results on both sides; Right = Better results in the right axilla; Left = Better results in the left axilla.

Table 3: Starch-iodine test

PATIENT	30 DAYS	1 YEAR
Patient 1	Similar	Similar
Patient 2	Similar	Similar
Patient 3	Similar	Similar
Patient 4	Similar	Similar
Patient 5	Similar	Similar
Patient 6	Similar	Similar
Patient 7	Similar	Similar
Patient 8	Right	Right
Patient 9	Similar	Right
Patient 10	Similar	Left
Patient 11	Similar	Similar
Patient 12	Similar	Similar

Note: No = It has neither improved nor worsened; Similar = Similar sweating on both sides; Right = Decreased sweating in the right axilla; Left = Decreased sweating in the left axilla.

test with continuity correction for assessing the difference in the intensity of sweating between the two sides was of 1,333, with p = 0.2482. For a p-value greater than α (significance level) Ho is accepted and H1, rejected. As a result, there is no significant difference between the two procedure types regarding the cause and effect of the difference in the results obtained for the intensity in sweating. The histologies performed before and 30 days after the procedure showed absence or decrease of the secretory ducts and acini on both sides (Figure 1A and 1B: right axilla, 2A and 2B: left axilla).

There was absence of intercurrences during the procedures. Postoperative intercurrences can be seen in Table 4. Four patients experienced pain only on the right side, 6 had pain in both sides and none reported pain only on the left side, with a maximum duration of 10 days, being well controlled with ketorolac trometamol. Local hematoma was observed on the right side in all cases, and in the left side in 5 cases. Regression took place in up to 10 days, with the use of a gel containing allantoin and sodium heparin. Temporary paresthesia was reported on the right side in 3 cases, with improvement of symptoms in roughly 90 days with prednisone and Vitamin B1. Skin erosion was reported only in 1 case, in the right side, with improvement in 30 days using silicone gel.

DISCUSSION

Primary axillary hyperhidrosis affects about 3% of the population in the USA and implies significant emotional and psychosocial consequences. Unlike secondary hyperhidrosis, PAH is not associated with any identifiable underlying condition. [1,3] The limited understanding about the precise pathophysiological mechanism means that its treatment is varied, with varying responses for each therapeutic modality. [2] The present study evaluated the liposuction of eccrine glands, comparing it with 915nm diode laser assisted axillary laserlipolysis. [6]

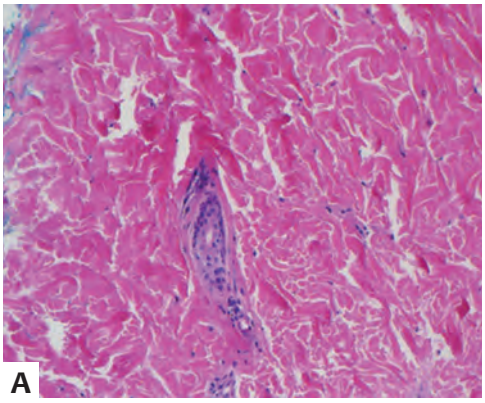


Figure 1: A. Right axilla before the treatment with an eccrine sweat gland unit comprising four secretory acini and one excretory duct

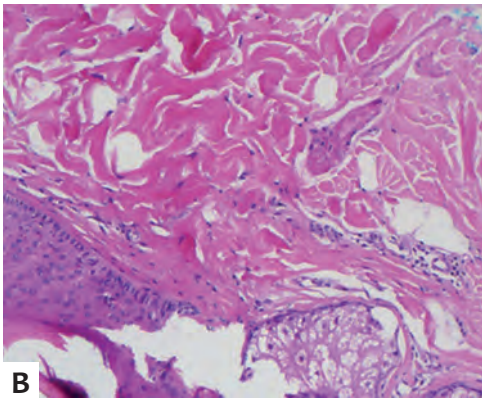


Figure 1: B. Right axilla after the treatment with absence of sweat glands

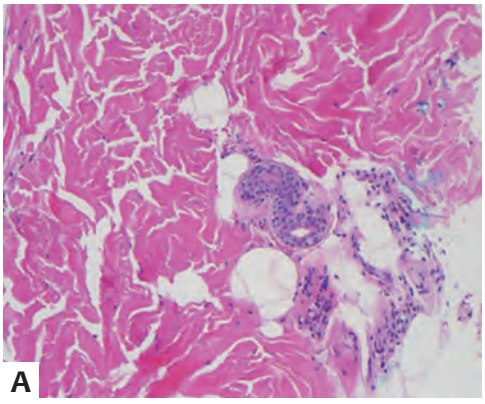


Figure 2: A. Left axilla before the treatment with an eccrine sweat gland unit predominantly comprising excretory ducts and rare secretory acini

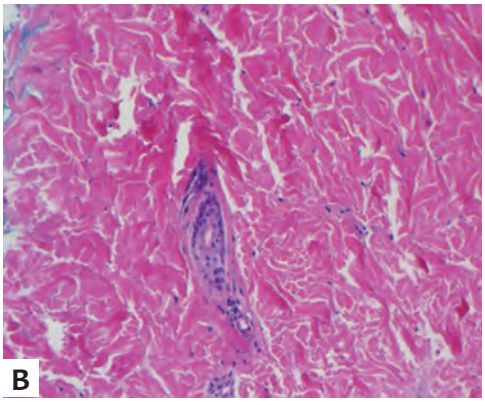


Figure 2: B. Left axilla after the treatment with absence of sweat glands, with only one excretory duct observed at the upper portion of the reticular dermis

Table 4: Intercurrences in the postoperative period						
PATIENT	PAIN		HEMATOMA		OTHER	
	Right axilla	Left axilla	Right axilla	Left axilla	Right axilla	Left axilla
Patient 1	Yes	No	Yes	Yes	Erosion	No
Patient 2	Yes	Yes	Yes	No	Paresthesia	No
Patient 3	Yes	Yes	Yes	Yes	No	No
Patient 4	Yes	No	Yes	Yes	No	No
Patient 5	No	No	Yes	Yes	No	No
Patient 6	Yes	Yes	Yes	No	Paresthesia	No
Patient 7	No	No	Yes	No	No	No
Patient 8	Yes	Yes	Yes	No	Paresthesia	No
Patient 9	Yes	Yes	Yes	Yes	No	No
Patient 10	Yes	No	Yes	No	No	No
Patient 11	Yes	Yes	Yes	No	No	No
Patient 12	Yes	No	Yes	No	No	No

Note: No: Absence; Yes: Presence.

The starch-iodine test demonstrated the presence of decreased sweating in all cases, both at 30 days and after 1 year of follow-up. The histological studies performed before the procedure and 30 days after showed absence or decrease of secretory ducts and acini in both sides. These outcomes are in line with the literature. Leclere [7] described reduced sweating in all evaluated therapeutic modalities, demonstrated by the decrease in the dark areas in the starch-iodine test in all studied groups: 975nm diode laser, association of 924/975nm lasers, isolated curettage, and curettage combined with the association of 924/975nm lasers. That article concluded that the group that underwent last treatment modality had a more significant decrease in sweating. [7]

Due to the emission of light beams from diode or 1.064nm Nd:YAG lasers, laserlipolysis generates heat in the axillary region, destroying the glands that produce sweat, promptly and conclusively interrupting its production. [1,6] Laserlipolysis' safety and effectiveness are recognized in the reviewed literature. [6,8] Caplin [8] demonstrated the 1.064nm Nd:YAG laser's efficacy using the starch-iodine test and patient satisfaction scales after 1 year of follow-up. He concluded that it is an effective therapy, with lower levels of adverse effects, [8] a finding that was also observed in the present study.

CONCLUSIONS

This study evidenced satisfactory outcomes during the 1 year follow up after the performances of liposuction and laserlipolysis procedures for the treatment of axillary hyperhidrosis refractory to clinical treatment with antiperspirants and botulinum toxin type A. Both techniques showed similar effectiveness at the end of the case's follow up, nevertheless axillary laserlipolysis can be considered a good alternative in the treatment of axillary hyperhidrosis due to the lower frequency of post-operative complications associated to it in the present study. Yet, further studies and more comprehensive patient follow-ups are required in order to confirm this paper's conclusions. ●

REFERENCES

1. Singh S, Davis H, Wilson P. Axillary hyperhidrosis: A review of the extent of the problem and treatment modalities. Surgeon. 2015;13(5):279-85.
2. Stashak AB, Brewer JD. Management of hyperhidrosis. Clin Cosmet Investig Dermatol. 2014 Oct 29;7:285-99.
3. Laser Therapy for Hyperhidrosis: A Review of the Clinical Effectiveness and Guidelines. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health; 2015. 19 p.
4. Mordon SR, Trelles MA, Leclere FM, Betrouni N. New treatment techniques for axillary hyperhidrosis. J Cosmet Laser Ther. 2016;16(5):230-5.
5. Lee SJ, Chang KY, Suh DH, Song KY, Ryu HJ. The efficacy of a microwave device for treating axillary hyperhidrosis and osmidrosis in Asians: a preliminar study. J Cosmet Laser Ther. 2013;15(5):255-9.
6. Brown AL1, Gordon J, Hill S. Hyperhidrosis: review of recent advances and new therapeutic options for primary hyperhidrosis. Curr Opin Pediatr. 2014;26(4):460-5.
7. Leclère FM, Moreno-Moraga J, Alcolea JM, Vogt PM, Royo J, Cornejo P, et al. Efficacy and safety of laser therapy on axillary hyperhidrosis after one year follow-up: a randomized blinded controlled trial. Lasers Surg Med. 2015 Feb;47(2):173-9.
8. Caplin D, Austin J. Clinical evaluation and quantitative analysis of axillary hyperhidrosis treated with a unique targeted laser energy delivery method with 1-year follow up. J Drugs Dermatol. 2014;13(4):449-56.

Immunohistochemistry and Mohs micrografic surgery: a pilot study

Imuno-histoquímica aplicada à cirurgia micrográfica de Mohs: estudo-piloto

DOI: http://dx.doi.org/10.5935/scd1984-8773.20168402

ABSTRACT

Introduction*:* In the dermatologic surgery practice, Mohs micrographic surgery is of great value in the excision of cutaneous neoplasias. Nevertheless, in certain types of neoplasia, immunohistochemistry can increase diagnostic accuracy.

Objective*:* To describe the use of Mohs micrographic surgery associated to immunohistochemistry and evaluate their effectiveness regarding traditional methods.

Method*:* Mohs micrographic surgery was performed in 5 cases of diverse cutaneous neoplasias. Tissue evaluation with hematoxylin-eosin and immunohistochemistry were carried out intraoperatively.

Results*:* There was greater prevalence of elderly female patients with higher frequency of recurred basal cell carcinomas in the face. In all cases it was possible to perform immunohistochemistry in the frozen specimen. In most cases, primary closure was carried out in the first stage of the Mohs surgery, without postoperative complications.

Conclusion*:* The combination of the two techniques can increase the procedure's sensitivity, guaranteeing the presence of free margins, leading to fewer recurrences and allowing the preservation of a greater amount of neoplasia-free tissue.

Keywords: mohs surgery, Immunohistochemistry, skin neoplasms

RESUMO

Introdução: *Na prática cirúrgica dermatológica, a cirurgia micrográfica de Mohs é de grande valia para a exérese de neoplasias cutâneas. No entanto, em determinados tipos de neoplasia, a imuno-histoquímica pode aumentar a acurácia diagnóstica.*

Objetivo: *Relatar o uso da cirurgia micrográfica de Mohs associada à imuno-histoquímica e avaliar sua eficácia em relação aos métodos tradicionais.*

Método: *Realizadas cirurgia micrográfica de Mohs em cinco casos de neoplasias cutâneas diversas e avaliação tecidual com hematoxilina-eosina e imuno-histoquímica, no intraoperatório.*

Resultados: *Maior prevalência de pacientes do sexo feminino, idosos, com maior frequência de neoplasias do tipo carcinoma basocelular recidivado, na face. Em todos os casos foi possível realizar a imuno-histoquímica na peça congelada e, na maioria dos casos, foi realizado fechamento primário no primeiro estágio da cirurgia de Mohs, sem complicações pós-operatórias.*

Conclusão: *A combinação das duas técnicas pode aumentar a sensibilidade, assegurando margens livres, permitindo menor número de recidivas e preservação de maior quantidade de tecido livre de neoplasia.*

Palavras-chave: *cirurgia de Mohs, imuno-histoquímica, neoplasias cutâneas*

Original Articles

Authors:
André Luiz Simião[1]
Marina de Almeida Delatti[2]
Larissa Mondadori Mercadante[2]
Amilcar Castro de Matos[2]
Marcela Baraldi Moreira[3]

[1] Head of the Tumors and Microscopic Mohs Surgery Ambulatory, Dermatology Service, Pontifícia Universidade Católica de Campinas (PUC-Camp) – Campinas (SP), Brazil.

[2] Dermatology Resident Physician, PUC-Camp.

[3] Pathologist Physician, PUC-Camp.

Correspondence:
André Luiz Simião
Av. 14 de Dezembro, 1265, apt. 112F - Vila Mafalda
Cep 13206 -105 –Jundiaí (SP)
Brazil
e-mail: andresimiao@gmail.com

Received on: 10/10/2016
Approved on: 14/11/2016

This study was performed at the Pontifícia Universidade Católica de Campinas (PUC-Camp) – Campinas (SP), Brazil.

Financial support: None
Conflict of interests: None

INTRODUCTION

Doctor Frederic Mohs pioneered the development of the micrograph surgery concept, in Wisconsin (USA), in 1930. While studying the effect of injecting different substances in neoplasias, he noticed that there was tissue necrosis in the presence of zinc chloride, however the microscopic structure was preserved as if it had been processed according to the anatomopathological routine. As a result, he inferred that the *in situ* fixation could be used in conjunction with surgical procedures to remove tumors in a microscopically controlled manner. In addition, Dr. Mohs also developed the idea of using frozen horizontal sections – rather than employing the traditional vertical cut – for evaluating 100% of the margins (deep and peripheral), with a higher cure rate. In 1941 he published his first scientific article, describing the treatment of 440 patients during a four-year period, rapidly attracting attention from the dermatological community. In 1951, Dr. Mohs developed the so-called Mohs micrographic surgery (MMS), in which tumors were removed for subsequent fixation – known as fresh tissue technique. This made the method faster, more tolerable for the patient and offered greater preservation of the healthy tissue, turning it into the gold standard technique for the treatment of some primary or recurrent cutaneous neoplasms. [1]

Over the years, this procedure started to be increasingly used, especially after the advent of tissue freezing, becoming the most reliable and more frequently used method for the removal of cutaneous malignancies.[2,3]

Immunohistochemistry (IH) is a technique used to detect specific antigens based on the use of previously selected antibodies, and can be performed in two ways: directly or indirectly. The direct form is less sensitive, requiring a greater amount of antibodies, consequently being progressively less used. The indirect form requires a lesser amount of antibodies, thus being more efficient, being the most used nowadays. The present study employed the indirect form of IH. [4,5]

Since 1980, IH has been incorporated into MMS aiming at lending greater sensitivity to the method, since it makes easier to interpret the anatomopathological results, nevertheless it is still little used today. [6] The present study's objective is to demonstrate the applicability, advantages and limitations of immunohistochemistry in MMS. This is the first study in the Brazilian literature to describe the use of that technique – which has application in several types of cutaneous neoplasms – in the dermatology service of a university hospital.

METHODS

Five surgical cases of patients being treated at a dermatology medical residency service in 2015 were reported. Mohs micrographic surgery was performed in different epithelial and mesenchymal tumors, with the procedure being performed according to the standards required by the technique, where the lesion's excision was followed by mapping, flattening of the fragments, freezing, cutting and preparation of the slides for hematoxylin-eosin (HE) staining, and immunohistochemical study.

Immunohistochemistry was performed in the corresponding specimens using BenchMarck Ultra device (Ventana Medical Systems, Inc. Roche, USA) automated system, and the following markers: AE1 and AE3 (pancytokeratins) for epithelial neoplasms, CD34 for mesenchymal tumors, and enolase for neural evaluation. Once verified the absence of neoplasia in the margins, the corrections of the surgical defects was carried out.

The study was conducted in accordance with the Declaration of Helsinki's ethical principles, which are aligned with the applicable good clinical practices and regulatory requirements. Also, it was performed according with the federal regulations in place and the International Conference of Harmonization (ICH)'s guidelines.

Each patient signed a free and informed term of consent before undergoing the procedures.

CASE DESCRIPTION

1. Seventy-four male patient (PG) under follow-up in the dermatology service due to various cutaneous neoplasms. In 2015, a new lesion emerged in the left lateral nasal wall: pearly-erythematous plaque, approximately 1.2 cm in diameter, with poorly defined borders and visible telangiectasia, covered by hematic micro crusts, diagnosed as a solid expansive basal cell carcinoma (BCC), after incisional biopsy. A decision was made for using MMS associated with IH for excising the lesion due to its highly sensitive location and poorly delimited margins, in addition to the proximity to previous surgical scar. The neoplasia's delimitation was defined observing 2mm surgical margins, with the lesion's exeresis being carried with preparation of the lateral and deep edges, and subsequent freezing of the specimens. The margins were analyzed with HE staining (Figure 1A) and IH technique using the AE1/AE3 cytokeratins panel. All surgical margins were found to be free of neoplasia after the first MMS' stage. The tumor's debulking was then performed, with subsequent freezing, HE staining, and AE1/AE3 IH, respectively aimed at visualizing the tumor and evaluating the IH of the frozen specimen (Figure 1B). Once all margins were found to be free of neoplasia, the reconstruction of the operative wound was carried out, and the patient was kept under clinical follow up.

2. Thirty-three years old male patient (TGZ) began to be followed up at the dermatology service in August 2015 due to an asymptomatic lesion that had emerged one year before in his left leg, with progressive growth. The patient had previously undergone exeresis of the lesion (May 2015), with diagnosis of dermatofibrosarcoma protuberans. The dermatological examination evidenced an infiltrated, well delimited brownish plaque measuring 1cm. The diagnosis hypothesis of recurrent dermatofibrosarcoma protuberans was then raised, with a decision having been made for using MMS, which is deemed the gold-standard procedure for the treatment of this type of neoplasia. The lesion exeresis was performed with 1cm margins, with the specimen being divided into eight fragments. In the freezing and subsequent HE staining, the fragments were found to be free of neoplastic involvement, with only one MMS stage being needed,

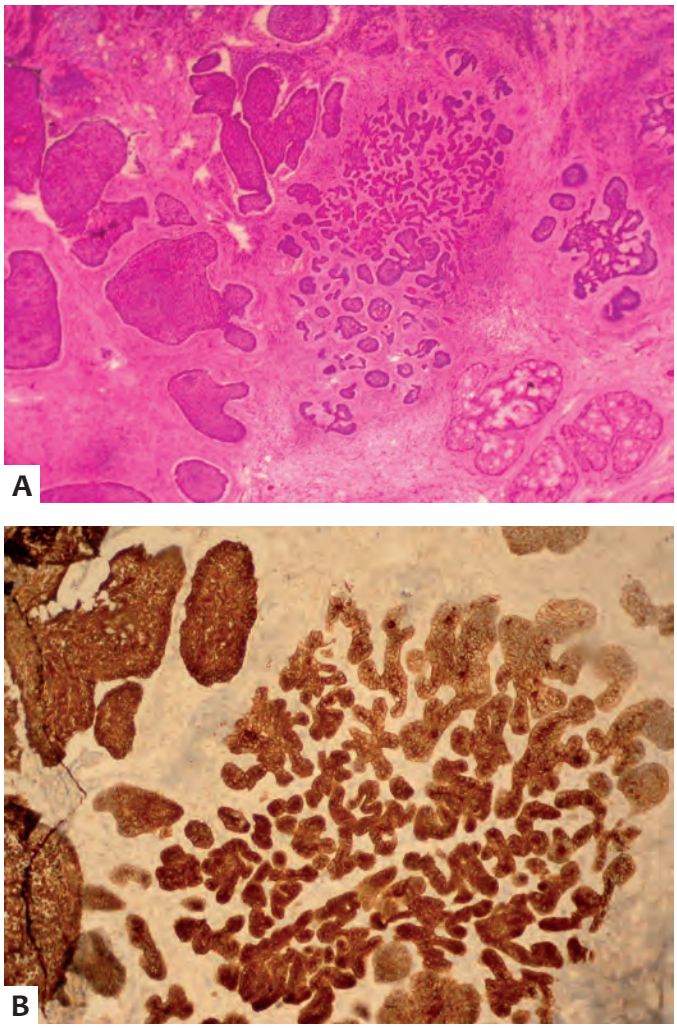


Figure 1: A - Case 1: Hematoxylin-eosin, micronodular BCC (debulking); **B - Case 1:** Positive immunohistochemistry with markers AE1/AE2, micronodular BCC (debulking)

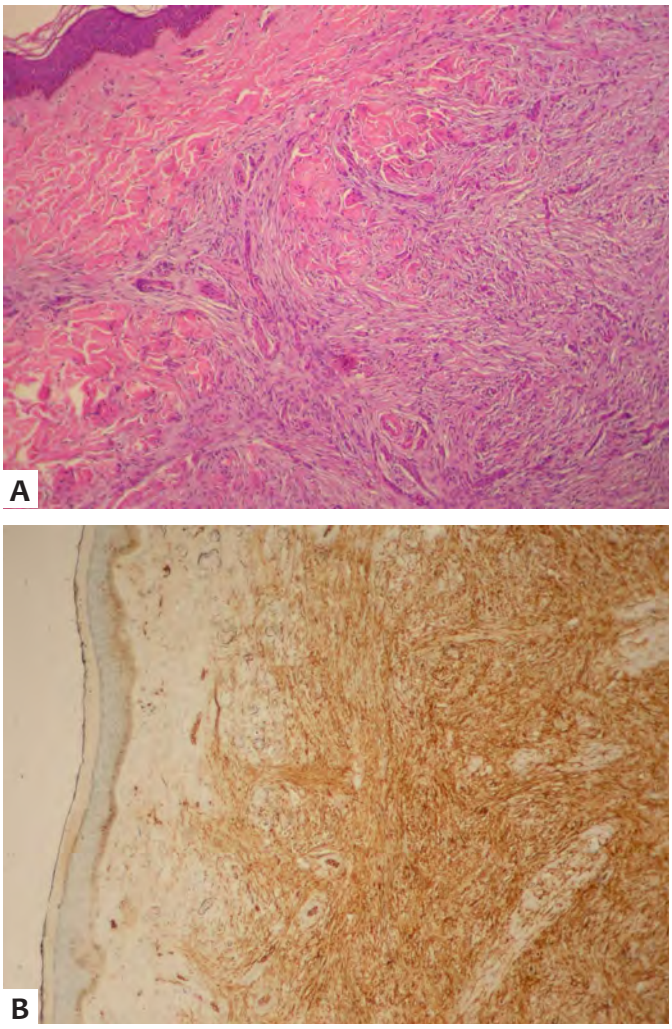


Figure 2: A - Case 2: Dermatofibrosarcoma protuberans HE (debulking); **B - Case 2:** Positive CD-34 IH for spindle cells suggestive of dermatofibrosarcoma protuberans (debulking).

followed by primary closure (Figure 2A). Tumor debulking was then carried out, with freezing, HE staining, and CD34 IH, respectively aimed at visualizing the tumor and performing the IH analysis of the frozen specimen (Figure 2B).

3.A sixty-six year-old female patient (PSL) being followed up at the dermatology service due to multiple actinic keratoses, was found to be bearing an pearly-erythematous 0.8cm papule with central ulceration in the right nasal wing, after a dermatological examination in July 2015. An incisional biopsy resulted in methatypic CBC with squamous differentiation. Due to the prime location and histologic subtype of the neoplasia, the patient was referred to MMS. Surgical margins of 2mm were defined and divided into four fragments, all of which were found to be free of neoplasia in the first stage. Pancytokeratins AE1 and AE3 based IH also did not evidenced tumor involvement in the margins (Figure 3). The reconstruction of the postoperative wound was performed via a transposition flap.

4.A 74 years old female patient (MCC) was referred to the dermatology service with a lesion in the left malar region and infiltrative BCC diagnosis after incisional biopsy underwent MMS. The margins were found to be free from neoplasia after the first stage, however large cells were visualized in margin B that were submitted to IH for confirmation of its histogenesis. Antibodies AE1/AE3 were negative in B's topography, leading to the conclusion that the surgical margins were free of cancer. The operative wound underwent primary closure.

5.A 47 year-old female patent (MCGS) was referred to the to dermatology service for clinical follow up after the complete exeresis of a solid and sclerodermiform BCC with neoplastic infiltration up until the deep dermis and perineural

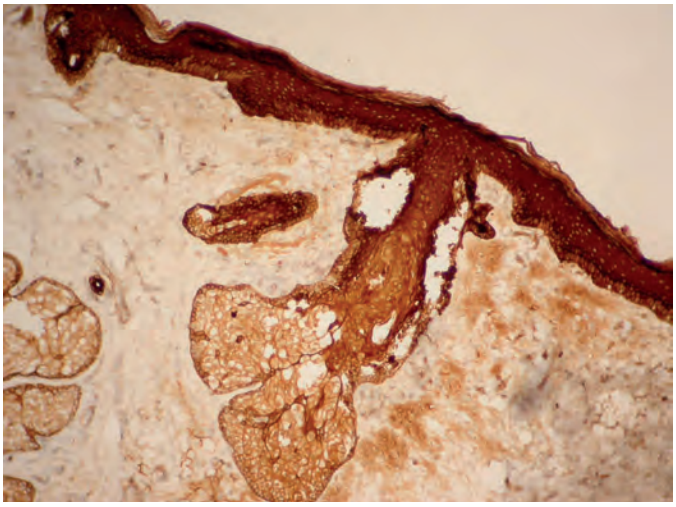


Figure 3: Caso 3 - AE1/AE3 IH showing epidermis and sebaceous gland (free margin)

invasion, located in the left hand side epicanthus. The initial dermatological examination only evidenced a scar with good aspect and no signs of recurrence. Nonetheless, three months after, an infiltrated, hardened, plaque with telangiectasia and measuring 1cm emerged in the medial region of the scar. The diagnosis of recurred BCC was hypothesized and a three-point incisional biopsy was performed. The anatomopathological examination showed an infiltrative BCC reaching the deep skeleton muscle tissue (Figure 4A). Due to the fact that deep tissues were found to be affected, MMS was performed in two stages, for the margins A, C and F were compromised in deep planes, demanding expansion. Immunohistochemistry was carried out with enolase aiming at evidencing the nerve bundle, which was found to be free of neoplastic involvement (Figure 4B). The surgical defect was corrected by direct closure.

RESULTS

Five male and female patients aged between 33 and 74 years old, were treated due to different skin neoplasms. It was possible to observe a higher prevalence in females with over 60 years of age (Graph 1). The most frequent location was the nose, with 80% of the neoplasms being located in the face and absence of postoperative complications in all cases. Histological diagnosis of infiltrative BCC was the most common, with 3 recurrent and 2 primary neoplasms (Table 1). The only surgery that required two MMS stages was that of a recurrent tumor, with most cases undergoing primary closure in the first stage. Regarding the immunohistochemical markers, decisions were made for the use of AE1/AE3, CD34 and enolase (Table 2). The possibility of using different immunohistochemical markers in the frozen specimens was demonstrated in the present pilot study, demonstrating the possibility of further increasing the sensitivity and effectiveness of free margins.

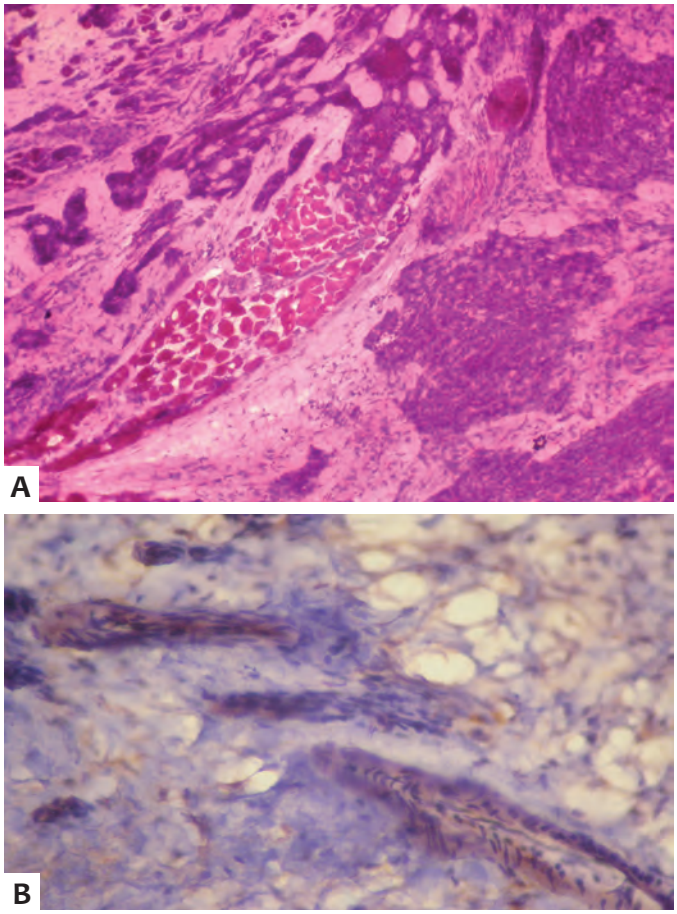


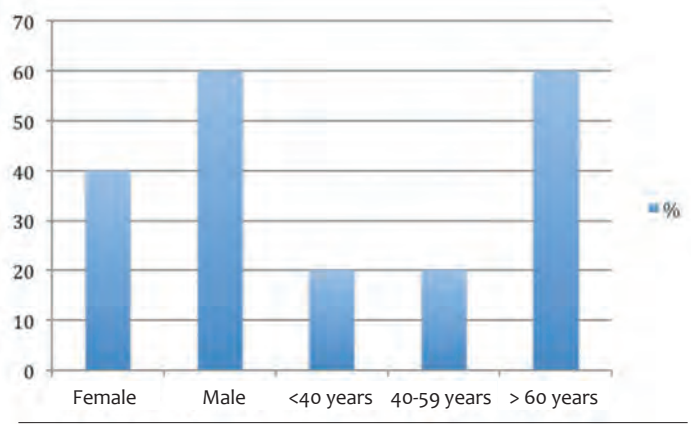
Figure 4: A - Case 5: HE, BCC with infiltration in the deep muscles. Free nerve bundle;
B – Case 5: Enolase IH, nerve bundle without tumor

DISCUSSION

Mohs micrographic surgery is a surgical technique consisting in initially delimiting the clinical margins of the tumor, subsequently delimiting those of the surgical margins, with a distance equal or greater than 2mm. The surgical specimen is divided in fragments and mapped for correct spatial orientation during its analysis. The fragment undergoes flattening in a way to allow the complete visualization of the epidermis and dermis in a single plane. Next, the tissues are frozen and the slides are prepared for histological evaluation, stained with HE, which is used for all cutaneous neoplasms. [3,7]

Once these procedures have been carried out, the dermatologic surgeon evaluates the slides in order to access the involvement of the margins. If the margins are found to be free of neoplasia, the reconstruction of the surgical defect can be performed immediately. In case the margins (both lateral and deep) are found to be compromised, new expansions are progressively performed up until all margins can be considered free of neoplasia. In this manner, the MMS technique allows complete histological control, with the evaluation of 100% of the margins. [3,7]

Indications for MMS are: recurrent tumors; incompletely excised tumors; non melanoma skin tumors greater than 0.4



Graph 1: Gender and age descriptive statistics

cm located in areas with high risk of local recurrence (central facial, periocular, periauricular); tumors located in areas where tissular preservation and high cure rates are important; tumors with poorly defined clinical margins; tumors with aggressive histological subtypes (micronodular, infiltrative, squamous or sclerodermiform BCCs, and SCC) or with evidence of perineural and perivascular invasion; tumors located over irradiated areas or scars; tumors in prime areas such as genital, anal, hands and feet; expanding tumors in immunosuppressed patients; in patients genetically predisposed to develop multiple skin cancers (xeroderma pigmentosum, Gorlin-Goltz syndrome). [3,4,7]

Immunohistochemistry is a laboratory technique used to detect specific antigens in tissue sections that can be performed in two ways. The original or direct method allows that a single antibody, previously conjugated to an enzyme, interact with the antigen present in the target cell. A substrate is then added, which reacts with fluorescence when in contact with the enzyme. This method requires high concentrations of antibodies, which decreases sensitivity. In the indirect method, the primary antibody binds to a specific antigen. A second antibody previously conjugated to an enzyme is then added and subsequently bound to the primary complex. A substrate is then added and, when in contact with the enzyme, fluoresces. As a result, a smaller concentration of antibodies is required, which increases the method's sensitivity and efficacy. [4,5] From 1980, IH was incorporated into MMS, since it allowed recognizing neoplastic cells more easily. Its applicability is however limited due to its protracted preparation, requiring longer surgical times. Moreover, it is expensive, there are few trained professionals who are able to perform it, and the literature about it is scarce. [6] This theme has been increasingly studied by many researches over the past 20 years, and more medical schools have gained know-how in order to provide training on the technique. As a result, the role of IH in MMS has been established, with the number of procedures in which it is used having doubled during the last decade. In addition, it has been proved that the freezing technique preserves the antigenic content, increasing the antibodies' ability to identify and trace antigens (tumoral cells). [5,6]

Currently, a number of markers can be used in the IH technique depending on the type of tumor in question. Examples are: Melan-A, S100, HMB45, cytokeratins, among others. [2,4,5]

The advantages of immunohistochemistry in MMS are linked to the increased ability to identify tumor cells, including more difficult cases, such as those whose neoplasms mimic normal structures or are intertwined with the dense inflammatory process or fibrotic tissue, and those with perineural invasion. It also provides a more accurate identification of free and compromised surgical margins, leading to a decrease in recurrence rates and unnecessary removal of healthy tissue. [2,5]

Table 1: Descriptive statistics: tumor location, anatomopathological diagnosis and presence of recurrence

VARIABLE	FREQUENCY	%
Localização tumoral		
Nose	2	40
Malar	1	20
Lateral epicanthus	1	20
Leg	1	20
Anatomopathological diagnosis		
CBC expansive solid	1	20
BCC metathype differentiation	1	20
infiltrative BCC	2	40
Dermatofibrosarcoma protuberans	1	20
Recurred Tumor		
Yes	3	60
No	2	40

Disadvantages include a longer implementation time and multiple steps required in the process of staining the tissues, in addition to the high cost and short shelf life that common reagents have. Increasing the number and improving the expertise of professionals in Mohs laboratories, including technicians and surgeons, as well as expanded waiting times for patients also are limiting factors. [2] Trimble et al [6] conducted a study in which accredited Mohs surgeons listed the main reasons for not using IH, which were, in order of appearance: increased surgical time, lack of training and high cost.

Nowadays, one of the main focuses of research in this field has been the reduction the time required by the staining process and of the surgery as a whole. Research show that swift protocols (up to 30 minutes) have already been developed and offer effectiveness levels similar to those of more traditional protocols (one hour on average), without compromising the method's reliability. [8,9]

CONCLUSION

The use of IH in MMS is unquestionably expanding, however more studies are still needed. The use of staining in frozen sections has been shown useful in the various types of cutaneous neoplasias, leading to an increase in the number of detections of tumor cells, nevertheless this in turn calls for an increase in the number of teams that are proficient in the technique.

Immunohistochemistry allows expansion and growth in the applicability of MMS, especially in tumors of difficult histological delimitation. As a result, it increases the sensitivity for the identification of tumor cells, making it possible to preserve a greater amount of healthy tissue and decrease recurrences, offering a higher quality treatment to patients. ●

REFERENCES

1. Trost LB, Bailin PL. History of Mohs Surgery. Dermatol Clin. 2011;29(2):135-9
2. Stranahan D, Cherpelis BS, Glass LF, Ladd S, Fenske NA. Immunohistochemical stains in Mohs surgery: a review. Dermatol Surg. 2009;35(7):1023-34.
3. Benedetto PX, Poblete-Lopez C. Mohs micrographic surgery technique. Dermatol Clin. 2011;29(2):141-51.
4. El Tal AK, Abrou AE, Stiff MA, Mehregan DA. Immunostaining in Mohs micrographic surgery: a review. Dermatol Surg. 2010;36(3):275-90.
5. Thosani MK, Marghoob A, Chen CS. Current progress of immunostains in Mohs micrographic surgery: a review. Dermatol Surg. 2008;34(12):1621-36.
6. Trimble JS, Cherpelis BS. Rapid immunostainig in Mohs: current applications and attitudes. Dermatol Surg. 2013;39(1 Pt 1):56-63.
7. Reis NA, Azevedo LCM, Stolf HO, Nouri K, Kimyai-Asadi A, Goldberg LH. Cirurgia micrográfica de Mohs. Surg Cosmet Dermatol. 2011;3(3):227-31.
8. Cherpelis BS, Turner L, Ladd S, Glass LF, Fenske NA. Innovative 19-minute rapid cytokeratin immunostaining of nonmelanoma skin cancer in Mohs micrographic surgery. Dermatol Surg. 2009;35(7):1050-56.
9. Cherpelis BS, Moore R, Ladd S, Chen R, Glass LF. Comparison of MART-1 frozen sections to permanent sections using a rapid 19-minute protocol. Dermatol Surg. 2009;35(2):207-13

Pulsed radiofrequency with multineedles for earlobe aging treatment

Radiofrequência pulsada com multiagulhas (RFPM®) no tratamento do envelhecimento do lóbulo da orelha

DOI: http://dx.doi.org/10.5935/scd1984-8773.20168403

ABSTRACT

Introduction*:* Numerous techniques have been described to treat the earlobe aging. Surgical and nonsurgical methods as peelings, CO_2 laser and fillings have been proposed to produce collagen remodeling.

Objective: The objective of this retrospective clinical study was to evaluate the effectiveness of microneedling assisted radiofrequency for earlobe aging.

Methods: Retrospective study of the technique's safety and effectiveness through the evaluation of the results with the application of a satisfaction questionnaire to patients and of the analysis of clinical outcomes by independent dermatologists.

Results: Twelvy patients aged between 48 and 67 years who underwent the technique were evaluated. One hundred percent of the patients reported satisfaction with the results, whereas in the comparative evaluation of the photographs carried out by two independent dermatologists the rate of improvement was 75% in four patients, 100% in eigth patients. Post-inflammatory hyperpigmentation was observed ten to 15 days after the treatment in five patients, though it was reversed after clinical treatment.

Conclusion: This new procedure emerges as an alternative treatment for earlobe aging.

Keywords: *ear cartilage; pulsed radiofrequency treatment; rejuvenation*

RESUMO

Introdução: Várias técnicas vêm sendo descritas para o tratamento do envelhecimento do lóbulo da orelha. Métodos cirúrgicos e não cirúrgicos, como *peelings*, laser fracionado de CO_2, e preenchedores vêm sendo propostos com o intuito de produzir remodelamento de colágeno dessa região.

Objetivo: O objetivo deste estudo clínico retrospectivo foi avaliar a eficácia da radiofrequência pulsada com multiagulhas (RFPM®) no rejuvenescimento do lóbulo da orelha.

Métodos: Estudo retrospectivo da segurança e efetividade da técnica mediante avaliação dos resultados por aplicação de questionário de satisfação aos pacientes e julgamento dos resultados clínicos por dermatologistas independentes.

Resultados: Foram avaliados 12 pacientes com idade entre 48 e 67 anos, submetidos à técnica, 100% dos quais relataram satisfação com os resultados, enquanto na avaliação comparativa das fotografias por dois dermatologistas independentes o índice de melhora foi de 75% em quatro pacientes e 100% em oito pacientes. A hiperpigmentação pós-inflamatória foi observada entre dez e 15 dias após o tratamento em cinco pacientes, tendo sido revertida após tratamento clínico.

Conclusão: Esse novo procedimento se apresenta como alternativa ao tratamento do envelhecimento do lóbulo da orelha.

Palavras-chave: cartilagem da orelha; tratamento por radiofrequência pulsada; rejuvenescimento

Original Articles

Author:
Emerson Vasconcelos de Andra de Lima[1]

[1] Coordinator, Cosmiatry and Dermatologic Surgery, Santa Casa de Misericórdia do Recife - Recife (PE), Brazil.

Correspondence:
Emerson Vasconcelos de Andrade Lima
Av. Agamenon Magalhães, 2939 / Sl. 402-404
Cep 52020-000 – Recife (PE), Brazil
Email: emersonderma@terra.com.br

Received on: 23/06/2015
Approved on: 20/03/2016

This study was performed at the Santa Casa de Misericórdia de Recife and at a private practice - Recife (PE), Brazil.

Financial support: None
Conflict of interests: None

INTRODUCTION

Aligned with the natural process of aging, the aging of the earlobe is characterized by sagging, excess skin, volume loss and the onset of rhytids. These alterations, secondary to the degeneration of this anatomical segment's tissue, cause the expansion of the earring orifice, a situation that can many times be worsened by the use of heavy adornments over the years, or even by traumas that form partial or total clefts in the earlobe. [1,2]

Surgical and non-surgical alternatives are available aimed at restoring the damage caused to this region, isolatedly or in association, observing the diversity of unsightly and progressive signals. [1,2] Among surgical correction techniques are: removing the excess skin and / or correcting the cleft; hyaluronic acid based cutaneous filling; the use of caustic substances, with application limited to the orifice or covering the lobe completely; or, still, the use of lasers, which is frequent in the therapeutic armamentarium. [3-5] More recently, pulsed radio frequency with multineedles was indicated by Lima for the rejuvenation of the eyelids. In the present study, the author describes outcomes showing important cosmetic improvement in 19 patients, with correction of sagging and wrinkles, and increased quality of the skin. [6]

Based on the findings regarding the aging process of the eyelid, an investigation was conducted aimed at verifying the applicability of the technique in cases of aging of the earlobe. The present study presents this investigation's results.

Pulsed radiofrequency with multineedles (RFPM®)

The use of fractional random high frequency energy beamed on the skin results in dermal regeneration at the papillary-reticular interface, through the stimulation of fibroblasts and subsequent synthesis of collagen and elastic fibers, as well as epidermal regeneration caused by the migration of keratinocytes.

This paper proposes an innovative approach for skin rejuvenation, based on subablative energy, using electrodes with several needles, connected to a radio-electrosurgery device.

This technique, performed in a well-delimited and accurate manner, does not compromise the tissue adjacent to the vaporized micropoints and causes significant tissular impact, thus enabling the stimulus for new collagen formation.

Electrodes called Lima 2, Lima 4 and Lima 8 – in a reference to the Author's name –(Figure 1) are required for performing RFPM®. They respectively consist of 2, 4 or 8 tungsten needles with a diameter of 100 thousands of a millimeter, with identical weight and length, arranged in parallel, aimed at reaching the same depth. Being 2mm long, these needles cross the epidermis and act in the dermis, stimulating the contraction and renewal of collagen (Figure 2).

The present retrospective clinical study was to evaluate the effectiveness of RFPM® in rejuvenating the earlobe.

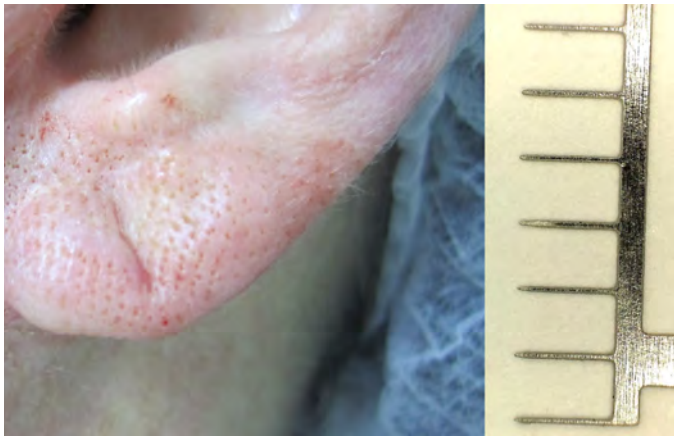


Figure 1: RFPM®'s immediate postoperative period and electrode with 100µ needles (depicted with great magnification)

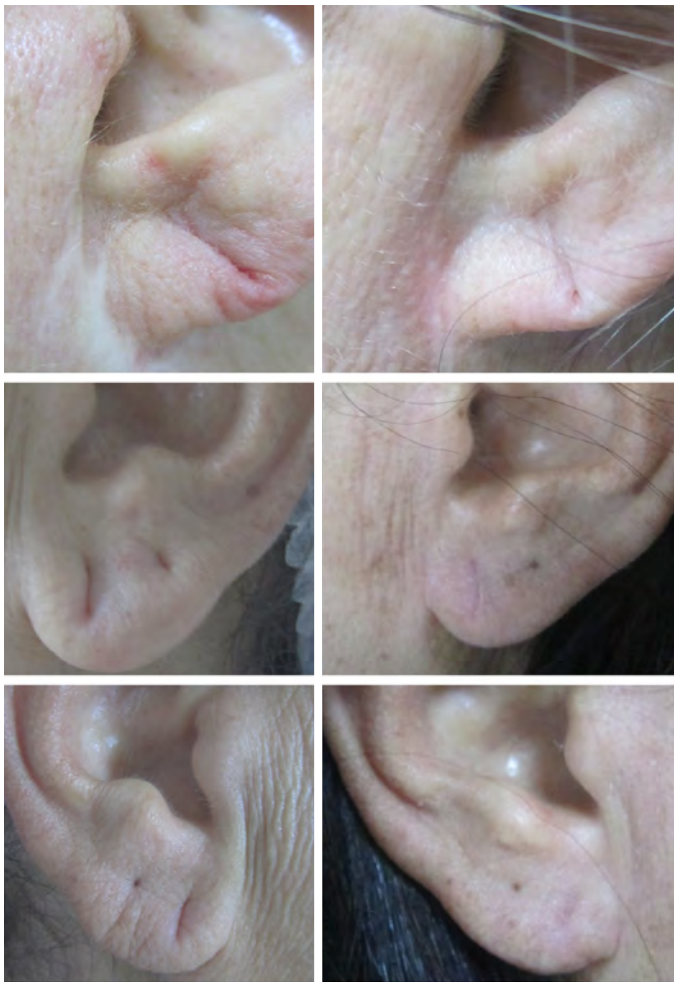


Figure 2: Earlobes before and 30 days after treatment with RFPM®

METHODS

The medical records of 12 female patients with aged earlobes treated with RFPM®, performed ambulatorially by the same physician, between March and December 2015, were analyzed. The photographic records were carried out with the same digital camera, under the same environmental conditions, immediately before and 1 month after a single intervention. The study was performed according to the Helsinki Declaration.

After antisepsis with 1% chlorhexidine, the earlobe was injected with 2% lidocaine without vasoconstrictor. The FRAXX® device (Loktal Medical Electronics, São Paulo, Brazil, Anvisa 10362610008) was used for the application of RFPM® in the single pulse mode, and with parameters set at levels guided by 12 months of investigative effort. The patients in this group were treated with the device set in the CUT mode, power at 30, Active at 30ms, using the Lima 8 electrode. A single pass was performed, avoiding overlapping. The earlobe was completely covered with the treatment and both faces – anterior and posterior – were punctured by the needles.

After the procedure, dressings with micropored bandage were applied and removed on the following day. The patients were instructed to use a skin regenerating cream (Ciclapast baume ® La Roche Posay, Rio de Janeiro, Brazil) in the postoperative period twice a day, in addition to an industrialized SPF 60 sunscreen.

The evaluation of results was performed based on patient satisfaction questionnaires and the judgment of clinical outcomes performed by independent dermatologist physicians.

The self-assessment questionnaire included questions on the degree of satisfaction with the procedure, measured with the ratings *poor*, *reasonable*, *good* and *very good*.

Photographs of before and 30 days after the procedure were evaluated by 2 dermatologist physicians unrelated to the study, who used the following scale: *regular* (for 25% of improvement), *good* (50% improvement), *very good* (for 75% improvement) and *excellent* (for 100% improvement).

Figure 1: Lima 8 electrode and earlobe immediately after the intervention.

RESULTS

Twelve women between 42 and 67 years old, treated at the author's private clinic and the Cosmiatry Ambulatory of the Santa Casa de Misericórdia do Recife were evaluated. The patients' Fitzpatrick phototypes ranged from II to IV. All patients reported satisfaction with the results, choosing the ratings *good* and *very good* for the questions asked in the questionnaire.

Based on the comparative evaluation of the photographs taken before and after the procedure, performed by 2 independent dermatologist physicians, the improvement indices were the following: 75% = *very good* (4 patients) and 100% = *excellent* (8 patients). Also, a substantial improvement was observed in the size of the earring orifice (Figure 2).

The pain during the treatment was considered tolerable, and tissue regeneration was observed between 5 and 7 days, with patients returning to their work activities after a significant reduction of the edema and hematoma resulting from the infiltrative anesthesia and the procedure. No infections, permanent dyschromia or unsightly scars were observed in this group.

Mild to moderate post-inflammatory hyperpigmentation was observed in 5 of the 12 patients after a period of 10 to 15 days after the treatment. Resolution was achieved in 15 to 30 days with the use of whitening formulations.

DISCUSSION

Earlobe sagging is a frequent complaint among patients seeking cosmetic treatments. The annoyance becomes more pronounced when earrings are no longer used due to the enlargement of the cleft, which loses its ability to hold the adornment well positioned because of the lobe's sagginess and looseness.

The corrective techniques used have offered satisfactory results, however some patients might respond poorly to the interventions, and the combination of procedures is often mandatory.[4,5]

When excess skin and sagging are intense, conventional surgical intervention might not be well accepted by the patient since it results in scars, even when the necessary preventative measures are taken. Peels or semi-ablative techniques can be insufficient for the improvement of the damage, especially in elderly patients. Hyaluronic acid, a common cutaneous filler aimed at treating this region's aging, volumizes and attenuates fine wrinkles and sagging, nevertheless has limitations regarding the improvement in the skin's quality and deeper static wrinkles, which many times behave as scars due to the intense elastosis. [3-7]

For rejuvenating this area, the Author of the present paper proposes the use of RFPM® with specific electrodes, a methodology that has been recently developed and studied in detail, based on results obtained in the treatment of periorbital aging. [6] The data presented in this article suggest that:

1. RFPM® is a promising therapeutic proposal for the rejuvenation of the earlobe, especially when there is absence of indication of or desire for conventional surgery, and when thin, sagging and wrinkled skin is the main complaint

2. The results obtained are reproducible using the methodology and the electrodes described in this article

3. The possibility of a swift return to the professional activities and few adverse effects observed in the evaluated group encouraged the Author of the present article to recommend the inclusion of this new proposal in the already available broad therapeutic armamentarium for intervention in this region.

4. Performing the procedure requires training and is technician-dependent. The operator needs be properly skilled and must have all necessary basic knowledge to ensure excellence of outcomes

The Author of the present article suggests that the technique be evaluated in other groups with a view to confirming the outcomes and conclusions presented in this paper. ●

REFERENCES

1. Beschloss J, Toren L, Bingham JL. Earlobe stabilization with 6-0 suture for repair of a complete split. Dermatol Surg. 2011;37(6):848–849.
2. Mendoça M, de Oliveira AR, Araújo JM, Silva Md, Gamonal A . Nonsurgical technique for incomplete earlobe cleft repair. Dermatol Surg. 2009;35(3):446–450.
3. Niamtu J 3rd. Eleven Pearls for Cosmetic Earlobe Repair . Dermatol Surg. 2002;28(2):180–185.
4. Bagatin E, Hassun K, Talarico S. Revisão sistemática sobre peelings químicos. Surg Cosmet Dermatol. 2009;1(1):37-46.
5. Ravanfar P, Alster TS. Laser earlobe revision. Dermatol Surg. 2013;39(7):1056–1061.
6. Lima E . Radiofrequência pulsada com multiagulhas: uma proposta terapêutica em rugas, flacidez e pigmentação periorbital. Surg Cosmet Dermatol. 2015;7(3):223-6.
7. Chiummariello S, Iera M, Arleo S. L-specular plasty versus double-round plasty: two new techniques for earlobe split repair. Aesth Plast Surg. 2011 35(3):398–401.

Nutritional supplementation effect ON THE nail PLATE'S strength and growing

Efeito de suplementação nutricional no fortalecimento e crescimento das lâminas ungueais

Original Articles

Author:
Flávia Alvim Sant'Anna Addor[1]

[1] Dermatologist Physician at private practice - São Paulo (SP), Brazil.

DOI: http://dx.doi.org/10.5935/scd1984-8773.201684867

RESUMO

Introdução: "unhas quebradiças", ou que não crescem, constituem queixa relativamente frequente na prática dermatológica; entretanto, há poucos estudos sobre a influência nutricional nessa queixa

Objetivo: avaliar a possível influência de suplemento nutricional na melhora da resistência da lâmina ungueal, bem como de seu crescimento

Material e Métodos: 45 pacientes com queixas de unhas frágeis/quebradiças foram observadas durante 16 semanas, sob uso de suplemento nutricional contendo vitaminas e oligoelementos em ingestão diária recomendada com avaliações clínicas e subjetivas em oito, 12 e 16 semanas.

Resultados: houve melhora nos parâmetros força, resistência, crescimento e integridade ungueais a partir de oito semanas, melhora que progride com o uso continuado do suplemento, permitindo afirmar que esse tratamento levou a perceptível melhora da qualidade da lâmina ungueal.

Conclusões: O suplemento nutricional avaliado se mostrou seguro e eficaz na melhora de sinais de enfraquecimento ungueal, como perda da resistência e redução da velocidade de crescimento.

Palavras-chave: doenças da unha; nutrientes; queratinócitos

ABSTRACT

***Introduction**: Brittle nails or nails that do not grow are relatively frequent complaints in the dermatological practice, nonetheless there are few studies on how nutrition influences these symptoms.*

***Objective**: To evaluate the possible influence of nutritional supplementation for improving the nail plate's resistance and growth.*

***Methods**: Forty-five patients complaining of fragile/brittle nails were observed for 16 weeks under recommended daily intake of a nutritional supplement containing vitamins and trace elements, having undergone clinical and subjective evaluations in Weeks 8, 12 and 16.*

***Results**: There were improvements in the parameters strength, resistance, growth and nail integrity from Week 8, with further progress after continued use of the supplement, allowing the conclusion that this treatment led to noticeable improvement of the nail plate's quality.*

***Conclusions**: The nutritional supplement evaluated was safe and effective in improving the signs of nail weakening, including loss of resistance and reduction of growth rate.*

***Keywords:** nail diseases; nutrients; keratinocytes*

Correspondence:
Flávia Alvim Sant'Anna Addor
Al. Campinas, 159, Alphaville 04
Cep 06486-110 - Santana de Parnaíba (SP), Brazil
e-mail: medci002@terra.com.br

Received on: 19/07/2016
Approved on: 03/12/2016

This study was performed at Medcin Instituto da Pele – Clinic Research Unit - Osasco (SP), Brazil.

Financial support: FQMDerma

Conflict of interest: FQMDerma supplied the study product, however the methodology, execution and analysis of results were performed by the researcher without interference of the company.

INTRODUCTION

The formation of the nail plate begins in the matrix, where keratinocytes multiply, differentiate and keratinize, in a process similar to that of hairs. The generated keratin stabilizes in a different pattern – disulfide bridges – that determines this adnexum's structural differences.

Its growth rate is of 2mm-3mm per month, leading to a total renovation of the exposed plate in 6-9 months, being slightly slower in the toes' nails. [1]

Although the fingers' movement and the physical friction of the nails are important factors that contribute for their growth by stimulating the plate's synthesis, systemic factors that alter the vascularization and nutrition of the ungual apparatus also influence the keratinogenesis' speed and, therefore, of the growth and quality of the nails formed. [2]

In this manner, nails are influenced by the individual's nutritional state, which have diverse manifestations. When there is deficiency of zinc, for instance, onycholysis and onychodystrophy are described. [2] The brittle nail syndrome affects roughly 20% of the adult population, being characterized by onychoscysia and onychorrhexis. [3] Although multiple factors have been investigated, there is clinical evidence that might be related to specific nutritional deficiencies.

Onychoses account for 10% of all dermatological complaints. [4] Nails that are brittle or do not grow are relatively frequent complaints in the dermatological practice, especially in women and on fingernails, even in the absence of some related dermatosis or onychosis. However, there are few studies in the world medical literature relating onychoses to nutritional alterations.

OBJECTIVE

The objective of the present study was to evaluate the possible influence of a nutritional supplement known as Eximia Fortalize® in improving the nail plate's resistance and growth, through a clinical and subjective evaluation.

ETHICAL ASPECTS

This study was conducted with the approval of the Research Ethics Committee. All invited patients received a detailed explanation of the study and signed a REC approved Free and Informed Term of Consent.

MATERIAL AND METHODS

A prospective clinical, monocentric, open study was carried out with 68 female patients (between 18 and 60 years old) who complained of weakness and brittleness in the fingernails. The exclusion criteria were pregnancy, lactation and use of hormonal drugs, as well as the presence of onychoses. All patients underwent dermatological examination for the clinical observation of the complaint.

After the data were collected, patients were instructed to take one tablet (orally) daily for 16 consecutive weeks. The evaluated product's composition is in Chart 1.

The patients were instructed to return to the institute for new evaluations after 8, 12 and 16 weeks. On these visits, the patients evaluated the nails' properties indicative of strength (thicker, harder, less brittle) and resistance (greater resistance to trauma and cut) by means of a questionnaire based on a five-rating system. An additional three-rating based questionnaire was applied for evaluating the perception of growth the nails. The clinical evaluations performed by dermatologist physicians assessed the nails' resistance (observation of onychoscysia and onychorrhexis signs) and integrity (morphological alterations such as onycholysis and onychomalacia).

Statistical evaluation

The percentage frequencies of the following variables were computed aimed at assessing the subjective effectiveness, according to the patient's satisfaction on each evaluation date: nail's *strength*, *resistance* and *growth*. The non-parametric Cochran's Q test was used (with a level of significance of 0.05) in order to test whether there was variation over time (from V0 to V4).

The same evaluations were performed for the nail plate's resistance and integrity, with the data collected in the clinical assessments (on the same experimental timepoints).

RESULTS

Of the 68 patients recruited, only 45 were included in the study due to absence of compliance with the inclusion and / or exclusion criteria. In the course of the study, one patient discontinued the use of the product for reasons unrelated to the study. Forty-four patients completed the research's protocol.

EFFECTIVENESS

Subjective evaluation

1.Stronger nails

According to Graph 1, the perception of improvement for the parameter *strength* increased gradually, with 61.4% of patients considering their nails strong from Week 8, 70.5% from

Chart 1: Nutritional supplement composition

COMPONENT	DOSE
Calcium pantetonate (Vitamin B5)	5mg
Magnesium	130mg
Ascorbic acid (Vitamin C)	45mg
Ferrous fumarate (Iron)	7mg
Tocopherol (Vitamin E)	10mg
Nicotinamide (Vitamin B3)	16mg
Zinc (Zinc oxide)	3,5mg
Betacarotene (Vitamin A)	600mcg
Cyanocobalamin (Vitamin B12)	2,4mcg
Thiamin (Vitamin B1)	1,2mg
Pyridoxine hydrochloride (Vitamin B6)	1,3mg
Riboflavin (Vitamin B2)	1,3mg
Folic acid	240mcg
Biotin	30mcg

Week 12, and 75% from Week 16. When compared to the perception at the beginning of the treatment, it was possible to observe that there had been a significant increase in the perception of very strong nails after Week 16 ($p < 0.023$) and strong nails after Week 8 ($p < 0.01$).

2.More resistant nails

At the initial visit, most patients (70.5%) considered their nails brittle. After eight weeks of treatment there was a significant reduction of this perception ($p < 0.001$). In addition, 68.2% and 65.9% of patients considered their nails more resistant after Week 12 and Week 16 of use of the product, respectively, as shown in Graph 2.

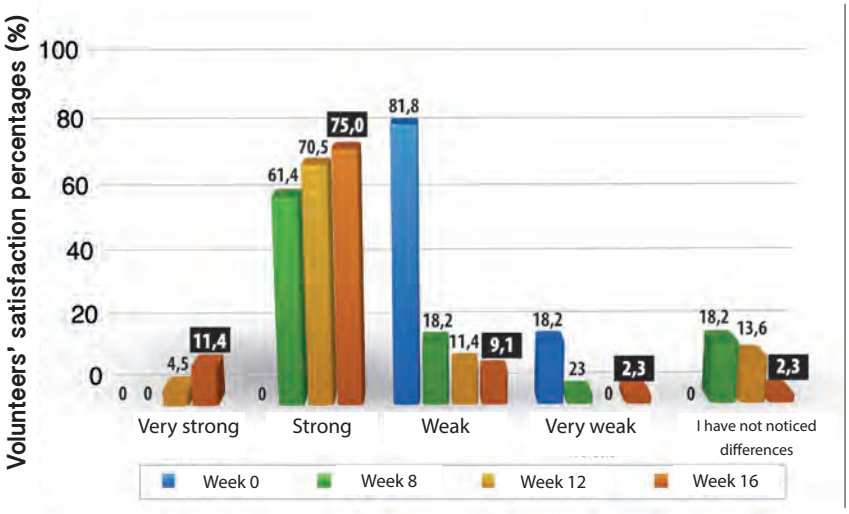
3. Nail growth

There was a significant increase in the perception of the nail's growth over time from Week 8. Of the 50% patients who perceived slow growth at baseline, only 6.8% remained with the same opinion in Week 8 ($p = 0.001$). The perception of greater growth was already significant after Week 8, with 20% of the patients referring this increase, as shown in Graph 3.

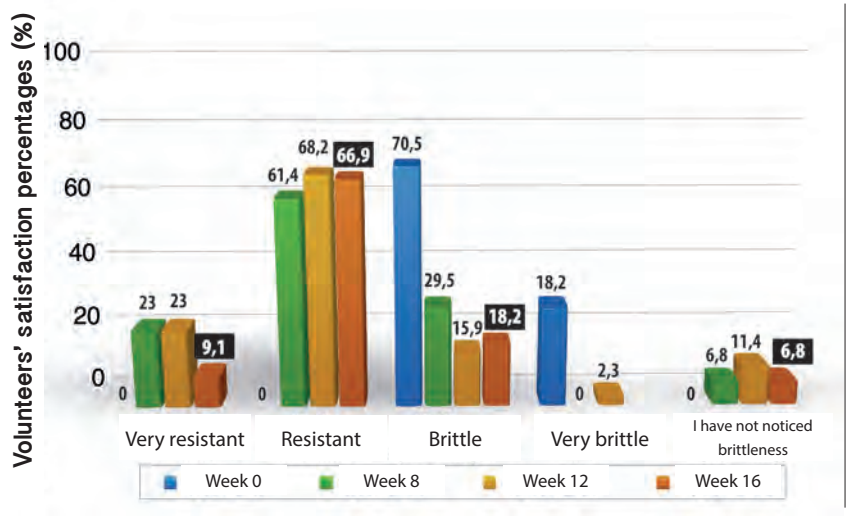
Clinical evaluation

1.Nail resistance

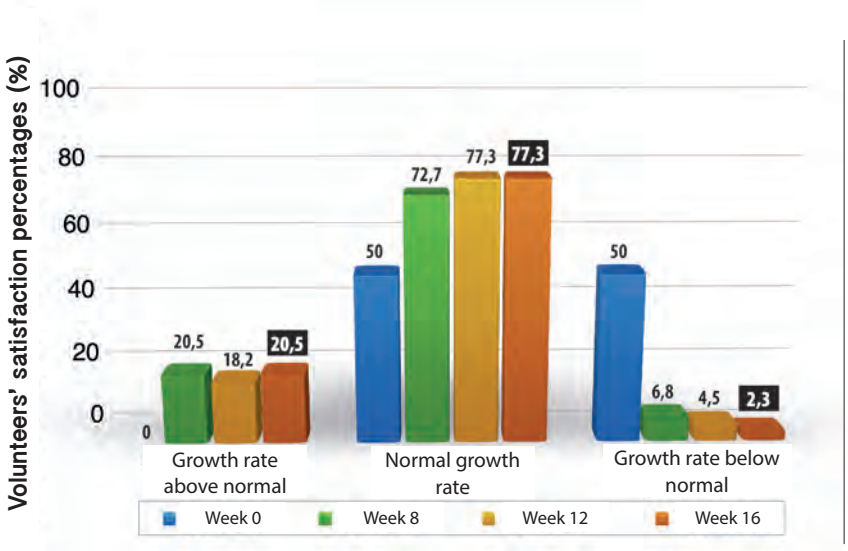
Graph 4 shows the percentage of ratings obtained for the clinical evaluation of the nails' resistance on the study's experimental timepoints. Graph 4 depicts the progressive clinical improvement of resistance over time, indicating a statistically significant increase in the resistance to trauma and cut: 47.7% in Week 8, 59.1% in Week 12, and 93.2% in Week 16 ($p < 0.001$). Weak / very weak nails, which accounted for 88.7% of the sample, decreased to 52.3% in Week 8, to 40.9% in Week 12, and to 6.8% in Week 16, confirming the presence of progressive and significant clinical improvement over time ($p < 0.001$).



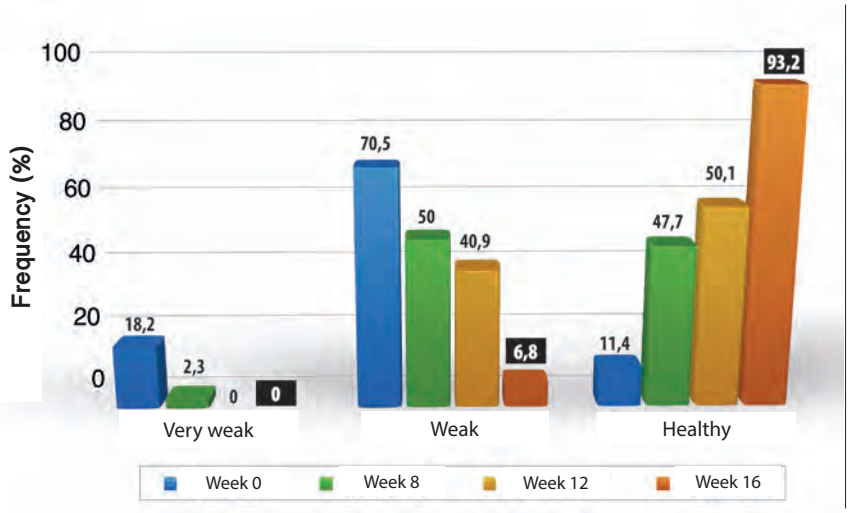
Graph 1: Percentages for the ratings attributed in the experimental timepoints (Weeks 0, 8, 12 and 16) in the subjective evaluation of perception of the nails' strength (n = 44)



Graph 2: Percentages for the ratings attributed in the experimental timepoints (Weeks 0, 8, 12 and 16) in the subjective evaluation of perception of the nails' resistance (n = 44)



Graph 3: Percentages for the ratings attributed in the experimental timepoints (Weeks 0, 8, 12 and 16) in the subjective evaluation of perception of the nails' growth rate (n = 44)



Graph 4: Percentages for the ratings attributed for the nails' resistance in the clinical evaluation in the experimental timepoints (Weeks 0, 8, 12 and 16) (n = 44)

2.Nail integrity

Clinical improvement of nail integrity, characterized by lower incidence and extent of onycholysis, was progressive over time and statistically significant: 72.2% of patients had brittle / very brittle nails at baseline, with 47.7 % in Week 8, 36.4% in Week 12 and 25.7% in Week 16 ($p < 0.001$). Seventy-nine point five percent had healthy nails after 16 weeks of treatment, as shown in Graph 5.

Tolerability

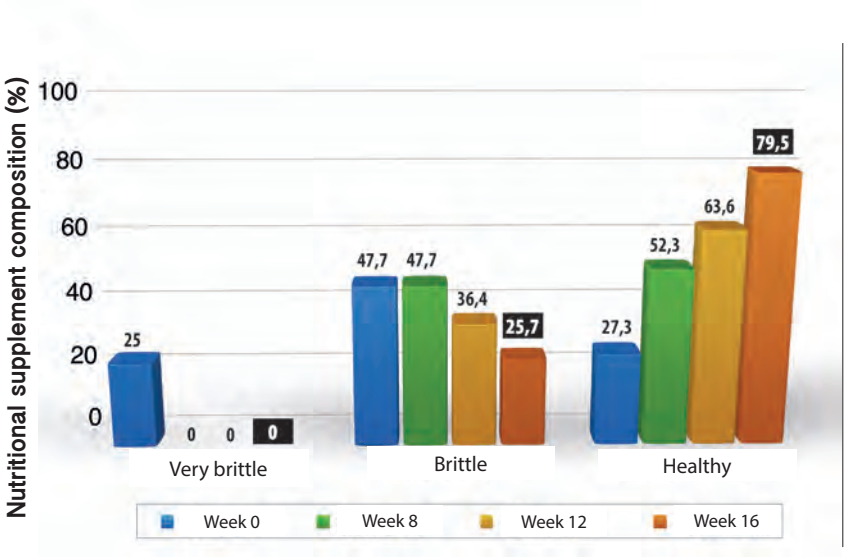
The use of the product in the recommended dosage (one tablet a day) was very well tolerated. None of the patients reported any discomfort during ingestion or adverse reaction of any nature during the study period.

DISCUSSION

The semiology of ungual alterations is subtle, and some signs may coexist on the same nail plate, as in the case of osteomalacia (reduction of the nail's resistance) and onychoschisis (cracking of the free border). Some of these findings are related to traumatic causes (both mechanical and chemical), such as onycholysis and onychorrhexis. [1]

However, onychoses have greater incidence in nails whose keratinogenesis is compromised, with one of the most common causes being linked to nutrition. [5]

Even if borderline, specific deficiencies of micronutrient and trace elements can lead to disorders in the formation of hair and nails, reflecting the adnexa's quality and growth rate. [6] A good example is iron deficiency anemia, which classically leads to koilonychia; nevertheless, alterations in the nail's integrity can be noticed in mild deficiencies. [1]



Graph 5: Percentages for the ratings attributed for the nails' integrity in the clinical evaluation in the experimental timepoints (Weeks 0, 8, 12 and 16) (n = 44)

There is evidence that the brittle nail syndrome, characterized by onychoschizia and onychorrhexis, is linked to deficiency of biotin. [7]

Oral carotenoids allow more effective concentration in regions with adnexa than their topical form, and are capable of normalizing the differentiation of keratinocytes, improving their metabolism and division, in addition to influencing the secretion of growth and transcription factors. [8]

The literature is however scarce when it comes to studies on nutritional deficiency involving nails. It makes sense to hypothesize that nutritional deficiencies responsible for alterations found in the hair also lead to problems in the nails given the similarity between these adnexa regarding the synthesis of keratin. [9]

The evaluated association of nutrients initially underwent a study in keratinocytes culture that demonstrated a significant increase in cell differentiation, with consequent greater keratinogenesis. [10] In the present study, the it was possible to observe a significant improvement in most of the parameters evaluated from Week 8 of use, and that the improvement increases with continued use. Although the nails' metric evaluation was not performed, the alignment of the clinical results with the data collected from the patients shows that the studied supplement led to a perceptible improvement in the quality of the nail plate.

CONCLUSION

The nutritional supplement evaluated was proven effective in improving the signs of ungual weakening (for instance, loss of resistance and decrease in the growth rate). The improvement in the quality of the nail plate was significant both in the clinical examination and in the patients' self-evaluation, demonstrating the nutritional supplement is safe in the approach of complaints involving weakness, brittleness, and low growth rates of the nails. ●

REFERENCES

1. Cashman MW, Sloan SB. Nutrition and nail disease. Clin Dermatol, 2010;28(4):420-5.
2. Boelsma E, Hendriks HF, Roza L. Nutritional skin care: health effects of micronutrients and fatty acids. Am J Clin Nutr. 2001;73(5):853-64.
3. Costa IMC; Nogueira LSC; Garcia PS. Síndrome das unhas frágeis. An Bras. Dermatol. 2007;82(3):263-7.
4. Maverakis E, Fung MA, Lynch PJ, et al. Acrodermatitis enteropathica and an overview of zinc metabolism. J Am Acad Dermatol. 2007;56(1):116-124.
5. Nandedkar-Thomas MA; Scher RK. An update on disorders of the nail. J Am Acad Dermatol. 2005;52(5):877-87.
6. Gupta MA; Gupta AK; Haberman HF. Dermatologic signs in anorexia nervosa and bulimia nervosa. Arch Dermatol. 1987;123(10):1386-90.
7. Oski, FA. The nonhematologic manifestations of iron deficiency. Am J Dis Child. 1979 Mar;133(3):315-22.
8. Szyszkowska B, Lepecka-Klusek C, Kozłowicz K, Jazienicka I, Krasowska D. The influence of selected ingredients of dietary supplements on skin condition. Postepy Dermatol Alergol. 2014;31(3):174-81.
9. Sato, S. Iron deficiency: structural and microchemical changes in hair, nails, and skin. Semin Dermatol. 1991;10(4):313-9.
10. Addor, FAS. Influência da suplementação de nutrientes no metabolismo de queratinócitos: estudo in vitro. Surgical and Cosmetic Dermatol. 2012;4(2):150-4.

Original Articles

Authors:
Andréa Santos Soares[1]
Ana Paula Dornelles Manzoni[2]
Carla Daniele Amorim de Souza[3]
Magda Blessmann Weber[4]
Tatiane Watanabe[1]
Leandra Camini[5]

[1] Dermatologist Physician, Universidae Federal de Ciências de Saúde de Porto Alegre (UFCSPA) – Porto Alegre (RS), Brazil.

[2] PhD. Preceptor, Dermatology Department, UFCSPA.

[3] Physician, UFCSPA.

[4] PhD, Assistant Professor, Dermatology Department, UFCSPA.

[5] Dermatologist Physician. Preceptor, Dermatology Department, UFCSPA.

Correspondence:
Andréa Santos Soares
R. Ogê Fortkamp, 111, apt 301 - Bloco A
cep 88036-610 – Florianópolis (SC), Brazil
e-mail: dea.ss@hotmail.com

Received on: 30/05/2016
Approved on: 26/08/2016

This study was carried out at the Dermatology Department of the Universidade Federal de Ciências de Saúde de Porto Alegre - Porto Alegre (RS), Brazil.

Financial support: None
Conflict of interests: None

Comparative analysis between sutured elliptical excision and shaving of intradermal melanocytic nevi: a Randomized Clinical Trial

Ensaio clínico randomizado sobre a análise comparativa entre excisão de nevos melanocítos intradérmicos por shaving versus excisão em elipse e sutura

DOI: http://dx.doi.org/10.5935/scd1984-8773.201684902

ABSTRACT

Introduction: Although the intradermal melanocytic nevi are benign lesions, many patients seek for dermatologists for their excision. However, there are no studies about the best method for this procedure.

Objective: To compare in a randomized clinical trial the excision of intradermal melanocytic nevi in the face for shaving and elliptical excision with suture

Methods: Patients with intradermal melanocytic nevi on the face were selected for removal by shaving or ellipse, randomly. The results were described regarding patient satisfaction and photographic records evaluated by a blinded physician.

Results: 18 patients underwent excision of intradermal melanocytic nevi. The mean scar size after six months of the procedure was of 8,11mm for the excision in ellipse and 2,92mm for the shaving ($p < 0.05$). The mean score of the patients after six months was 9.67 (ellipse) and 9.57 (shaving) ($p = 0.8$). The mean by the blinded physician was of 7.78 (ellipse) and 7.86 (shaving) ($p = 0.91$). 28.6% of patients undergoing shaving had recurrence of the nevus.

Conclusions: The two forms are of excision are equivalent concerning patients satisfaction and the judgment of medical team about the aesthetic results of the scar. However, ellipse with suture excision has the advantage of having a lower relapse.

Keywords: nevus, intradermal; ambulatory surgical procedures; skin; therapeutics

RESUMO

Introdução: *apesar de os nevos melanocíticos intradérmicos serem lesões benignas, muitos pacientes recorrem ao dermatologista para sua exérese. Entretanto, não existem estudos sobre o melhor método para esse procedimento.*

Objetivo: *comparar em ensaio clínico randomizado a exérese de nevos melanocíticos intradérmicos na face, por shaving e excisão em elipse com sutura*

Métodos: *foram selecionados pacientes com nevos melanocíticos intradérmicos na face para os dois métodos, randomicamente. Os resultados foram descritos quanto à satisfação do paciente e aos registros fotográficos avaliados por médico cegado.*

Resultados: *18 pacientes foram submetidos à exérese de nevos melanocíticos intradérmicos. A média de tamanho da cicatriz após seis meses foi de 8,11mm para as lesões excisadas por fuso e de 2,92mm para as por shaving ($p < 0,05$). A média da nota dos pacientes após seis meses foi 9,67 (fuso) e 9,57 (shaving) ($p = 0,8$). A média pelo médico cegado foi 7,78 (fuso) e 7,86 (shaving) ($p = 0,91$). Ocorreu recidiva da lesão em 28,6% dos pacientes submetidos ao shaving.*

Conclusões: *As duas formas de excisão se equivalem quanto à satisfação do paciente e nota dada pela equipe médica quanto aos resultados estéticos da cicatriz. Contudo, a exérese por fuso tem a vantagem de apresentar menor índice de recidiva.*

Palavras-chave: *nevo intradérmico; procedimentos cirúrgicos ambulatoriais; pele; terapêutica*

INTRODUCTION

Acquired melanocytic nevi are benign lesions originated from melanocytes, and can be classified as junctional, compound or IMN. [1,2] The progressive decrease in its growth rate and the emergence of differentiation of cells in melanocytic nevi lend the benign characteristic to the lesion, which are generally solid and can vary in size. [1] IMN (IMN) are nevi with little presence or absence of melanocyte proliferation in the epidermis, and its main characteristic is the presence of clusters of nevus cells in the dermis. [1] The cells that are located more deeply in the dermis tend to assume neuroid or fibroblastic morphology, and lose their melanin synthesizing capacity, meaning that the vast majority of IMNs are clinically not pigmented. [1] The diagnosis of IMN is usually clinical, and its malignization risk is low. [1] On examination, the lesions appear to be papular, normochromic or slightly pigmented, [1,2] and are most commonly found on the face. Telangiectasias and terminal hairs may be present. [1] Differential diagnosis of IMN includes dermatofibromas, neurofibromas, fibroepithelial polyps, and basal cell carcinomas, among others. [2]

The excision of IMN is indicated when there are proven clinical or dermoscopic changes and atypical appearance of the lesion, nevertheless they are more often excised due to aesthetical reasons or repeated local traumas. [2]

Currently, there is no consensus on the best way to excise an IMN, and it is up to the dermatologist to use the shaving technique or the elliptical excision followed by suture.

Shaving – or saucerization – is the removal of the lesion by cutting its base parallel to the skin, using a scalpel or scissors. Elliptical excision corresponds to the ellipse-shaped exeresis of the skin around the lesion. It allows the removal of all skin layers up until the hypodermis and requires suturing. The present study was aimed at comparing the two procedures regarding the patients' and dermatologist physicians' satisfaction with the aesthetic results, and the lesion's risk of recurrence.

METHODS

A comparative randomized clinical trial, blind to an observer, was carried out at the Dermatology Service, Universidade Federal de Ciências de Saúde de Porto Alegre (UFCSPA), Porto Alegre, Brazil, including 18 patients with clinical diagnosis of IMN on the face, from August 2014 to June 2015. The study was approved by the Research Ethics Committees of both UFCSPA and the health center Santa Marta (Porto Alegre, RG, Brasil).

Patients of both genders bearing intradermal nevi diagnosed based on the classical clinical manifestations (normochromic melanocytic papular lesions) and dermoscopic characteristics (focally located globules or structures similar to globules, whitish areas without structure, and thin linear vessels or in the shape of a comma), located on the face, which corresponds to the area of highest prevalence of IMN. Patients were aged between 18 and 80 years, had Fitzpatrick's phototypes I to IV (Table 1), and accepted to take part in the study by signing the Term of Free and Informed Consent. Patients whose nevi had undergone previous procedures, those with undiagnosed or poorly controlled clinical diseases (for example diabetes, Thyroiditis, hypertension), previous history of Keloid, use of medications that alter wound healing (eg. isotretinoin and immunosuppressants), were exclusion factors. Also, patients who did not follow the evaluation schedule or who did not have confirmation of the clinical diagnosis by histology after undergoing exeresis of the lesion were excluded.

The patients were alternately selected to undergo shaving or excision, followed by suture, observing the order of inclusion in the study. The lesions that had been randomized to undergo for ellipse exeresis (always observing the skin's tension lines for better incision and suture) were demarcated so as to maintain a 30º angle at the ellipses' borders, restricting the incision's length to three times the width's length, maintaining a margin of 1mm to 3mm from the intradermal nevus. Sutures were performed with separate single stitches, using a 6/0 nylon thread. Micropore was applied on the suture, with patients being instructed to remove it after 24 hours, and carefully cleanse the surgical wound once day with water up until the stitches have been removed in the 7th post-operative day, at UFCSPA's Dermatology Service.

The lesions that were randomized for the shaving procedure underwent excised by the means of an incision carried out at the base of the lesion, flush to the skin, using a scalpel blade number 15. The hemostasis was performed only with local compression. Micropore was applied on the site and the patients

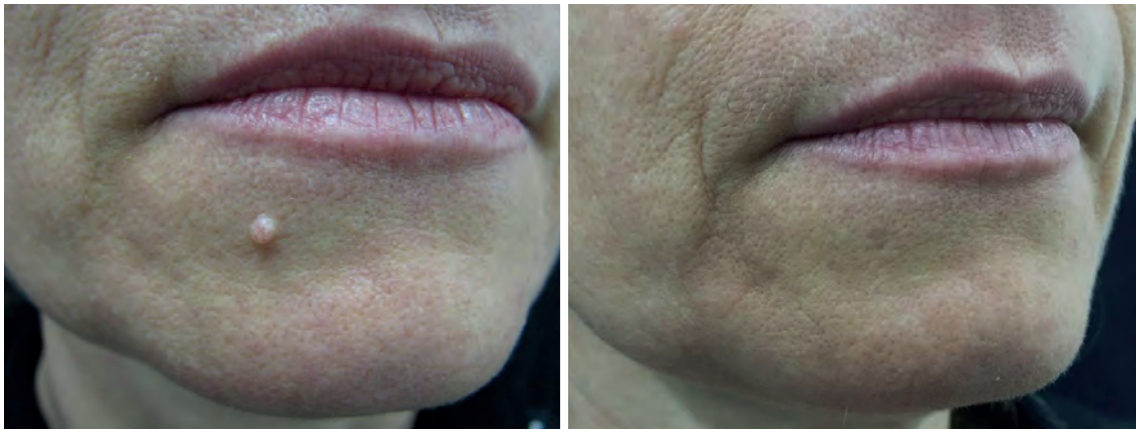


Figure 1: *Intradermal melanocytic nevus in the mentum region, before and after resection using the shaving technique*

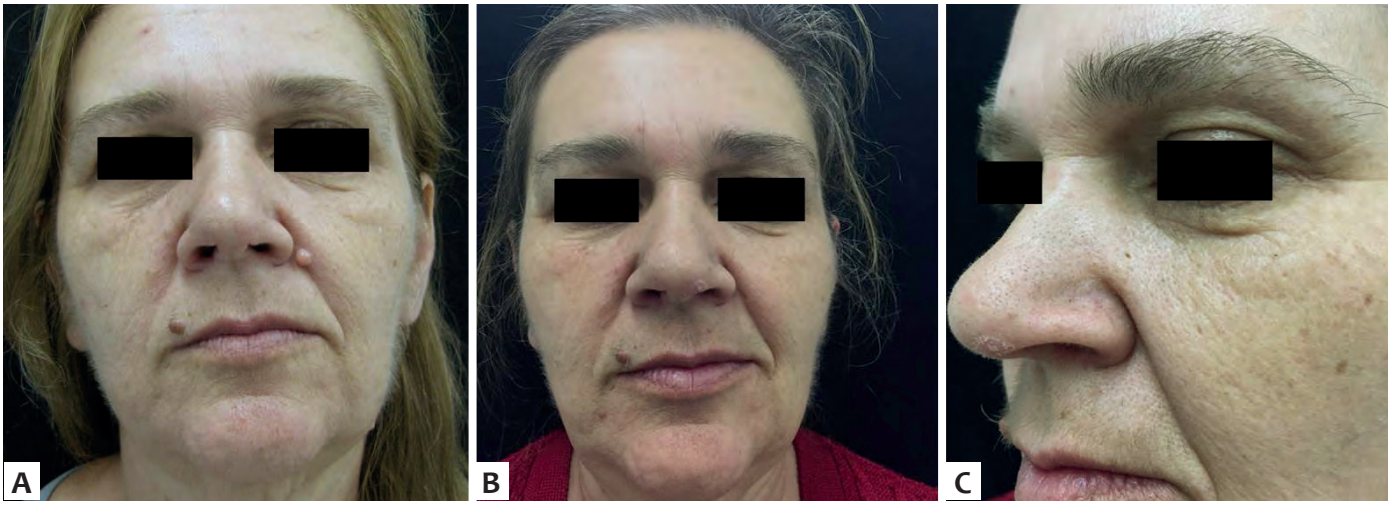


Figure 2: Intradermal melanocytic nevus in the nasolabial fold region, before **(A)** and after resection performed using the shaving technique **(B and C)**.

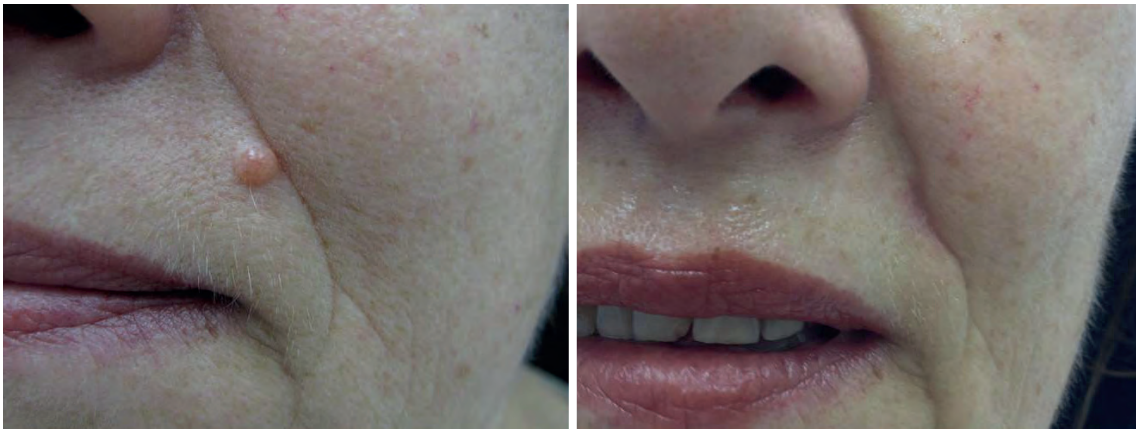


Figure 3: Intradermal melanocytic nevus in the nasolabial folds region, before and after elliptical exeresis and suture

Chart 1: Fitzpatrick phototyping scale of the skin

Cutaneous phototype	Skin reaction to UV-R
I	Always burns
II	Never tans
III	Easily burns
IV	Minimally tans
V	Moderately burns
VI	Moderately tans
	Minimally burns
	Easily tans
	Rarely burns
	Easily tans and almost never burns
	Easily tans and almost never burns
	Tans immediately and intensely

Source: Brazilian Photoprotection Consensus 2014. [3]

were instructed have it removed 24h after, with gentle cleansing with water once a day. All surgical procedures and advice were given to the patients by the same dermatological surgeon on all follow-up visits.

Regarding the patient follow-up visits, all were contacted 48h after the procedures for the classification of the intensity of discomfort with the excision. This classification was based on an analogue scale of pain graded from "zero" (absence of discomfort) up to "10" (unbearable discomfort), with the patients being advised that "discomfort" would include the presence of pain, bleeding, restriction to movement, and difficulty to sleep.

The patients returned to the UFCSPA's Dermatology Service after 3 and 6 months of the procedure for postoperative evaluation and having their surgical wound photographed. Pre- and post-procedure photographs were taken under standardized environmental, lighting, and technical parameters (including the camera and the photographer), and the lesion was measured in millimeters before the procedure and at all subsequent visits. All patients were instructed to use sunscreen with at least SPF30 (reapplied each 4 hours), in addition to physical protection for at least 6 months.

Regarding the statistical evaluation, the qualitative data were assessed using frequency and percentage analysis, while the quantitative data were assessed based on mean values and standard deviation (when normally distributed) and median and interquartile range (when the distribution was not normal).

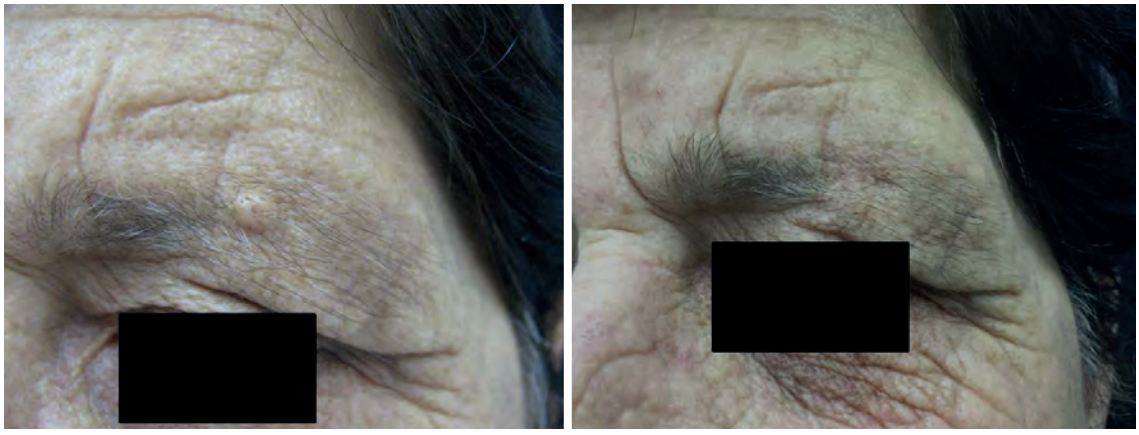


Figure 4: Intradermal melanocytic nevus in the eyebrow region, before and after resection performed using ellipse and suture

The data normality was verified using the Shapiro-Wilk test. The comparisons between the different types of treatment were performed using the Fisher exact test (qualitative variables), the Student's t-test (normally distributed quantitative variables) and the Mann-Whitney test (non-normally distributed quantitative variables). The comparisons between the assessments performed by the physician and the patient were analyzed by using the Student's t-test, according to the assessment timepoint and the treatment. The data were recorded on an electronic spreadsheet and analyzed using the software SPSS V21A. The statistical significance was 5% (p-value < 0.05).

RESULTS

Eighteen patients with lesions on the face underwent excision of IMN. The histological analysis revealed the following diagnoses: IMN (16 cases, 88.9% of the sample cases); compound melanocytic nevus (1 case) and hemangioma (1 case). As a result, 11.5% of the facial lesions had discordant histological and clinical diagnoses. These patients were excluded from study.

The analyzed sample had 16 patients (2 men, 14 women). The profile of the patients included in the study is described in Table 1, evidencing the sample homogeneity regarding the patients' age, gender and phototype. Patients were followed-up for up to 6 months.

The average IMN size studied was 3.94mm for those excised with the elliptical technique, and 3.92mm for those excised using the shaving technique. The sample was homogeneous for all groups described (Table 1).

The average scar size after 6 months was 8.11mm for lesions excised with the elliptical technique, and 2.92mm for those excised with the shaving technique ($p < 0.05$), as seen in Table 2. In the evaluation performed 6 months after the procedure, the mean rating attributed by the patients regarding the procedure's final outcome was 9.67 for those who underwent fusiform (elliptical) excision and 9.57 for those who underwent the shaving procedure ($p = 0.8$). Regarding the evaluation performed by the blinded physician, the average rating regarding the procedure's final outcome was 7.78 for the patients undergoing fusiform (elliptical) resection and 7.86 for those who underwent shaving exeresis ($p = 0.91$) (Table 3).

Only two patients reported discomfort after the procedure (attributing the rating "1" on a scale from "zero" to 10), with each of them belonging to one of the groups (elliptical excision and shaving procedure) (Table 2).

None of the patients developed hypertrophic scarring or keloid during the follow-up period the procedure. Regarding the recurrence of the lesion after the procedure, none of the patients who underwent fusiform (elliptical) excision experienced recurrence while 28.6% of those ho underwent the shaving procedure in the same group had recurrence (Table 2).

DISCUSSION

There is lack of scientific literature effectively comparing options and indicating the best treatment for IMN. Some studies evaluate the durations of the healing, bleeding and infection, however there are no studies comparing the shaving technique with fusiform excision followed by suture.

Histological analysis in the present study evidenced that 88.9% of the lesions excised were IMN, as previously clinically diagnosed. The discordant cases were: one compound melanocytic nevus and one hemangioma. This fact shows a high level of agreement between the histology and the clinical manifestations of IMN, nevertheless it highlights the paramount importance of submitting all excised lesions to histological examination. In the present study, all discordant lesions were benign, however differential diagnoses, such as amelanotic melanoma and basal cell carcinoma, should not be overlooked. [2,4]

In the present study, the scars from lesions excised via the shaving technique were significantly smaller than those excised using fusiform excision (Figures 1 and 2) – and even smaller than the lesions before undergoing the procedure (Figures 3 and 4) ($p < 0.05$). The outcomes corroborate the literature findings, which state that approximately 45% of the facial nevi excised using the shaving technique generate scars that are smaller than the original lesions. [1] The smaller size of the scar as compared to the initial nevus lesion after shaving excision is possibly due to the cicatricial retraction of the tissues. On the other hand, the fusiform (or elliptical) technique requires that the length of the surgical piece be roughly three times larger than the nevus, which leads to an increase of the scar in this technique. [1]

TABLE 1: Sample characterization

Variables	Face		
	Elliptical (n = 9)	Shaving 9n = 70	p -value
Age, mean ± SD	53.22 ± 9.42	49.29 ± 8.99	0,412#
Sex, n (%)			> 0,999*
Female	8 (88.9)	6 (85.7)	
Male	1 (11.1)	1 (14.3)	
Phototype, n (%)			> 0,999*
2	6 (66.7)	4 (57.1)	
3	3 (33.3)	(42.9)	
Treatment of nevus			
(mm), mean ± SD	3.94 ± 0.88	3.93 ± 1.24	0,976#

DP: Desvio-padrão; # Teste t; ⋆ Teste exato de Fisher / SD: standard deviation; # Test t; ⋆ Fisher's exact test

TABLE 2: Comparison

	Variables	Fuso	Shaving p-value
Hypertrophic scar / keloid, n (%)			–
Yes	–	–	
No	9 (100)	7 (100)	
Recurrence, n (%)			0,175*
Yes	–	2 (28,6)	
No	9 (100)	5 (71,4)	
Scar size after 3 months, mean ± DP	8.11 ± 2,72	3.00 ± 1,83	0,001#
Scar size after 6 months, mean ± DP	8.11 ± 2.62	2.93 ± 1,79	0,001#
Pain, median [25%;75%]	0.0 [0,0-0,0]	0.0 [0,0-0,0]	0,854##

DP: Desvio-padrão; # Teste t; ##Teste Mann-Whitney; = SD: standard deviation; # Test t; ## Mann-Whitney test;

⋆ *Fisher's exact test; Test not calculated*

All patients included in the study (in both groups) were very satisfied with the procedures' outcomes. The difference between the average rating for the patients' satisfaction with the shaving technique and with exeresis followed by suture was little, with a slightly greater satisfaction with the elliptical excision, however without statistical significance (p = 0.8). In their study, Lee et al. also demonstrated a significant patient satisfaction index associated to the shaving technique used for the removal of IMN. [5]

TABLE 3: Assessments regarding patient and physician satisfactions

Evaluator	Period	Face		
		Fuso	Shaving	p - value
Patient	3 months	9.89 ± 0.33§	9.57 ± 0.79§	0,348#
	6 months	9.67 ± 0.71§	9.57 ± 0.79§	0,803#
Physician	3 months	7.33 ± 1.00	7.29 ± 1.89	0,949#
	6 months	7.78 ± 1.48	7.86 ± 1.57	0,919#

 # Teste t; Teste não calculado; § Diferença significativa em relação à avaliação do médico para o mesmo período avaliado (p < 0,05; teste t de Student) = # T test; Test not calculated; § Significant difference regarding the physician's evaluation for the same period evaluated (p <0.05, Student's t-test)

In the present study, none of the patients developed hypertrophic scar or keloid during the follow-up period. This may be linked to the fact that patients with lower phototypes (II and III) were selected, in addition to the small size of the studied sample. [6]

It was possible to observe a low recurrence rate linked to the excision of facial lesions using the shaving technique. It is known that the most superficial excision caused by the shaving technique increases the risk of recurrence of the nevus as compared to the excision up until the hypodermis followed by suture. Nonetheless, the real reason for the recurrence and its correlation with that technique needs to be better studied.

CONCLUSION

It is possible to conclude that the two excision techniques are equivalent in terms of patient satisfaction and the rating attributed by the medical team to the esthetical outcomes of the scar. Nevertheless, the fusiform (or elliptical) exeresis has the advantage of having a lower recurrence rate. Despite the results that were obtained, more studies are necessary aimed at consolidating the present paper's findings. ●

REFERENCES

1. Burns T, Breathnach S, Cox N, Griffiths C. Rook's Textbook of Dermatology. 8th ed. Oxford: Wiley-Blackwell; 2010.
2. Bolognia JL, Jorizzo JL, Schaffer JV. Dermatology. Rio de Janeiro: Elsevier; 2015.
3. Schalka S, Steiner D, Ravelli FN, Steiner T, Terena AC, Marçon CR, et al. Consenso Brasileiro de Fotoproteção. An Bras Dermatol. 2014;89(6 Suppl 1):S6-75.
4. Arjona-Aguilera C, Gil-Jassogne C, Jiménez-Gallo D, Albarrán-Planelles C. Intradermal Melanoma Associated With an Intradermal Melanocytic Nevus. Actas Dermosifiliogr. 2015;106(9):776-7.
5. Lee JM, Lee H, Lee TE, Park M, Baek S. Second intention healing after shave excision of benign tumors on the lid margin. Ann Dermatol 2011;23(4):463-7.

Original Articles

Authors:
Marisa Gonzaga da Cunha[1]
Francisca Daza[2]
Flávia Cury Rezende[3]
Carlos D. Apparecida Machado Filho[4]

[1] Dermatologist Physician, Doctoral student in Health Sciences. Head of the Cosmiatry Sector, Dermatology Department, Faculdade de Medicina do ABC (FMABC) - Santo André (SP), Brazil.

[2] Cpllaborating Dermatologist Physician, Cosmiatry Sector, Dermatology Department, FMABC.

[3] Intern Physician, Dermatology Department, Faculdade de Medicina do ABC (FMABC) - Santo André (SP), Brasil.

[4] Full Professor, Dermatology Department, FMABC.

Correspondence:
Marisa Gonzaga Da Cunha
Rua Gonçalo Fernandes 153, salas 83-84 - Bela Vista
Cep 09090-410 - Santo André (SP), Brazil
e-mail: dramarisagonzaga@yahoo.com.br

Received on: 12/11/2016
Approved on: 01/12/2016

This study was performed at Faculdade de Medicina do ABC (FMABC) - Santo André (SP), Brazil.

Financial support: Galderma Brazil.

Conflict of interests: Galderma Brazil supplied 28 bottles of the studied product free of charges, however the researchers carried out the methodology, implementation and analysis of the obtained results without interference from the company.

Poly-L-lactic acid injections in sagging body skin

Aplicação de ácido poli-l-lático para o tratamento da flacidez corporal

DOI: http://dx.doi.org/10.5935/scd1984-8773.20168404

ABSTRACT

Introduction*:* The treatment of sagging skin in body areas is still a big challenge, as there are few aesthetic procedures aiming to improve it.
The poly-L-lactic acid (PLLA) is an injectable synthetic polymer of the alpha-hydroxy acids family, which injection into the deep dermis or superficial hypodermis induces a local and gradual reaction, with synthesis of new collagen by the fibroblasts and consequent increase of dermal thickness.
Purpose: Evaluate the effects of poly-L-lactic acid on the sagging skin of the body.
Methods: Fourteen patients with sagging in gluteal region underwent two applications of poly-L-lactic acid with a 45 days interval between them. We performed an initial clinical evaluation and after six months of the second application, photos before and after six months of treatment, questionnaires answered by the patient and by the evaluating physician and ultrasound examination of all patients to assess the increase of dermal thickness. The adverse effects observed were also evaluated.
Results: In patient's opinion, 85% presented improvement of general appearance of the skin and 71% noticed improvement of sagging. For the evaluating physician, 100% of patients presented improvement of general appearance of the skin and improvement of sagging, but in different degrees and not proportional to the initial degree of severity. There was no significant side effects in the period evaluated.
Conclusions: The results are promising and should be confirmed with studies with a larger sample size.
Keywords: cutis laxa; skin; Buttocks

RESUMO

Introdução*: O tratamento da flacidez cutânea corporal constitui grande desafio, pois poucos são os procedimentos destinados a melhorá-la. O ácido poli-L-lático é polímero sintético injetável da família dos alfa-hidroxiácidos, cuja injeção na derme profunda ou hipoderme superficial induz reação local e gradual, com síntese de novo colágeno pelos fibroblastos e consequente aumento da espessura dérmica.*
Objetivo: *Avaliar os efeitos do ácido poli-L-lático na flacidez da pele do corpo.*
Métodos: *Quatorze pacientes que apresentavam flacidez de região glútea foram tratadas com duas aplicações de ácido poli-L-lático com intervalos de 45 dias entre elas. Foram realizadas avalição clínica inicial e seis meses após a segunda aplicação, fotos prévias e seis meses após o tratamento, bem como foram aplicados questionários às pacientes e ao médico avaliador, e realizado exame ultrassonográfico de todas as pacientes para verificação do aumento de espessura dérmica. Foram avaliados também os efeitos adversos observados.*
Resultados: *Na opinião das pacientes, 85% apresentaram melhora no aspecto geral da pele e 71% na flacidez. Para o médico avaliador, 100% das pacientes apresentaram melhora no aspecto geral da pele e na flacidez, porém em graus variáveis e não proporcionais ao grau de gravidade inicial. Onze pacientes tiveram aumento da espessura dérmica acima de 20% dos pontos. Não houve efeitos colaterais importantes no período avaliado.*
Conclusões: *Os resultados são promissores e devem ser confirmados com a realização de estudos com casuística maior.*
Palavras-chave: *flacidez; pele; região glútea*

INTRODUCTION

Beauty and attractiveness are important sociocultural factors that tend to dictate how individuals are judged and accepted by the society.[1] As the world's population progressively ages and cosmetic procedures become increasingly popular, adults of all age and socioeconomic groups seek aesthetic improvement.

Currently, there is a great variety of procedures and materials for the treatment of facial aging, which opens up a series of possibilities and combinations that will have synergistic effects – e.g. the use of different cutaneous fillers at different points in time or of different products in different facial sites. [2] Concomitantly to the improvement of the facial appearance, the search for a perfect body is a concern for most of the population, particularly for women. However, the treatment of sagging skin continues to be a major challenge, since there are few procedures aimed at improving it.

The changes caused by the skin's chronological aging result from the normal physiological process, where there are epidermal, dermal and hypodermic thinning, which in turn are aggravated by photoaging. [1] In addition to aging, several factors contribute to the onset or aggravation of skin sagging, for instance restrictive diets, weight loss, liposuction and post-pregnancy, all of which favor the loss of the skin's elasticity, even in young patients.

Innovative treatments are being constantly developed, however few studies have been published on the treatment of sagging in the body's skin in general. Knowledge of the relationship between the various skin layers – especially that between the dermis and the hypodermis – and the changes they undergo, triggering skin sagging, is crucial for understanding the indications of possible treatments, based on their mechanisms of action. Given that the poly-L-lactic acid's (PLLA) mechanism of action induces a local and gradual reaction that can lead to recovery of the hypodermis and collagen network that were lost during the aging process, the hypothesis of its use for the treatment of general body skin sagging was raised.

Poly-L-lactic acid is an injectable synthetic polymer from the alpha-hydroxy acid family. It is biocompatible and biodegradable, has very low cytotoxicity, [3] and has been used for many years in absorbable surgical suture threads. Once injected, PLLA induces local and subclinical inflammatory response shortly after application, recruiting monocytes, macrophages and fibroblasts. It is then hydrolyzed into lactic acid monomers and eliminated; nonetheless there lingers an increased deposition of collagen produced by fibroblasts, with the resulting increase in dermal thickness. [3,4] It is this fibroplasia that will determine the cosmetic results. [5] Since PLLA is a biostimulating agent that depends on the host's reaction, its effects will not be immediate, and will be observed in a gradual and progressive manner, during the months ensuing its application. [6]

The present study was performed at the Cosmiatry Sector, Dermatology Department of the Faculdade de Medicina do ABC (FMABC), in Santo André (SP), Brazil, aimed at analyzing the treatment of sagging skin in the gluteal region with subdermal applications of PLLA. It was approved by the Research and Ethics Committee of FMABC and conducted according to the Good Clinical Practice directives.

The choice for the gluteal region was linked to the fact that it is frequently linked to complaints – even in young patients – often being associated with the presence of cutaneous striae, in addition to the fact that this location is not significantly influenced by muscular sagging – unlike the inner part of the arms, for example, in this age group. The study's secondary objective was to evaluate the influence of improved sagging on the improvement of cellulitis.

PATIENTS AND METHODS

Fourteen women between 27 and 37 years of age with complaints of cutaneous skin sagging in the gluteal region were selected.

Inclusion criteria: women with skin sagging.

Exclusion criteria: pregnancy, breastfeeding, vegetarian diet, history of hypertension, diabetes, allergies and skin diseases, previous treatments in the studied area, and weight gain during the study period.

The evaluation was carried out clinically, and the scoring system used in the initial evaluation was as follows:

Skin sagging: (0) absence of skin sagging, (1) little skin sagging, (2) moderate skin sagging, (3) intense skin sagging.

Striae: (0) absence of striae, (1) up to 5 striae, (2) between 6 and 15 striae, (3) more than 16 striae.

Gynoid-lipodystrophy cellulite (GLD) Grade II: (0) absence, (1) mild, (2) moderate, (3) severe.

The total score corresponded to the sum of the evaluated criteria's scores.

The patients and the applicator physician answered a detailed questionnaire about the local conditions of the skin, presence of striae, sagging, and degree of cellulite before the application. At the pretreatment stage, the degree of sagging ranged from mild (3), moderate (5), and severe (6), and was not correlated to the severity of the striae, due to the fact it was possible to observe that despite the presence of more pronounced sagging in some patients, they had only a few striae. At baseline, 90% of the patients had moderate GLD Grade II in the treated site.

The pre-treatment photographic evaluation was performed in three positions: frontal, dorsal and profile.

Two applications were performed in the gluteal region bilaterally with a 45-day interval, using one PLLA vial in each session. Each vial was diluted two days before in 9 ml of distilled water, leading to a final volume at the moment of the application of 8ml, to which 2ml of lidocaine without vasoconstrictor were added.

The applications were performed under local anesthesia with anesthetic cream. The skin was marked with squares with sides of approximately 2cm, as shown in Figure 1. A solution volume of 0.04ml per square was applied in the deep dermis-superficial hypodermis, in a puncture made in the center of each square. After the applications, local massage was applied for 5 minutes. The numbers of points of hematoma in the applications

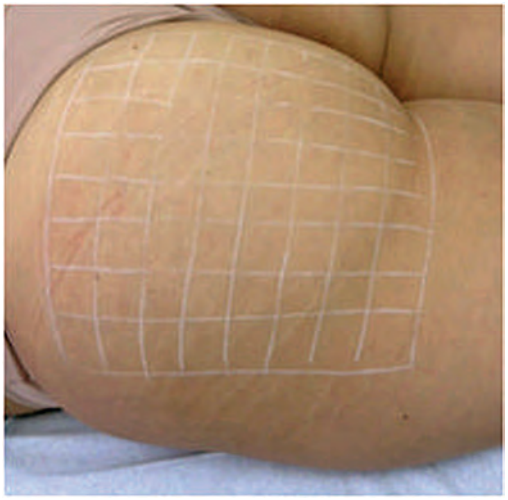


Figure 1: Marking of the skin to be treated. The applications were performed in the central point of each square

sites were recorded.

Six months after the second application, a new clinical evaluation was carried out by the patient and the evaluator physician, using the same questionnaire applied at baseline. The improvement score was as follows:

Absence of improvement (0), little improvement (1), moderate improvement (2), intense improvement (3). The total score corresponds to the sum of the responses to the treatment for each adopted criterion. In addition to the questionnaires answered by the patient and the evaluator physician, ultrasound examinations were performed in the various predefined application points (10 in total), for evaluation of the increase in the skin thickness in the treated areas.

The photographic evaluation was performed in three positions, 6 months after the second application.

The adverse effects were evaluated as follows:

Pain: (0) absence of pain, (1) mild, (2) moderate and (3) intense;

Number of points of hematoma observed after each application: (0) absence of hematoma, (1) up to 3 points of hematoma, (2) from 4 to 7 points of hematoma, (3) more than 8 points of hematoma.

Table 1: Pre-treatment period's severity score

PATIENT	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Skin sagging	1	1	1	2	2	3	2	3	3	2	3	3	2	3
Striae	2	2	0	3	1	2	2	2	1	2	3	3	2	2
GLD	2	3	1	2	2	2	2	2	1	1	1	1	1	3

Regarding skin sagging: it ranged from mild (3 patients), moderate (5 patients) and severe (6 patients). Regarding striae: absence of striae (1 patient), up to 5 striae (2 patients), between 6 and 15 striae (8 patients) and more than 16 striae (3 patients). Regarding GLD Grade II: mild (5 patients), moderate (6 patients) and severe (2 patients).

Table 2: Degree of improvement in the patient's opinion

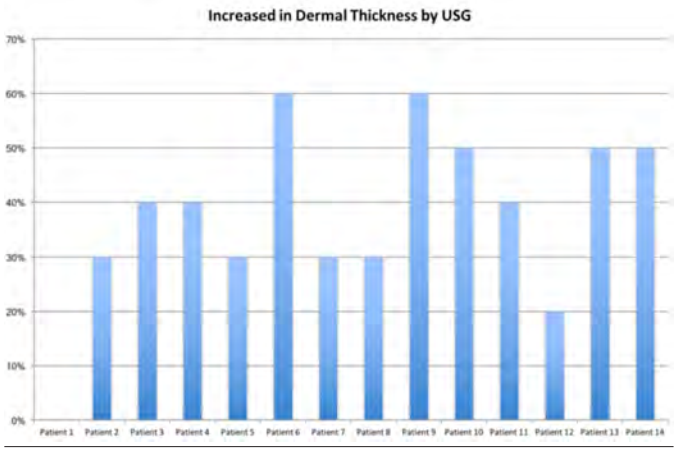
PATIENT	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Skin sagging	2	1	0	1	1	2	2	0	0	3	3	0	3	2
Striae	2	0	0	1	1	2	0	1	0	3	2	1	3	1
GLD	2	0	0	1	1	1	-1	1	0	0	3	1	2	3
GAS	3	1	0	1	1*	3	1	1	0	3	3*	3	3	2

LDG - Gynoid lipodystrophy. GAS - General appearance of the skin. (*) After having experienced pain, Patient 5 underwent only one application. Patient 11 also underwent only one application due to concerns with overcorrection after observing great improvement after the 1st application. Three patients reported intense improvement in skin sagging; Four reported moderate improvement; Three noticed little improvement; And four reported absence of improvement.

Table 3: Degree of improvement in the evaluator physician's opinion

PATIENT	1	2	3	4	5*	6	7	8	9	10	11*	12	13	14
Skin sagging	2	1	1	2	1	3	2	2	2	3	3	3	2	2
Striae	3	2	2	2	2	2	2	2	3	3	2	3	1	2
GLD	3	0	0	2	0	3	0	2	0	0	3	1	1	3
GAS	3	3	1	2	2	3	2	2	2	3	3	3	1	3

Intense improvement was observed in 4 patients, moderate improvement was observed in 7 patients (78% of patients), and little improvement was observed in 3 patients. LDG - Gynoid lipodystrophy. GAS - General appearance of the skin.



Graph 1: Ultrasonography measurement of the percentage of points that presented increase in the thickness greater than 10%: 11 patients had an increase in dermal thickness above 20% of the points. (*) In both patients who underwent only one application, the improvement of the score can be observed in the USG

RESULTS

Regarding the answers given in the questionnaires, the initial scores (baseline) of the patient and the applicator physician were equal (Table 1):

According to the patients' opinion, the improvement score 6 months after the second application (Table 2) indicates that 50% of the participants had moderate or intense improvement:

According to the evaluator physician's opinion, the improvement score 6 months after the second application (Table 3) suggests that 78% of the participants reported moderate and intense improvement.

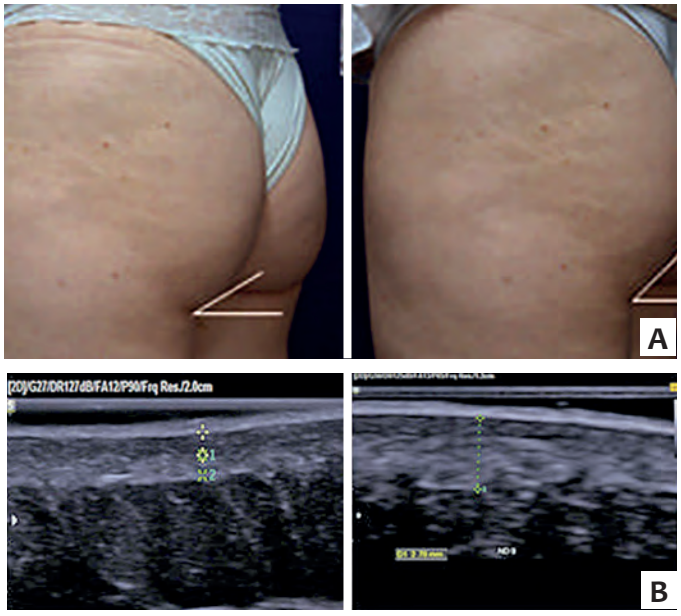
The evaluation of the ultrasonographic examination was expressed in percentage points (Graph 1). The response was considered good only for values that were above 10% of the baseline thickness, as this is the expected intraobserver variation, taking into account the extremely small dimensions of these measurements, despite the fact that the zoom feature has been used aimed at avoiding greater errors. The values presented correspond to the percentage of points that had the thickness increased.

In the photographic analysis, it was possible to observe an increase in the angle formed in the gluteal fold, while the ultrasound examination detected a significant increase of the dermal thickness in 11 patients (Figures 2 and 3)

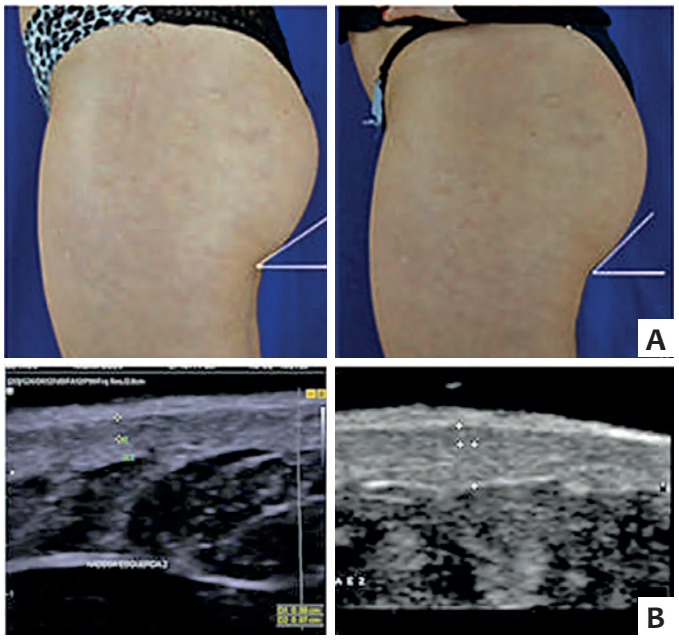
Shows adverse effects and hematoma after the first and second application (Table 4). None of the patients presented newly formed or late nodules.

Table 4: Adverse effects

PATIENT	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Pain	2	1	3	2	3	2	2	1	3	1	3	2	2	2
Hematoma	1	3	2	2	1	2	2	2	1	1	1	1	1	1
Edema	0	0	1	0	-	0	0	0	0	0	-	0	0	0



Figures 2: Patient 1 - An increase is observed in the angle formed by the gluteal fold **(A).** Same patient's ultrasound examination **(B),** with increased dermal thickness



Figures 3: Patient 10 - An increase is observed in the angle formed by a horizontal line **(A).** In the detail, ultrasonographic examination of the same patient with increased dermal thickness **(B).**

DISCUSSION

New and innovative treatments are being constantly developed, however few studies have been published on the treatment of sagging in the body's skin in general.

The changes that take place in the skin's mechanical properties during adult life include the progressive loss of elasticity and an increase in the time required for the skin to return to its original state after being pinched. This process begins after the age of 20, and leads to a significant, linearly steady reduction of the cutaneous thickness over the years. [5] Clinically, the skin seems thinner, drier and less elastic, beginning to wrinkle and fall. These changes in texture can occur associated to changes in color (arising as hypopigmentation or hyperpigmentation areas) and to the emergence of visible vessels in areas exposed to the sun, worsening as a result of the patients' life-style related habits, such as smoking, for instance. [6]

The thinning of the dermal thickness observed in chronological aging occurs due to biochemical and structural changes in the properties of the collagen and elastic fibers, and the ground substance, with a reduction in the synthesis of collagen and an increase in its degradation due to increased levels of collagenase. The elastic fibers decrease in number and diameter, and the amount of mucopolysaccharides in the ground substance decreases, especially that of hyaluronic acid, which negatively influences the skin's turgor, in addition to influencing the deposition, orientation and size of collagen fibers. [6] As a result, the dermis becomes thinner and the skin loses elasticity.

Moreover, the reduction of serum estrogen levels in women is also associated with the reduction of the dermal content of collagen, further increasing skin extensibility and reducing elasticity. These changes are more related to menopause than chronological aging, [6] which explains the worsening of sagging in the climacteric. Associated with chronological aging, body

skin sagging is aggravated by the presence of striae, which arise due to the rupture of collagen fibers and disorganization of elastic fibers. In addition to the disorganization of extracellular matrix fibers in the dermis, the thinning of the hypodermis caused by the loss of adipose tissue due to aging, weight loss and the practice of high-performance sports (with a reduction of the BMI) manifests in patients by the loose skin sensation. On palpation, the skin feels thin and lacking in consistency, lacking "filling". These changes are observed even in younger patients.

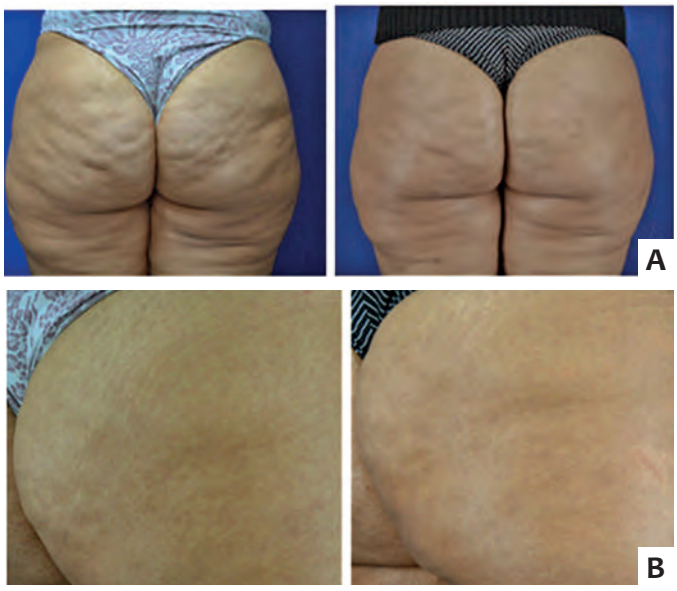
Poly-L-lactic acid is an injectable synthetic polymer of the alpha-hydroxy acid family. It is biocompatible and biodegradable, has very low cytotoxicity, [7] and has been used for many years in absorbable suture. Injections of PLLA into the deep dermis or superficial hypodermis induce local and progressive reaction, with subclinical inflammatory response soon after application, recruiting monocytes, macrophages and fibroblasts. The new collagen begins to form a month after the application and continues to increase during a period varying from 9 months to 1 year. In the 6th month, many PLLA particles become porous and surrounded by macrophages. It is then hydrolyzed into lactic acid monomers and eliminated, however the increased deposition of collagen produced by fibroblasts lingers, resulting in the increase of dermal thickness, [7,8] nevertheless without evidence of fibrosis. [6,7]

This fibroplasia determines the aesthetic outcomes and [5] the improvement of skin sagging. Due to the fact it is an stimulating agent, it promotes the production of collagen in the deep dermis, [3]which, in turn, will act by increasing the tissular volume progressively, [5,7] possibly leading to the recovery of the collagen network. Its mechanism of action has important implications on how the product should be applied in order to improve outcomes and avoid adverse effects. [9]

Given that PLLA is a biostimulating agent that depends on the host's reaction, its effects are not immediate, but will gradually and progressively be observed during the months following its application. [6] Results might not be evident for weeks after the application, and it is important to wait for the biological response to occur between application sessions aiming at avoiding overcorrection. [9] Regarding the face, the literature recommends 2 to 4 applications observing intervals of 30 to 60 days between them. [5,9]

It is important to note that the PLLA treatment's final outcome depends on the amount of product used, the age of the patient, the quality of the treated tissue and its ability to stimulate collagen. [5] Loss of cutaneous fat and poor skin quality can be treated successfully, however greater amount of product and number of applications will be required for a satisfactory final outcome. On the other side, younger patients who feel the first signs of cutaneous lipoatrophy, and report skin thinning, usually respond rapidly to the treatment. In this manner, a decision was made for 2 applications with intervals of 45 days between them, as well as for evaluations before (baseline) and 6 months after the second application.

According to the self-assessment, 85% of patients showed improvement in the general appearance of the skin while 71% noticed improvement in sagging. According to the evaluator physician, 100% of patients had some improvement in the general aspect and sagging of the skin, which were confirmed by the photographic evaluation. This fact demonstrates that the patient's perception is not objective and varies according to her or his expectation regarding the treatment.



Figures 4: Patient 14 - An improvement is observed in the general appearance of the skin when comparing the baseline with the after-treatment experimental timepoint (six months after the second application) **(A).** In the detail **(B),** it is possible to observe improvement of striae

It is important to highlight that some patients had little or no improvement in sagging, which could be related to the number of applications. As the response is variable and individual, it may be the case that some patients needed a greater stimulus to achieve better outcomes, since the improvement of striae has been observed in almost all patients, a finding that should be considered in future studies.

Regarding GLD (cellulitis), little improvement was observed in general. Nevertheless, one of the patients who had an edematous GLD picture, experienced an important improvement (Figure 4), probably linked to the improvement of skin sagging and striae (Figure 4, detail). Also, a patient who had a hard or fibrous GLD picture, experienced a slight worsening, perhaps linked to the increase in local fibroplasia, evidenced by the improvement in the striae (Figure 4, detail). Therefore, it can not be stated that PLLA is an appropriate treatment for GLD, for it can improve its appearance due to the improvement in skin sagging that is commonly associated with GLD cases with a higher degree of edema, however it can even cause aggravation in the case of GLD with a higher degree of fibrosis.

Reported adverse reactions related to the use of PLLA (such as ecchymoses, hematomas, edema, papules, nodules and granulomas) mainly arise at the sites of product injection. [10,11]

The response to treatment occurred in varying degrees

and were not proportional to the initial degree of severity. For instance, even bearing a more severe degree of skin sagging, Patient 6 had a better response than Patient 2, who had a mild degree of sagging skin, reinforcing the hypothesis that the clinical response depends on the host and varies from patient to patient.

Regarding the adverse effects observed in the present study, pain was described by all patients, ranging from mild to intense, causing one of the patients to drop out before the second application. As for hematomas, an interesting fact was the improvement in their formation in the second application in 100% of the patients, which may correspond to an improvement of vascular fragility in the treated site. There were no cases of early formation of nodules or late granulomas.

CONCLUSION

The application PLLA for improving facial skin sagging is already well known, however there are few reports on its use in other body sites.[12] In the present study, the authors described a technique for treating skin sagging in the gluteal region with applications in the deep dermis-superficial hypodermis with considerably promising results. These findings should be confirmed by more encompassing studies aimed at better evaluating both the beneficial and adverse effects and ideal number of applications, ideal doses and duration of the results of PLLA injections.

Aknowledgements: We would like to thank Dr. Ayrton Pastore for performing the ultrasound examinations.

REFERENCES

1. Langlois JH, Kalakanis L, Rubenstein AJ, Larson A, Hallam M, Smoot M. Maxims or myths of beauty? A meta-analytic and theoretical review. Psychol Bull. 2000; 126(3):390-423.
2. Beer K. Dermal fillers and combinations of fillers for facial rejuvenation. Dermatol Clin. 2009; 27(4):427-32.
3. Lacombe V. Sculptra: a stimulatory filler. Facial Plast Surg. 2009 May;25(2):95-9.
4. Tan CY, Statham B, Marks R, Payne PA. Skin thickness measurement by pulsed ultrasound: its reproducibility, validarion and variability. Br J Dermatol. 1982;106(6):657-667.
5. Fitzgerald R, Vleggaar D. Facial volume restoration of the aging face with poly-l-lactic acid. Dermatol Ther. 2011;24(1):2-27.
6. Varani J, Dame MK, Rittie L, Fligiel SE, Kang S, Fisher GJ, Voorhees JJ. Decreased collagen production in chronologically aged skin: roles of age--dependent alteration in fibroblast function and defective mechanical stimulation. Am J Pathol. 2006;168(6):1861-1868.
7. Lam SM, Azizzadeh B, Graivier M. Injectable poly-L-lactic acid (Sculptra): technical considerations in soft-tissue contouring. Plast Reconstr Surg. 2006;118(3 Suppl):55S-63S.
8. Yang J, Liu F, Tu S, Chen Y, Luo X, Lu Z, et al. Haemo-and cytocompatibility of bioresorbable homo- and copolymers prepared from 1,3-trimethylene carbonate, lactides, and epsilon-caprolactone. J Biomed Mater Res A. 2010;94(2):396-407.
9. Bauer U, Graivier MH. Optimizing injectable poly-L-lactic acid administration for soft tissue augmentation: the rationale for three treatment sessions. Can J Plast Surg. 2011;19(3):e22-7.
10. Machado Filho CDS, Santos TC, Rodrigues APLJR, Cunha MG. Ácido Poli-L-Láctico: um agente bioestimulador. Surg Cosmet Dermatol. 2013;5(4):345-50.
11. Rendon MI. Long-term aesthetic outcomes with injectable poly-l-lactic acid: observations and practical recommendations based on clinical experience over 5 years. J Cosmet Dermatol. 2012;11(2):93-100.
12. Coimbra DD, Amorim AGF. Ácido Poli-L-láctico na região medial dos braços. Surg Cosmet Dermatol. 2012;4(2):182-5.

Original Articles

Supra-Auricular Lifting With Fillers: New Technique

Lifting supra-auricular com uso de preenchedores: nova técnica

Authors:
Daniel Dal'Asta Coimbra[1]
Betina Stefanello de Oliveira[2]

[1] Cosmiatry Instructor, Instituto de Dermatologia Rubem David Azulay, Santa Casa de Misericórdia do Rio de Janeiro – Rio de Janeiro (RJ), Brazil.

[2] Instructor, Instituto de Dermatologia Rubem David Azulay, Santa Casa de Misericórdia do Rio de Janeiro.

Correspondence:
Daniel Dal'Asta Coimbra
R. Casuarina 705 - Humaitá
Cep 22261-160 - Rio de Janeiro (RJ), Brazil
e-mail: drcoimbra@gmail.com

This study was performed at Dr. Daniel Dal'Asta Coimbra's private practice, Rio de Janeiro (RJ), Brazil.

Financial support: None

Conflict of interests: Dr. Daniel Dal'Asta Coimbra works as a speaker for Allergan in domestic and international events.

DOI: http://dx.doi.org/10.5935/scd1984-8773.20168405

ABSTRACT

Introduction: The evolution of filling techniques allowed a three-dimensional approach to the face: nowadays volumetric restoration is more important than grooves.
Objective: Description of an unpublished technique of facial volumization through the injection of filler in the supra-auricular region, with a detailed review of the regional anatomy.
Methods: A retrospective case-control study was conducted in patients presenting skin mobility in the temporo-parietal region. The injection of Hyaluronic Acid for volumetric replacement was done using cannulae, bolus and fan techniques in the supra-auricular region, limited antero-superiorly by the area of hair implantation and inferiorly by the tragus. The patients were evaluated clinically, photographed and had their data analyzed by statistics.
Results: 152 women and 13 men aged 24 to 84 years were treated between July and September 2016. The volume of Hyaluronic Acid used in the patients ranged from 0.6 to 2.6 ml. In 8 cases local edema was observed due to hematoma during application, that was controlled by digital compression. Significant improvement of the facial contour was observed.
Conclusion: The use of fillers in the supra-auricular region allows a three-dimensional approach and promotes static and dynamic rejuvenation of the entire face.
Keywords: dermal fillers, hyaluronic acid; rejuvenation

RESUMO

Introdução: *A evolução das técnicas de preenchimento possibilitou uma abordagem tridimensional da face: deixando-se de valorizar sulcos e optando-se pela restauração volumétrica.*
Objetivo: *Descrição de técnica inédita de volumização facial por injeção de preenchedor na região supra-auricular, com revisão detalhada da anatomia regional.*
Métodos: *Foi conduzido estudo retrospectivo de análise de casos, em pacientes apresentando mobilidade da pele na região têmporo-parietal. A injeção de ácido hialurônico para reposição volumétrica foi feita com cânulas, utilizando-se técnicas em bólus e em leque, na região supra-auricular, limitada ântero-superiormente pela área de implantação do cabelo e inferiormente pelo trágus. Os pacientes foram avaliados clínica e fotograficamente e tiveram seus dados analisados por estatística.*
Resultados: *Foram tratados 152 mulheres e 13 homens de 24 a 84 anos, entre julho e setembro de 2016. O volume de ácido hialurônico utilizado nos pacientes variou de 0,6 a 2,6ml. Em oito casos observou-se abaulamento local devido a hematoma durante a aplicação, controlado por compressão digital. Constatou-se melhora significativa do contorno facial.*
Conclusão: *O uso de preenchedor na região supra-auricular permite a abordagem tridimensional e promove o rejuvenescimento estático e dinâmico de toda a face.*
Palavras-chave: *preenchedores dérmicos; ácido hialurônico; rejuvenescimento*

INTRODUCTION

Beauty is a characteristic – or set of characteristics – that are pleasant to the eye and capable of captivating the observer. The concept of beauty varies according to the culture and personal opinion. Nevertheless, proportionate, symmetrical, well-marked faces with rounded contours and high cheeks appear to be more attractive. [1]

The rhytidectomy has always been considered the gold standard in the treatment of facial sagging and in the promotion of facial rejuvenation since its emergence at the beginning of the 20th century. [2] In 1920, Bettman improved the technique, describing the pre-auricular and temporal access that led to a more unnoticeable scar, similar to those obtained nowadays. Over time, the development of techniques has brought increasingly natural results, however, as a consequence of the risks, and the definitive and not always satisfactory outcomes, the surgical approach is limited to treating the consequences of aging in the vast majority of cases. [3,4]

During the last decades, there has been a better understanding of the facial aging process, specially regarding the knowledge about fat compartments [5,6] and the measurement of facial bone remodeling. [7] Concomitantly, new filling substances have been developed aimed at restoring the volume, while botulinum toxin began to be employed for the reeducation of muscles. As a result, a new era was established in the facial rejuvenation treatment, where non surgical liftings have been standing out, yielding outcomes that are both surprising and natural. [1,8,4,9]

The search for filling substances that are safe, long lasting, and whose effects are predictable and natural, has led to hyaluronic acid (HA), which is a polysaccharide (glycosaminoglycan compounded by alternating and repetitive units of D-glucuronic acid and N-acetyl-D-glucosamine) with hydrophilic properties, which causes an increase in the injected tissue. [10,11] The initial filling effect is directly related to the volume of filler injected; however, studies have demonstrated that there is an indirect effect when it is injected into the dermis due to the activation of fibroblasts. The need for a filler aimed at deep applications in the face (fat compartments and/or juxta-periosteum) led to the development of volume restoration-specific HA, [12] which have higher concentrations of HA and crosslinking than the HA fillers used in the dermis or superficial subcutaneous. This brought increased durability and viscosity to the gel, generating an increase in its lifting capacity against the skin's pressure. [11] The duration of the HA based fillers and of those aimed at restoring volume in general ranges from 12 to 24 months. [10]

The search for natural results has led to the development of different facial rejuvenation treatment techniques using fillers (e.g. MD Codes®) in order to avoid distortions, exaggerations or overcorrections that are very often observed when the wrong techniques are employed. [4,13] Nowadays, in addition to the three-dimensional static improvement of the face, the maintenance or improvement of facial motion stand out in facial rejuvenation treatments with fillers, with facial expressions being key in the choice of the application sites. In this way, applications cease to be static and become dynamic three-dimensional procedures based on the facial mimicry, where the filling material can hinder muscle contraction by mechanical block or facilitate the muscle movement via a deep support effect, reducing the force needed for the muscle to exert contraction. [13,14]

ANATOMY

The ear is disposed over the temporal bone. The temporal region is formed by the temporal bone, which articulates with the occipital, parietal, zygomatic, sphenoid and mandible bones.

The temporal region's tissue layers are: skin, subcutaneous fat, superficial temporal fascia (STF), deep temporal fascia (DTF) and temporal muscle. The STF is the continuation of the superficial muscular aponeurotic system (SMAS) of the face and the galea aponeurotic system of the scalp. This multilaminated fascial layer (also called temporoparietal fascia) is loosely adhered to the subcutaneous fat and is closely associated with the frontal branch of the facial nerve and the superficial temporal vessels. The loose areolar tissue, denominated subaponeurotic plane, separates the STF from the DTF and is the dissection plane that is commonly used in surgical approaches of the temporal region.

The DTF is a dense conjunctive tissue layer adhered to the superior temporal line that covers the temporal muscle. A few centimeters above the zygomatic arch, the DTF splits into superficial and deep layers. Between these two layers is the superficial temporal fat pad, which is irrigated by the middle temporal artery. In the direction of the DTF's deep layer lies the deep temporal fat pad, corresponding to the superior extension of the buccal adipose body. This extension runs superiorly and deeply regarding the zygomatic arch, to lay between the DTF's deep layer and the temporal muscle. [15,16]

The superficial temporal artery and the temporal branch of the facial nerve are two noble anatomical structures that should be well known for the approach of this region with the use of fillers.

The superficial temporal artery is the terminal branch of the external carotid artery. It originates within the parotid gland, rising roughly 10mm anteriorly to the tragus, to cross the zygomatic arch. The superficial temporal artery gives rise to numerous terminal branches, including the facial transverse, the medial temporal, the parietal and the frontal branches (Figure 1). [16,17]

The temporal branch of the facial nerve emerges from the superior margin of the parotid gland 1.7 cm anteriorly to the tragus, and crosses the zygomatic arch to supply the superior auricular and the anterior auricular muscles, the frontal part of the occipitofrontalis muscle, and, most importantly, the upper orbicularis muscle of the eye. The temporal nerve, which runs close to the deep face of the STF, is located superficially when it crosses the zygomatic arch and is loosely adhered to the adjacent facial layers. The vulnerability of the temporal branch is located at the level of the middle third of the zygomatic arch. Its path continues towards the frontotemporal region, always close to the deep face of the SMAS, up until penetrating the frontal muscle in its deep face. Its lesion causes palpebral ptosis and permanent difficulty to raise the eyebrow. [18] (Figure 1)

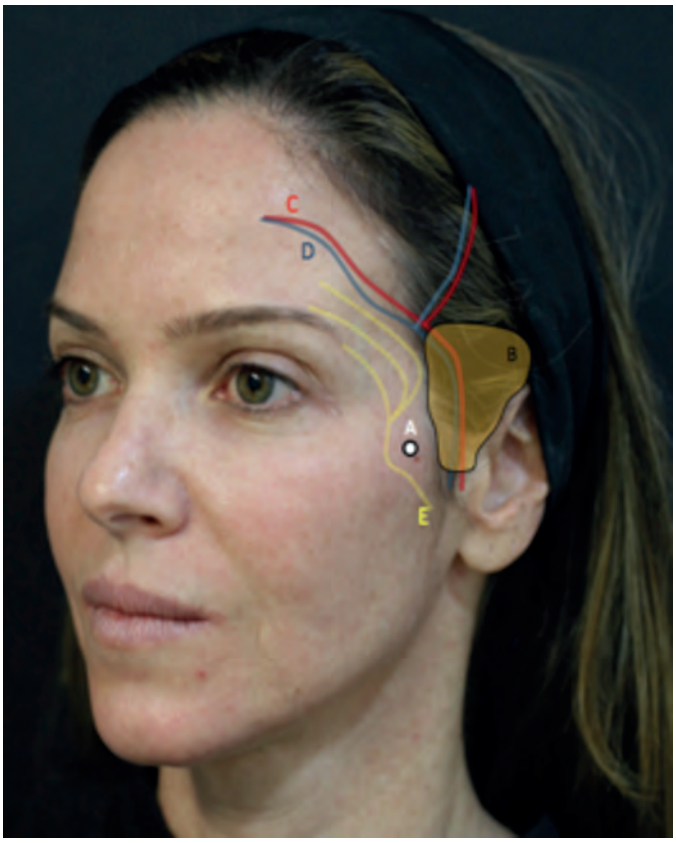


Figure 1: A. Entry location of the cannula. **B.** Supra auricular region. **C.** Temporal artery. **D.** Temporal vein. **E.** Temporal nerve branch of the facial nerve

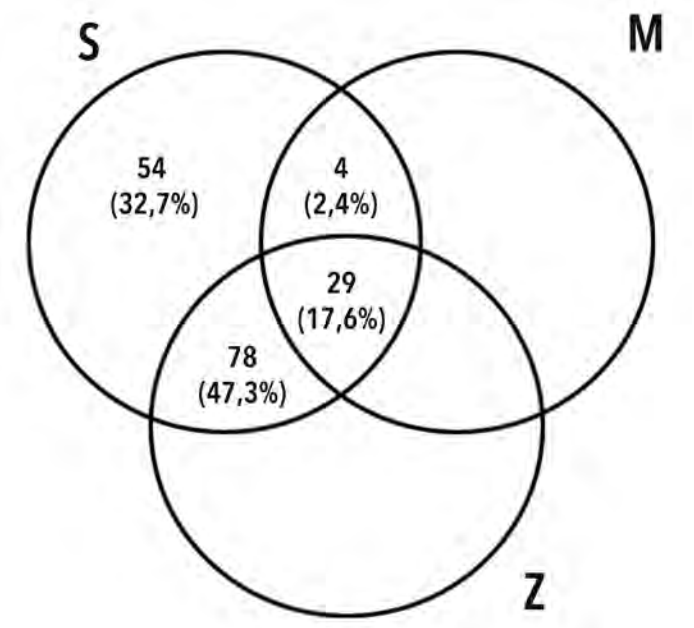


Figure 2: Venn diagram for the distribution of the number of patients and percentage according to the facial area of application in the supra auricular lifting technique

OBJECTIVE

To describe an unprecedented technique of non-surgical facelift based on the application of volumetric replacement HA cutaneous filler in the supra auricular region, promoting beneficial changes in the motion of the facial mimicry and rejuvenating the entire face.

METHODS

A retrospective case-control study was performed for the introduction of an unpublished technique of supra-auricular cutaneous filling aimed at performing a pan-facial facelift, carried out at the private practice of one of the authors, in the city of Rio de Janeiro (RJ), Brazil, from July to September 2016.

A total of 165 patients who sought care with indication for treatment of improvement of the facial contour received cutaneous filler in the supra-auricular region, having been distributed according to the Venn diagram in Figure 2.

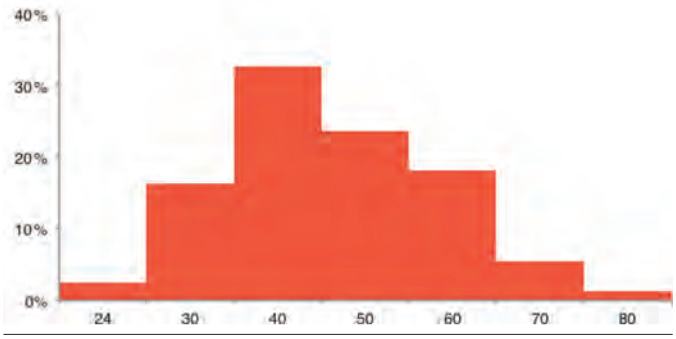
Of these, 152 patients were women, and 13 were men. Their ages ranged from 24 to 84 years (mean = 51 years, median = 49 years) (Graph 1).

For the selection of the patients, a test was carried out by stretching the skin from the temple towards the parietal region using the index finger's pulp. The patients who experienced motion in this tissue were included in the study for the filling of this region. There was no restriction regarding gender, age or phototype. Thirty-three patients (20%) had already undergone rhytidectomy. The study complied with the ethical directives of the 2000 Helsinki Declaration.

THE TECHNIQUE

With the patient lying down at 60 degrees, asepsis was carried out with 2% alcoholic chlorhexidine solution on the entire face and the temporal region covered by the hair. Next, an orifice was performed so as to allow the cannula to enter the temporal region, over the zygomatic bone. A 24G or 25G cannula was inserted through the orifice and slid through the subcutaneous up until it reached the supra-auricular region, where a bolus of 0.1 to 0.2ml of volumetric replacement HA was injected with lidocaine into the subcutaneous tissue. Digital pressure was then exerted on this bolus in order that the dispersion of the product produced anesthetic effect in the region. This was followed by the application of a new volume of the substance, using the fan technique, applying little force and with slow, gentle movements in the entire supra auricular area – with the area of hair implantation being the antero-superior limit, and the tragus, the inferior limit (Figure 1). A greater amount of the product was deposited in the region closer to the ear, in a more depressed area easily demarcated by digital palpation.

Due to the lifting effect produced by this lateral application, there was flattening and decreased anterior projection of the zygomatic region in some patients. In these patients, after the supra-auricular application, 0.33 ml of the product, on average, were injected on each side at the point of greatest anterior



Graph 1: Patients' age distribution histogram. Practice X - Rio de Janeiro (RJ), Brazil (n = 165), July to September 2016

Source: Database containing the records collected during the Authors' medical consultations.
Mean age = 51 years, median age = 49 years

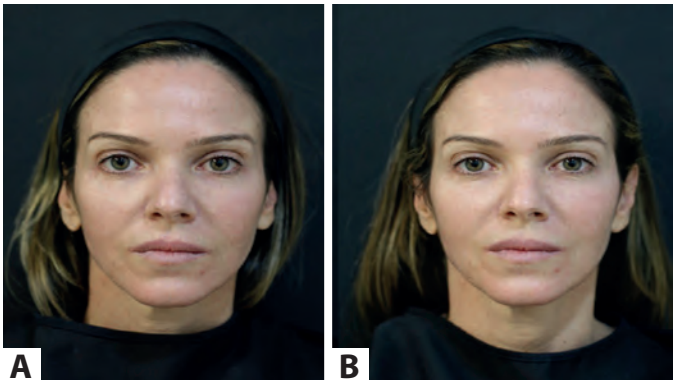


Figure 3: Forty-four year-old patient **(A)** pre-treatment and **(B)** after undergoing only supra-auricular filling with 0.8 ml of HA on the left hand side

projection of the Zygomatic bone, using the same orifice for the introduction of the cannula, but this time moving it towards the anterior region of the face.

RESULTS

A total of 165 patients were treated (152 women = 92%, 13 men = 8%). Their ages ranged from 24 to 84 years (mean = 51 years). Of these patients, 33 (20%) had already undergone facelift (Table 1). A total of 57 (34.5%) patients were seeking care for the first time, while 108 (65.5%) had previously attended consultations.

The total amount of product injected in the supra auricular region ranged from 0.6 ml to 2.6 ml, with an average of 1.68 ml (total injected volume). There was no statistical correlation between age and amount of product applied. In 107 patients (64.9%), it was necessary to complement the product in the zygomatic region with a mean volume of 0.33 ml per side.

After the application, a significant improvement of the entire facial contour was observed, related to the lifting effect caused by the product deposited in the treated region. In addition, there was improvement and softening of the facial expressions, generating static and dynamic rejuvenation in the entire face, which was very evident when a treated hemiface is compared with the contralateral hemiface before the treatment (Figure 3).

Despite the fact that block or topical anesthetic were not used, patients reported only mild pain, with a few patients who had previously undergone surgical facelift at the site regarding it as moderate. Edema in the region was reported as imperceptible and in 8 cases there was presence of local bulging due to hematoma during the application, which were immediately controlled by digital compression, not having externalized in the skin on the days following the procedure. All patients realized improvement in the photographic evaluation performed immediately after the procedure, having been instructed to return to their normal activities. No paradoxical depression of the temple was observed due to a possible excess of product in the supra-auricular region.

DISCUSSION

The search for naturalness in facial rejuvenation, associated with a better understanding of the aging process and the development of new techniques and volumetric replacement HA based fillers, have led to increasingly extraordinary results, often compared to those obtained only through surgical facelifts.

The three-dimensional approach of the face with the use of fillers is a safe method that yields natural and long lasting outcomes when adequately used. A thorough knowledge of each region's anatomy and changes linked to the aging process is of paramount importance so that the treatment can early address the causes – such as volume replacement in the fat pads or in juxta-osseous locations – in order to avoid, attenuate or postpone consequences arising on the surface, such as lines and furrows in the skin. Currently, in addition to this static three-dimensional improvement of the face, the maintenance or improvement of the facial motion has stood out in rejuvenation treatments with fillers, where facial expressions are key in the choice of the application sites.

After six years using volumetric replacement AH fillers with a three-dimensional approach of the entire face, a total of 7,194 ml of Juvederm Voluma® (Allergan Inc., Irvine, USA) have been applied in the upper, middle and lower thirds of patients' faces, in procedures carried out at one of the present study's authors' private practice, located in the city of Rio de Janeiro (RJ), Brazil. Initially the applications were mainly focused on the improvement of the shadow areas, concavities and projection of the lower contour of the face, in a static way. The practice with the use of fillers, the improvement of the technique, as well as the personal experience of the injector physician in the treatment of patients with facial paralysis using fillers resulted in the

Table 1: Profile of patients treated with facial restorative acid filler in the supra-auricular region. Practice X - Rio de Janeiro (RJ), Brazil - July to September, 2016

Characteristics	Up to 40 years old (n1 = 85)	50 years and over (n2 = 80)	Total (n1+n2 = 165)
Number of men	10 (11.8%)	3 (3.8%)	13 (7.9%)
Number of women	75 (88.2%)	77 (96.2%)	152 (92.1%)
1st consultation (= yes)	30 (35.3%)	27 (33,8%)	57 (34.5%)
Returning patient (= yes)	56 (65.9%)	53 (66,3%)	109 (65.5%)
Underwent supra-auricular treatment? (= yes)	85 (100%)	80 (100%)	165 (100%)
Supra-auricular (r + l) (total amount in ml)	144	133	277
Supra-auricular (r + l) (average amount in ml)	1.69	1.66	1.68
Minimum amount (in ml)	0.60	0.30	-
Maximum amount (in ml)	2	2.60	-
Underwent zygomatic treatment in addition to supra-auricular treatment? (= yes)	60 (70.6%)	47 (58.8%)	107 (64.8%)
Zygomatic (r + l) (total amount in ml)	35.10	34	69.10
Zygomatic (r + l) (average amount in ml)	0.59	0.72	0.65
Underwent malar treatment in addition to supra-auricular treatment? (= yes)	18 (21.2%)	15 (18.8%)	33 (20%)
Malar (r + l) (total amount in ml)	15.10	14.60	29.70
Malar (r + l) (average amount in ml)	0.84	0.97	0.90
Underwent malar, zygomatic and supra-auricular treatment? (= yes)	14 (16.5%)	15 (18.8%)	29 (17.6%)
Malar, zygomatic and supra-auricular (r + l) (total amount in ml)	42	49.70	91.70
Malar, zygomatic and supra-auricular (r + l) (average amount in ml)	3	3.31	3.16
Surgical lifting (= yes)	2 (2.4%)	31 (38.8%)	33 (20%)
Supra-auricular (r + l) (average amount in ml)	1.30	1.64	1.62
Zygomatic (r + l) (average amount in ml)	0.80	0.70	0.71
Surgical lifting (= no)	83 (97.6%)	49 (61.3%)	132 (80%)
Supra-auricular (r + l) (average amount in ml)	1.70	1.68	1.69
Zygomatic (r + l) (average amount in ml)	0.40	0.25	0.35

Source: Database containing the records collected during the Authors' medical consultations. Age (years): mean = 51, median = 49, min = 24, max = 84.

Obs: Observed complications: (i) hematoma (4.8% of cases), pain and/or local pressure (7.2% of cases).

development of a dynamic three-dimensional approach. More recently, this approach led to the description of the treatment of the body site described in the present study, which is unprecedented in the world literature, thus being now considered by the authors as the first and most important facial region for volumetric replacement.

Based on the palpation of a depressed area in the temporal region covered by hairs and the lifting effect caused by the digital traction of the skin from that area towards the parietal region, it was possible to verify that the patients could benefit from the volumetric replacement with HA at that body site. Using the technique described above, the authors of the present article performed the application of the product in the site, with an immediate lifting effect occurring in the entire face, in addition to a decrease in the ptosis of the malar and nasolabial fats above the nasolabial folds, an increase of the cutaneous tension in the lower eyelid due to lateral traction, the elevation of labial commissures, and the improvement of the mandibular contour. In addition to these static effects and for the surprise of the authors, there was an elevation in the brow's tail, given that during the smile, a greater amplitude of the mouth was generated (greater exposure of the lateral teeth) and an increase in the ocular opening,

Figure 4: Forty-four year-old patient. **(A)** Pre and **(B)** post-treatment dynamics. The filling treatment has been performed with 1.2 ml of HA only in the left supra-auricular region. **(C)** Pre and **(D)** post-treatment dynamic profiles showing greater ocular opening, greater smile amplitude (smiles with naturalness, showing the teeth more intensely), and improvement of facial contour

probably due to the decrease in the need for using the upper lip elevator muscle, in addition to a slight decrease in the hypertrophic platysmal bundles, promoting a non-surgical Dynamic Three-dimensional Lifting®. (Figures 4 and 5)

As already mentioned, the authors did not find any report of similar technique in the literature, with the three-dimensional approaches linked to filler injection based rejuvenation that have already been described usually beginning in the zygomatic and malar regions. [4,12] The approach proposed in the present study is unpublished and differs from those that have been studied in that the middle third's volumization begins in the supra auricular area covered by the hair, which is an almost imperceptible, safe area when the correct technique is employed – and practically painless when HA is used with lidocaine in its formulation. The possibility of immediately returning to daily activities provided a high degree of patient satisfaction. In addition, the facelift effect generated by the filler in this new area led to a decrease in the amount of AH needed in the zygomatic and malar regions, which generated less anterior projection of the face and extremely natural outcomes both statically and during facial mimicry.

Due to the lateral traction caused by the supra-auricular filling, 64% of patients presented a slight flattening and decrease of the anterior projection of the zygomatic region. In these patients, after the supra-auricular application, small volumes (on average 0.33 ml) of AH were injected into the zygomatic region on each side on the same occasion. It is important to note that the aging process is dynamic and occurs throughout the face, and other regions can be treated with fillers on the same occasion or in new sessions, depending on the needs of each face. After treatment of these regions, some patients were also treated in the malar region and in the upper and lower thirds of the face, however in the present study the authors considered only the influence of volume replacement in the supra auricular region in the middle facial third. (Table 1) Despite the fact that the authors use a considerable amount of the product (on average 0.84 ml on each side), they have not observed paradoxical depression of the temples, given that the treated area is covered by hair.

Of the patients treated, 57 (34.5%) had sought care for the first time, while 108 (65.5%) were patients who had already been previously seen. Comparing the two groups, the amount of product injected into the supra auricular region was lower in the new patients (1.57 as compared to 1.74 ml), nonetheless the concomitant treatment of the zygomatic and malar regions was significantly more frequent in the new patients group (84.2% as compared to 54.6% in patients also treated in the zygomatic region, and 40.4% as compared to 5.6% in those who were treated both in the zygomatic and malar regions). It was probably in the group of patients who had previously been seen and undergone treatment with fillers that there was less need to treat the zygomatic and malar regions, since they had already been treated in these regions before this new area has been described. These data demonstrate the importance of evaluating and treating the entire middle third of the face, especially in patients who have not undergone facial volumization, with the ideal treatment sequence proposed by the authors of the present article is to start

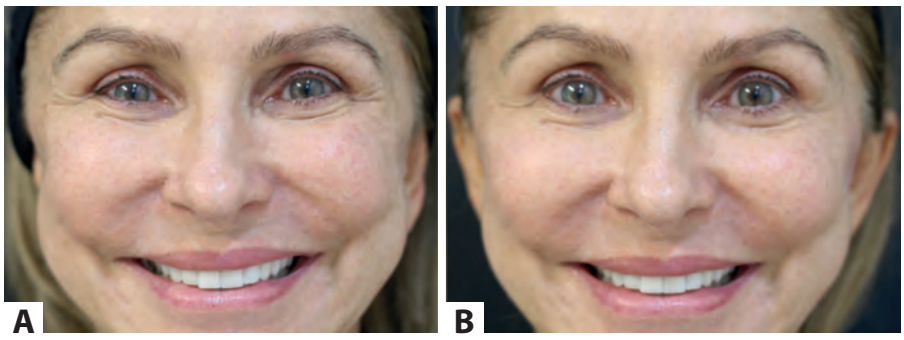


Figure 5: Fifty-six year-old patient. **(A)** Pre and **(B)** post-treatment only in the supra auricular region with 1 ml in each hemiface. It is possible to observe an increase of the ocular opening during the smile

with the supra auricular region, move on to the zygomatic, and finally treat the malar area.

Due to the important vascular-nervous structures present in the temporal region, the authors of the present study believe it is essential to use cannulas for the application of the product.[19] The choice to enter via an orifice over the zygomatic bone entails that the cannula will have to travel a path perpendicular to the large vessels (temporal artery and vein), which would minimize the risk of intravascular injection. The movements should be slow and gentle, and aspirations can be made if there is any doubt as to the positioning of the cannula in relation to the vessels.[20] The authors of the present study chose 24 and 25G cannulas based on their personal injecting experience, however cannulas of greater caliber can be used. Cannulas 27 and 30G should be avoided due to the increased risk of vascular accidents.[21,22]

The predominance of the female gender in the sample can be explained by the fact that the search for aesthetic procedures is still more frequent among women. The age ranged from 24 to 84 years, indicating the versatility of the filling procedure, which can be performed as long as the clinical examination identifies the need for it. In the experience of the author of the present study, young faces and still with little mobility of the skin at the site required smaller amounts of the product, however in the study's sample there was no statistical correlation between the age and the amount of product applied. The complex TMJ (temporomandibular joint) is located in the temporal region, and due to its almost constant motion and contraction, it is an area that undergoes intense bone remodeling and fat resorption, which justifies the treatment of this region even in young patients.

Of the study patients, 20% had already undergone a surgical facelift. In general and despite the cutaneous mobility present at the clinical examination, there was greater resistance to the passage of the cannula in the subcutaneous of these patients. In the studied sample, patients who had previously undergone surgical facelifts required treatment in the zygomatic region with significantly greater amounts when compared to those who had not undergone surgery (0.71ml x 0.35ml). Seven (87.5%) of the 8 patients who presented hematoma during the procedure – probably due to lesion to the temporal vein – had undergone surgical facelift at the site.

The choice for volumetric replacement AH (Juvederm Voluma® Allergan Inc., Irvine, USA) was based on the fat that the treated region is an area with great osteoarticular mobility, demanding a malleable product, however with a great capacity for lifting and deep tissue support. Further studies with hyaluronic acids from diverse brands should be carried out aimed at reproducing the results obtained in the present study.

Finally, due to the fact that the technique introduced by the present article is a recent and unprecedented, it is not yet possible to estimate the duration of the product's permanence in this region. Thus, further studies are needed to evaluate the long run results of supra auricular filling.

CONCLUSION

The authors of the present study have described a new technique for the three-dimensional rejuvenation of the face using fillers, in which volumetric replacement AH applied in the supra-auricular region promotes a non-surgical pan-facial lifting effect, with static and dynamic facial improvement. This new region is part of what the authors of the present study have termed *Dynamic Three-dimensional Lifting*® with the use of fillers, where the volumizing approach is based on facial mimicry. This description may serve as a platform for further studies related to the better understanding of the effect of fillers in the process of static and dynamic aging.

ACKNOWLEDGMENTS

The Authors of the present article would like to particularly thank the biostatistician and physician Dr. Luiz Felipe Pinto for contributing in the review of data and statistical analysis, and Natalia Caballero Uribe for the illustrations. ●

REFERENCES

1. Coimbra DD, Uribe NC, Oliveira BS. "Quadralização facial" no processo do envelhecimento. Surg Cosmet Dermatol. 2014;6(1):65-71.
2. Neligan PC. Plastic surgery: 6 volume. 3rd ed. St. Louis, MO: Elsevier Saunders; 2012.
3. Kim YB. The History and Future of Plastic and Reconstructive Surgery. Arch Plast Surg. 2015;42(5):515-6.
4. Maio M. The minimal approach: an innovation in facial cosmetic procedures. Aesthetic Plast Surg. 2004;28(5):295-300.
5. Gierloff M, Stöhring C, Buder T, Gassling V, Açil Y, Wiltfang J. Aging changes of the midfacial fat compartments: a computed tomographic study. Plast Reconstr Surg. 2012 129(1): 263-273.
6. Pessa JE, Rohrich RJ. Discussion: Aging changes of the midfacial fat compartments: a computed tomographic study. Plast Reconstr Surg. 2011;129(1):274-5.
7. Mendelson B, Wong CH. Changes in the facial skeleton with aging: implications and clinical applications in facial rejuvenation age-rela- ted changes of the orbit and midcheek and the implications for facial rejuvenation. Aesthet Plast Surg. 2012;36(4):753–60.
8. Coimbra DD, Oliveira BS, Uribe NC. Preenchimento nasal com novo ácido hialurônico: série de 280 casos. Surg Cosmet Dermatol 2015;7(4):320-6.
9. Carruthers J, Carruthers A. Técnicas de Preenchimento. New York: Elsevier; 2005.
10. Carruthers J, Cohen SR, Joseph JH, Narins RS, Rubin M. The science and art of dermal fillers for soft-tissue augmentation. J Drugs Dermatol. 2009;8(4):335-50.
11. Carruthers J, Carruthers A, Tezel A, Kraemer J, Craik L. Volumizing with a 20 mg/ml smooth, highly cohesive, viscous hyaluronic acid filler and its role in facial rejuvenation therapy. Dermatol Surg, 2010;36 Suppl 3: 1886-1892.
12. Raspaldo H. Volumizing effect of a new hyaluronic acid sub-dermal facial filler: a retrospective analysis based on 102 cases. J Cosmet Laser Ther. 2008;10(3):134-42.
13. Cotofana S, Schenck TL, Trevidic P, Sykes J, Massry GG, Liew S, Graivier M, Dayan S, de Maio M, Fitzgerald R, Andrews JT, Remington BK. Midface: Clinical Anatomy and Regional Approaches with Injectable Fillers. Plast Reconstr Surg. 2015;136(5 Suppl):219S-234S.
14. Sapijaszko MJ. Dermal fillers: Ever expanding options for esthetic use. Skin Therapy;12(8):4-7.
15. Breithaupt AD, Jones DH, Braz A, Narins R, Weinkle S. Anatomical Basis for Safe and Effective Volumization of the Temple. Dermatol Surg. 2015;41 Suppl 1:S278-83.
16. Salasche S, Bernstein G, Senkarik M. Surgical anatomy of the skin. New York: Appleton & Lange; 1988. 200-15.
17. Tamura BM. Anatomia da face aplicada aos preenchedores e à toxina botulínica – Parte II. Surg Cosmet Dermatol. 2010;2(3):205-14.
18. Silva MLA; Aboudib JH; Castro CC. Anatomia aplicada do ramo temporal do nervo facial: estudo do risco potencial de lesão durante a cirurgia do rejuvenescimento facial. Rev. Bras. Cir. Plást. 2010;25(4):604-613.
19. Vartanian AJ, Frankel AS, Rubin MG. Injected hyaluronidase reduces restylane-mediated cutaneous augmentation. Arch Facial Plast Surg. 2005;7(4):231-7.
20. Vliana GAP, Osaki MH, Cariello AJ, Damasceno RW. Tratamento dos sulcos palpebromalar e nasojugal com ácido hialurônico. Arq Bras Oftalmol. 2011;74(1):44-7.
21. Bellman B. Complication following suspected intra-arterial injection of Restylane. Aesthet Surg J. 2006;26(3):304-5.
22. 22. Lowe NJ. Arterial embolization caused by injection of hyaluronic acid (Restylane). Br J Dermatol. 2003;148(2):379; author reply 379-80.

Original Articles

Comparative and Randomized Study of Rich-Platelet Plasma in Male Androgenetic Alopecia

Estudo comparativo e randomizado do Plasma Rico em Plaquetas na Alopecia Androgenética Masculina

Authors:
Camila Carneiro Marques[1]
Denise Steiner[2]
Gabriela Momente Miquelin[1]
Mariana Morais Tavares Colferai[1]
Eduardo Figueiredo Gatti[1]

[1] Dermatology Resident Physician, Universidade de Mogi das Cruzes (UMC) - São Paulo (SP), Brazil.

[2] Head of the Dermatology Service, UMC.

Correspondence:
Camila Carneiro Marques
R. Dom Antônio Cândido Alvarenga, 170 - Centro
Cep 08780-070 - Mogi das Cruzes (SP), Brazil
Email: cam_tn1@hotmail.com

Received on: 14/10/2016
Approved on: 04/12/2016

This study was performed at Universidade de Mogi das Cruzes (UMC) - São Paulo (SP), Brazil.

Financial support: None
Conflict of interests: None

DOI: http://dx.doi.org/10.5935/scd1984-8773.20168406

ABSTRACT

Introduction: Male androgenetic alopecia, has high prevalence and causes great discomfort in patients. The platelet-rich plasma generates an environment acts to create a suitable microenvironment for tissue repair and possibly prolongs the anagen phase of the hair follicles.

Objective: To evaluate the safety, efficacy and viability of the PRP use for the treatment of male androgenetic alopecia. Methods: We selected 08 male patients with androgenetic alopecia. Participants had the side of the scalp randomized scalp to receive PRP or placebo. 3 were performed monthly applications.

Results: Patients who received treatment realized some degree of improvement especially as regards the fall. The results were obtained through the analysis dermatoscopic was evaluated as "trichoscale". We observed an increase of anagen hairs, down telogen hairs and vellus wires and increase terminal wires. The results were statistically significant as the reduction of vellus wires and increase of terminals wires.

Conclusions: This study showed a clinical improvement observed for photos as well as positive results documented by analysis "trichoscale". There was statistical significance of data obtained especially after the first month of treatment.

Keywords: alopecia; platelet-rich plasma; men

RESUMO

Introdução: *A alopecia androgenética masculina, tem grande prevalência e provoca grande desconforto nos portadores. O plasma rico em plaquetas gera um ambiente propício atuando de modo a criar um microambiente adequado para a reparação de tecidos e possivelmente prolonga a fase anágena dos folículos pilosos.*

Objetivo: *Avaliar a segurança, eficácia e viabilidade do uso do plasma rico em plaquetas para o tratamento da alopecia androgenética masculina.*

Métodos: *Foram selecionados 08 pacientes masculinos com alopecia androgenética. Os participantes tiveram o lado do couro cabeludo randomizado para receberem plasma rico em plaquetas ou placebo. Foram realizadas 3 aplicações mensais: de um lado do couro cabeludo com placebo e do outro com plasma rico em plaquetas.*

Resultados: *Os pacientes que receberam o tratamento perceberam algum grau de melhora principalmente no que se refere à queda. Os resultados foram obtidos através da análise dermatoscópica que foi avaliada pelo software "trichoscale". Observamos um incremento de fios anágenos, com redução de fios telógenos e de fios velus e aumento de fios terminais. Os resultados foram estatisticamente relevantes quanto à redução dos fios velus e aumento de fios terminais.*

Conclusões: *Neste estudo observamos uma melhora clínica observada por fotos além de resultados positivos documentados por análise com "trichoscale". Houve relevância estatística nos dados obtidos principalmente após o primeiro mês de tratamento.*

Palavras-chave: *alopecia; plasma rico em plaquetas; homens*

INTRODUCTION

Male androgenetic alopecia is the most prevalent form of alopecia, and although it is socially accepted, it generates great discomfort, low self-esteem and social problems in many of the affected individuals.

In this form of alopecia, the following changes can be observed: alterations in the hair cycle, with miniaturization of follicles, which become thinner and less pigmented (similarly to the vellus), shortened anagen phase, and a greater number of follicles that remain in the chenogen phase, when the follicle is empty.

Its pathogenesis is multifactorial and involves hormonal and genetic factors. In men, the most active androgen is the testosterone, which is converted into dihydrotestosterone by the 5-alpha-reductase type II's action in the dermal papilla, anatomically close to the hair follicle. Dihydrotestosterone has greater affinity to androgenic receptors than to testosterone. Men bearing androgenetic alopecia have higher levels of 5-alpha-reductase in the frontal region as compared to the occipital region. Most of the patients present normal serum androgen levels, meaning that the hormonal mechanism in androgenetic alopecia can be explained by a possible increase in androgens production in the pilosebaceous unit, or by an overexpression or hyperresponsiveness of the androgens' receptors.

Family history is usually positive in male androgenetic alopecia, and there is also a strong genetic association, probably due to polygenic inheritance.

Treatment options for androgenetic alopecia are very limited and include topical application of minoxidil and oral finasteride (FDA approved), isolatedly or in combination. However, there are several secondary side effects have been described, such as headache and increase in other body hairs (with minoxidil), and loss of libido (with oral finasteride).

Platelet-rich plasma (PRP) is produced from processed autologous blood, from which a concentrate of platelets, rich in growth factors (released by the platelets) is obtained. The use of PRP has shown positive effects in the fields of plastic, orthopedic and cardiac surgery, due to its potential tissue repair effect.

The presence of some leukocytes in PRP leads to a natural resistance to infectious processes, reducing the risk of infections in the site to be treated. Platelets are the essential components of this concentrate for they are able to release important growth factors that are important for the tissular cicatricial modulation. The platelets' alpha granules release a number of growth factors, which act by binding to cellular receptors that transmit the signal to the interior of the cells. Platelet-derived growth factor (PDGF) was one of the first factors to be identified. The platelets' PDGF begins the repairing process, stimulating the synthesis of DNA, the chemotaxis and collagen synthesis, processes that are crucial for the wound repair. The transforming growth factors beta (TGF-b) are a group of local mediators that regulate the proliferation and functions of most of the body's cells. Growth factors also activate the proliferative phase and differentiation of the ciliated cells and hair follicular stem cells, producing new follicular units. It has been reported that activated PRP stimulates the proliferation of cells in human dermal papillary layer, increasing the hair follicle cells' survival through its anti-apoptotic effects, and possibly stimulating hair growth, prolonging the anagen phase. [1,2,3]

OBJECTIVE

The objective of the present study was to evaluate the safety, effectiveness and viability of using PRP for the treatment of male androgenetic alopecia.

METHODS

A randomized, placebo-controlled blinded trial was carried out.

Eight male patients with androgenetic alopecia were selected. All met the following inclusion criteria: 18-45 year-old men, clinical diagnosis of androgenetic alopecia, and absence of previous treatment – including the use of finasteride for at least 3 months.

The following factors were the exclusion criteria: bearers of diseases with systemic hormonal alterations (for example hypothyroidism, hematological pathologies, diabetes mellitus, cancer, hypertension, patients in use of hormone-acting drugs, and patients with platelet levels below 130,000.

The participants of the study had the sides of the scalp randomized to receive either PRP or placebo. A computerized system was used to perform the randomization and to ensure the secretiveness of the sides draw. Both patients and the evaluator physician were blinded.

Three consecutive monthly sessions were performed, with subcutaneous injections of PRP and placebo, each applied on one of the sides of the scalp.

The PRP was obtained from autologous blood, meaning that each patient supplied his own blood for the preparation of the infusion to be applied into his own scalp. A 45 ml sample of whole blood was collected in the presence of anticoagulant, whose composition does not damage the platelets (sodium heparin). This sample was subjected to a double and continuous centrifugation process, during which a volume of 45 ml of whole blood was inoculated into a single 50 ml capacity tube, in a fully enclosed environment and isolated from the external air. The tubes were centrifuged at room temperature, resulting in three basic components: red cells, platelet-rich plasma (PRP), and platelet-poor plasma (PPP). The PRP volume of roughly 5ml was collected within the double tube, specifically developed for that end, with 4ml of 10% calcium chloride being subsequently added. The material was then infused subcutaneously on the previously randomized side of the scalp.

The evaluation of the primary outcome was performed using the Trichoscale® software (FotoFinder Systems, Inc., Columbia, Maryland, USA). The software is runs by the FotoFinder® device, which is a digital dermoscopy system developed by a German company in conjunction with the Tubigen University in Germany, and which magnifies cutaneous lesions by 20 to 70 times. The software component was developed for a more accu-

rate analysis of the scalp, and builds a digital trichogram. It is able to evaluate the following parameters: hair density (strands per square centimeter), percentage of anagen and telogen strands, vellus and terminal hair densities, and measurement of follicular units. The evaluation performed by the software was carried out on previously established and standardized areas: two circular areas with 1.5cm in diameter, located in the parietal region of each side of the skull, 14cm from the mastoid process on the respective side. The evaluation was carried out on three timepoints: 15 days before the first application, and at 30 and 60 days after the end of the treatment.

Secondary outcomes were determined by clinical and photographic evaluations of the scalp. In addition, the authors of the present article assessed the procedure's safety by recording the adverse events that were reported on all scheduled encounters (treatment and follow-up visits).

RESULTS

Of the 8 patients selected, one dropped out and another did not attend the last PRP application session.

The 6 patients who received the complete treatment noticed some degree of improvement, especially regarding the hair loss. The photographic assessment can be seen in Figures 1 and 2.

The results from the statistical analysis of the data performed by the Trichoscale® software are presented in Table 1, with a comparison of the mean values obtained from the sides treated with PRP and placebo. The Student t-test was used in order to obtain the results mean values.

Based on the analysis of Table 1, it is possible to infer that there was an increase in the percentage of anagen strands and a reduction in telogen strands in both of the treated sides, however the improvement was more significant on the PRP side. Both the increase in anagen hairs and the decrease in telogen hairs continued in the second month after treatment.

Furthermore, there was a statistically significant reduction in vellus hairs ($p = 0.035$) on the PRP side after the first month of treatment, however this reduction was not maintained in the second month.

Regarding the terminal hairs, there was an important increase in the PRP side, with statistical significance ($p = 0.035$) after the first month of treatment. The result was not maintained in the second month.

Regarding adverse effects, the only symptom reported by the patients was pain during the application, being that 4 patients reported pain a few hours after the application. Even though, the pain was rated as tolerable by the patients, and there was no need for analgesia even for those who complained of pain after the procedure. No signs of erythema, edema or heat sensation was observed in the application site.

DISCUSSION

Platelet-rich plasma contains growth factors that have effects on the cells' maturation and the wound repair process. Its use in wound repair, and orthopedic and cardiac surgeries is

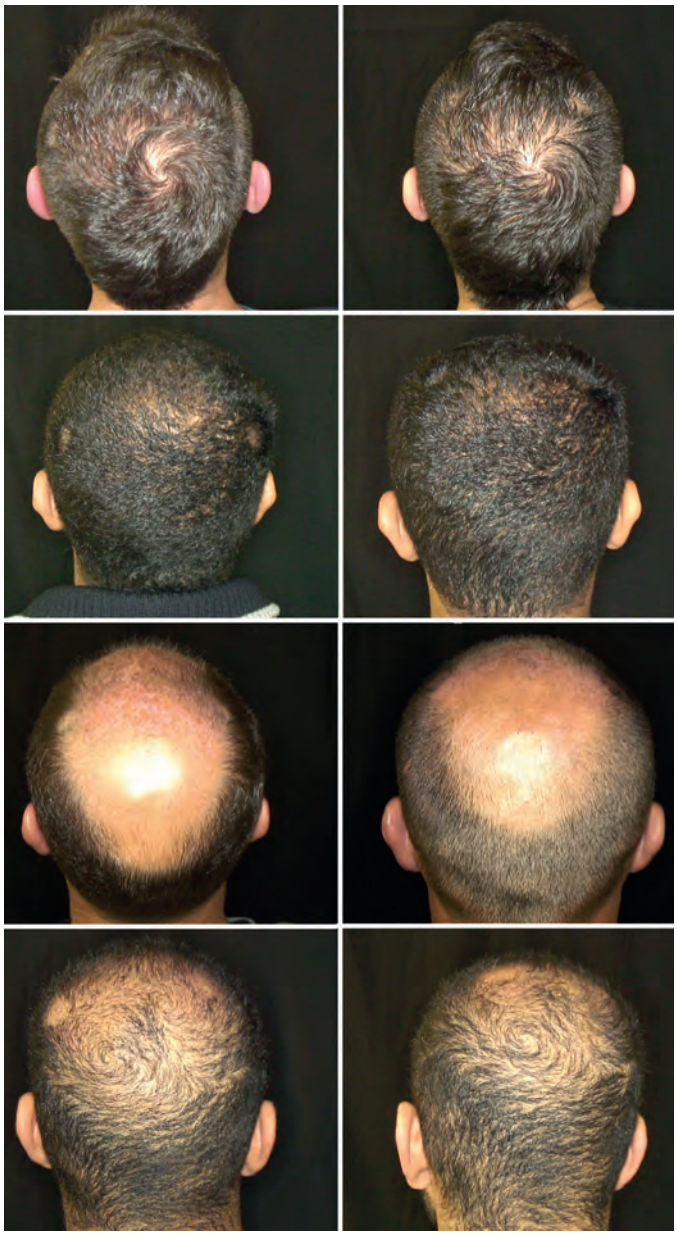


Figure 1: Photographs before (left) and after (right) the treatment with PRP

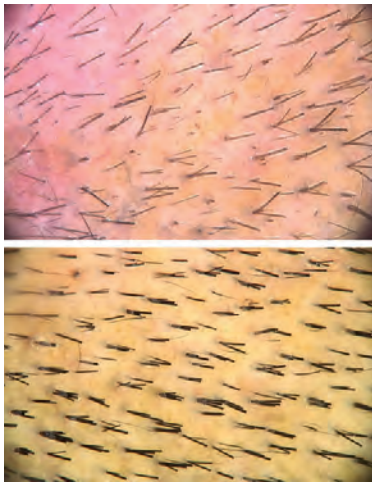


Figure 2: Dermoscopic image before (top) and after (bottom) the treatment with PRP

Table 1: Measurement of the data obtained using the Trichoscale® analysis software before and after the treatment with PRP

	Follow-up	Side treated with placebo (mean)	Side treated with PRP (mean)	Valor de P
Anagen %	Pre-treatment	53.733	49.550	0,194
	1 month after	66.683	77.050	0,141
	2 months after	65.400	66.967	0,68
Density of terminal hairs	Pre-treatment	129.900	132.483	,819
	1 month after	132.500	138.567	,201
	2 months afters	139.850	122.333	0,061
Vellus hairs density	Pre-treatment	27.300	42.450	0,257
	1 month after	37.467	23.050	0,053
	2 months afters	41.567	42.800	0,91
Telogens %	Pre-treatment	46.267	45.950	0,955
	1 month after	33.317	23.117	0,144
	2 months afters	34.600	33.533	0,753
Terminal %	Pre-treatment	81.383	76.083	0,178
	1 month after	76.383	84.133	0,035
	2 months afters	76.917	74.783	0,664
Follicular Units	Pre-treatment	97.50	102.17	0,348
	1 month after	99.83	97.00	0,393
	2 months afters	101.83	99.33	0,522
Vellus %	Pre-treatment	18.617	23.917	0,178
	1 month after	23.617	15.900	0,035
	2 months afters	23.083	25.217	0,664

growing increasingly. In the treatment of androgenetic alopecia, PRP has been studied with good prospects to emerge as an effective and safe treatment.

A study by Gentile et al with a sample of 23 patients compared the injection of PRP on one side versus placebo on the other side, for treatment of androgenetic alopecia. After 3 monthly cycles of treatment, the patients showed clinical improvement in the average number of hairs per analyzed area. A microscopic evaluation evidenced increased epidermal thickness and number of hair follicles. There was also an increase in Ki67 (a marker of cell proliferation), in epidermis' keratinocytes, and in follicle bulge cells. [4]

Another study, carried out by Singhal el al., tested the infusion of PRP in the scalp of 8 patients diagnosed with androgenetic alopecia, while the control group received a different drug therapy. In the PRP group, there was hair growth after 12 weeks of treatment and a reduction of 65% in the hair traction test. The control group did not experienced the same outcomes.[5]

A prospective cohort study of 20 patients with the application of PRP every 21 days and a new small volume application after six months showed a reduction in hair loss, which after 3 months reached normal levels. Furthermore, it was possible to notice increased hair density as compared to the baseline. [6]

A study conducted by Schiavone et al. with 64 male and female patients with androgenetic alopecia analyzed the application of two injections of leukocyte plasma rich in platelets (L-PRP) with the addition of concentrated plasma proteins. Two independent evaluators assessed photographs taken at baseline and after 6 months. Some degree of improvement was observed in all patients by one of the evaluators while the other identified improvement in 62 patients. In this study, it was possible to observe that the proposed treatment can induce some degree of clinical improvement for the male and female baldness.[7]

The great potential of PRP is linked to the concentration of growth factors contained in platelets. Many of them are involved in the regulation of morphogenesis and hair growth, and in the cyclic transformation of the hair follicle, acting as biological switches that are turned on and off during the different phases. [5,8] The main growth factors involved in the hair follicle growth are: vascular endothelium growth factor (VEGF), epidermal growth factor (EGF), insulin-like growth factor (IGF), and fibroblast growth factor (FGF). Platelets release large amounts of growth factors derived from platelets (PDGF), EGF and VEGF.[5]

Activated PRP seems to promote the differentiation of hair follicular stem cells through the stimulation of b-catenin transcription activity. In addition, it induces the *in vitro* proliferation of dermal papilla cells, increasing the growth of cells through the activation of kinase-dependent extracellular signaling (ERK). Platelet-rich plasma also appears to prolong the anagen phase of the hair growth cycle by increasing the expression of the fibroblast growth factor 7 (FGF-7), and to increase cell survival via the inhibition of apoptosis. [1] Another mechanism of action is the increase in the levels of VEGF and PDGF, stimulating angiogenesis in the perifollicular vascular plexus. [3,5]

The results of the present study were obtained through the dermoscopic analysis evaluated by the Trichoscale® software. There was an increase in anagen hairs, with a reduction of telogen and vellus hairs, and an increase in terminal hair. The results were statistically relevant for the reduction in vellus hairs and the increase in terminal hairs. The evaluation also included a 2-month follow-up after the treatment. Failure to maintain good results in this follow-up may be related to the androgenic hormonal stimuli that act on the progression of the disease. That fact contributes with the hypothesis that PRP therapy could be indicated as an adjuvant treatment in androgenetic alopecia. Also, there was an improvement on the side treated with placebo, which could be explained by the PRP's action from distance.

The present study's advantage was that the used PRP material was prepared according to a protocol, as described in the "Methods" section. For the evaluation of results, the authors used dermoscopic images analyzed by the Trichoscale® software, an assessment method that is more objective than the isolated photographic analysis.

The limitations of the present study were the small number of participating patients and the fact that the outcomes were not followed-up more prolongedly.

CONCLUSION

Androgenetic alopecia is a frequent complaint in the dermatology practices. There are several established treatments; however obtaining an effective treatment is still a challenge.

In the present study, a clinical improvement evidenced by photographs was observed, and positive results were documented by the Ttrichoscale® analysis. There was statistical relevance in the data obtained, especially after the first month of treatment.

In light of the results obtained and the considerable therapeutic potential of platelet-rich plasma, the authors of the present study believe that this new therapeutic resource will certainly add up to the dermatologists' armamentarium for the treatment of androgenetic alopecia.

Further studies should be carried out aiming at scientifically evidencing PRP's real effectiveness. ●

REFERENCES

1. Li ZJ, Choi HI, Choi DK, Sohn KC, Im M, Seo YJ, et al. Autologous platelet-rich plasma: A potential therapeutic tool for promoting hair growth. Dermatol Surg. 2012;38:1040-6.
2. Maria-Angeliki G, Alexandros-Efstratios K, Dimitris R, Konstantinos K. Platelet-rich plasma as a potential treatment for noncicatricial alopecias. Int J Trichol 2015;7:54-63
3. Arshdeep, Kumaran MS. Platelet-rich plasma in dermatology: Boon or a bane? Indian J Dermatol Venereol Leprol. 2014;80:5-14.
4. Gentile P, Garcovich S, Bielli A, Scioli MG, Orlandi A, Cervelli V. The Effect of Platelet-Rich Plasma in Hair Regrowth: A Randomized Placebo-Controlled Trial. Stem Cells Transl Med. 2015;4(11): 1317-23
5. Singhal P, Agarwal S, Dhot PS, Sayal SK. Efficacy of platelet-rich plasma in treatment of androgenic alopecia. Asian Journal of Transfusion Science. 2015; 9 (2):159-62.
6. Gkini MA, Kouskoukis AE, Tripsianis G, Rigopoulos D, Kouskoukis K. Study of platelet-rich plasma injections in the treatment of androgenetic alopecia through a one-year period. J Cutan Aesthet Surg. 2014;7:215-21
7. Schiavone G, Raskovic D, Greco J, Abeni D. Platelet-Rich Plasma for Androgenetic Alopecia: A Pilot Study. Dermatol Surg. 2014 (40): 1010-19
8. Lin WH, Xiang LJ, Shi HX, Zhang J, Jiang LP, Cai PT et al. Fibroblast Growth Factors Stimulate Hair Growth throughβ -Catenin and Shh Expression in C57BL/6 Mice. Biomed Res Int. 2015;2015: 9p.

Review article

Overview and management of fillers complications

Manejo de complicações de preenchedores dérmicos

Authors:
Meire Brazil Parade[1]
Camila Cazerta[1]
João Paulo Junqueira Magalhães Afonso[1]
Danielle Ioshimoto Shitara Nascimento[1]

[1] Dermatologist Physician, Private Practice - São Paulo (SP), Brazil.

Correspondence:
Meire Brasil Parada
Av. Ibirapuera, 2120 – Conj. 115
Cep 04028-001 – São Pailo (SP), Brazil
Email: mbparada@uol.com.br

Received on: 04/08/2016
Approved on: 03/12/2016

This study was performed at the authors' private practice, São Paulo (SP), Brazil.

Financial support: None

Conflict of interests: None

DOI: http://dx.doi.org/10.5935/scd1984-8773.201684897

ABSTRACT

Filler injections are among the most popular cosmetic procedures performed worldwide. Although fillers have a safety profile, there has been a rise in litigation as a result of treatments in the USA. In the Brazilian scenario, the number of non-surgical procedures has increased in the past years, mainly due to the increase of filler options available in the Brazilian market, as well as in the type of professionals allowed to perform injectable procedures. Therefore we sought to review the related literature regarding semi-permanent and temporary fillers adverse effects and outline a practical guide for complications avoidance, diagnosis and management.

Keywords: Granuloma; Ischemia; Esthetics; Hyaluronic Acid; Dermis; Subcutaneous fat; Biofilms; Infection

RESUMO

O preenchimento cutâneo Figure entre os procedimentos cosméticos mais realizados. Apesar de os tratamentos estéticos possuírem perfil de segurança favorável, ocorreu um aumento nos processos jurídicos deles resultantes nos Estados Unidos. No Brasil, o número de procedimentos não cirúrgicos apresentou crescimento nos últimos anos devido não apenas ao maior número de opções de materiais para preenchimento disponíveis no mercado, mas também devido à maior quantidade de profissionais com permissão para executar esses procedimentos. O objetivo do presente estudo foi revisar a literatura, assim como delinear um guia prático para prevenção, diagnóstico e manejo das complicações secundárias ao uso de preenchedores semipermanentes e temporários.

Palavras-chave: *granuloma; isquemia; estética; ácido hialurônico; derme; gordura subcutânea; biofilmes; infecção*

INTRODUCTION

According to the American Society for Aesthetic Plastic Surgery, more than 13.5 billion dollars were spent on surgical and nonsurgical procedures in the USA in 2015, with nonsurgical procedures accounting for 42% of the total value[1]. While nonsurgical cosmetic procedures have increased by 44% in the past 5 years, injection based procedures have increased by 21%.

In the survey conducted by the International Society of Aesthetic Plastic Surgery, 20 million cosmetic procedures were performed worldwide in 2014, with Brazil ranking third for non-surgical procedures. Nonsurgical procedures accounted for 51% of the total procedures, with botulinum toxin and cutaneous filler injections being the most popular. Botulinum toxin and hyaluronic acid accounted for 71% of non-surgical procedures[2].

In the United States, with the increased use of soft-tissue fillers, there has been a concomitant rise in litigation asserting harm as a result of treatments. The most common lesion giving rise to litigation was the formation of granuloma or autoimmune reaction[3].

The number of cosmetic filler options available in the Brazilian market has increased in the past years. Although soft tissue fillers have a very favorable safety profile, between 2003 and 2008 the US Food and Drug Administration has received 930 post-marketed reports of adverse effects, with 823 of those having been classified as severe[4]. Therefore the authors of the present study sought to review the literature regarding semi-permanent and temporary fillers adverse effects, as well as outline a practical guide for avoiding, diagnosing and managing complications.

Pre-treatment considerations: clinical assessment and informed consent

Assessing the patient prior to the injection procedure is vital, not only aiming at evaluating the patient's expectations, choosing the optimal product, planning the injection, and choosing the injection points, but also evaluating the risks involved.

Patients should be thoroughly queried regarding medical history of bleeding disorders, herpes, auto-immune diseases, pregnancy, allergies, keloid formation and use of medicaments, such as blood thinners (including coumadin and non-steroidal anti-inflammatory drugs), or vitamins/herbal supplements associated with prolonged bleeding – examples include (vitamin E, chondroitin, feverfew - Tanacetum parthenium, ginger, garlic, ginseng, gingko-biloba, kava-kava, celery root, and fish oils)[5, 6]. Herbal medications should be discontinued 7-10 days prior to the procedure to reduce the risk of hematomas. Regarding patients under use of anticoagulant medication, if it has been is prescribed for a limited period of time, it may be prudent to postpone the injection treatment until the patient has stopped taking the drug. Nevertheless, if the medication has been prescribed indefinitely, the benefit-risk of discontinuing these drugs should be carefully evaluated [5,7].

The history of aesthetic procedures should be assessed observing the types of previous aesthetic procedures the patient has undergone and the types of fillers used, as well as previous allergic reaction to fillers or anesthetics.

Overall, fillers should be avoided in case of active adjacent site of infection (intraoral, mucosal, dental or even sinusitis), adjacent inflammatory process, immunosuppression, allergy to filler components or lidocaine, pregnancy and breastfeeding [8,9].

In case of active adjacent site of infection, the procedure should be postponed and the infection should be treated before any injection. If the patient is under dental treatment, Parahitiyawa *et al*. also recommend to postpone the procedure, due to the fact that dental treatment can cause transitory bacteremia, which is already proven to have systemic impact and lead to diseases, and in theory can also cause colonization of the filler and formation of a bacteria biofilm[10]. The patient should be advised of the risks in case the physician chooses to perform the procedure during an active infection. The use of prophylactic antibiotic is debatable.

The use of semi-permanent or temporary fillers in an area where permanent fillers have already been injected should be avoided due to the risk of exacerbation or stimulation of nodule formation[11]. Nevertheless, injection in areas different from those where permanent fillers have already been injected could be performed after careful evaluation of the permanent filler's location assisted by imaging techniques (high-frequency ultrasound - HFUS, optical coherence tomography, MRI and scintigraphy) [12-15] is carried out prior to the treatment, clearly defining the area that should be avoided. High frequency ultrasound has proven to be the first line tool (quick and cost-effective) for assessing filler site and class (temporary vs permanent). In complicated cases, MRI seems to be very helpful in correctly evaluating filler migration and identifying subcutaneous abscesses or granulomas[15].

Photographs should be taken aimed at documenting the patients' appearance before the procedure, as well as for better analyzing the patient's areas of concern and eventual asymmetries. The patient's objectives and corresponding best filler types for his or her needs, risks and costs involved in the procedure should be discussed with the patient prior to the treatment, aiming at setting real expectations (7). The patient should read and sign a free and informed term of consent and the data in Table 1 should be well documented [16].

Intra-procedure general recommendations

In order to prevent infections and biofilm formation, all makeup and other potential contaminants present on the skin should be removed. In addition, the skin should be cleansed with an antimicrobial preparation, such as aqueous or alcoholic 2-4% chlorhexidine[11,17]. Chlorhexidine should be avoided in the periocular area due to risk of keratitis[7]. Also, it may be useful to have the patient rinse the mouth with a mouthwash before an injectable procedure to reduce oral microbiota. Oral 0.12%-0.2% chlorhexidine mouthwash was the most effective in reducing tooth biofilm *in vivo* [18, 19].

Even though it has not been proven that the use of non-sterile gloves and alcoholic chlorhexidine is insufficient in preventing filler infections, employing sterile technique through-

Chart 1: Important data to be included in the patients' records

Patient data

Medical history (bleeding, herpes, autoimmune diseases, pregnancy, allergies, tendency for keloids, dental treatments and medications)

Pre-treatment photographs
Physical examination: asymmetries, infection in adjacent areas (intraoral, mucosal, dental or even sinusitis), adjacent inflammatory process
Previous aesthetic procedures (type of filler used, sites injected, allergic reactions prior to fillers or anesthetics)

Free and Informed Term of Consent

Intra-procedure details

Type of antimicrobial used
Sterile (or non sterile) gloves
Injection points
Filler volume injected per point
Type of filler (expiration date, batch)
Needle or cannula (expiration date, gauge, batch)
Post-procedure recommendations

Patient and intraprocedure details with recommendation of inclusion in the patient's records.

out the procedure (i.e. using sterile gloves, drapes, gauze), in some authors' opinion may reduce the risk of these complications[7,11]. Making sure that good illumination is used during the procedure also helps to identify and avoid superficial vessels, reducing the risk of hematoma.

Injecting the product in the correct plane is critical to minimize adverse events, such as superficial placement. Some visual cues help the dermatologist physician to recognize the right plane for injection. For instance, in the superficial planes, the gray of the needle can be observed and the skin whitens. In the deep dermis, the gray of the needle is not seen, however its shape can be recognized. The supra-periosteal plane is reached inserting the needle perpendicular to the skin, until the periosteum can be palpated with the tip of the needle (7). The needle should be then pulled back slightly for better product placement.

Post-procedure general recommendations

Patients should not apply non-sterile make up in the first 4 hours after the procedure[7]. If massage is needed, for example after the injection of poly L-lactic acid (PLLA), aqueous or degerming chlorhexidine can be useful.

Managing adverse events

I) Early reactions (from a few days to several days)

A) Local reactions

Local reactions can be related to the injection alone, including local inflammation, hyperemia, tenderness, and hematoma. These are mainly influenced by the needle's gauge, physico-chemical properties of the injected material, and speed of injection[4]. Injection techniques that increase the dissection of the sub-epidermal plane (i.e. fanlike technique, rapid injection, rapid flow rates, higher volumes) have been associated with an increased number of local adverse events, due to tissue distension and trauma[6,20]. The use of blunt-tipped cannulas may decrease bleeding, hematoma and pain due to reduced intra-tissue trauma and number of punctures[21].

B) Erythema

Transient erythema can occur, especially if massage is performed after the procedure. Anti-histamine and topical steroids can help minimize transient redness. In case of persistent erythema, after exclusion of hypersensitivity reaction and infection (22), the use of light treatments such as IPL and LED has been described[6, 23].

C) Swelling

Swelling is one of the most common complications associated with fillers. Edema is usually localized and self-limiting. Most prone areas are the lips and periorbital region. The correct choices of product for the treatment area, as well as of correct plane for the treatment help prevent swelling. Applications of ice, anti-histamines and short time prednisone use, as well as the elevation of the head, have been described[6]. A rare form of recurrent and intermittent swelling that occurs after alcohol intake, sunlight exposure or vigorous exercise, has been reported.[9]

D) Superficial placement of fillers

The superficial placement of fillers can lead to blanching or, in case of hyaluronic acid (HA), bluish discoloration in the injection area (Tyndall effect)[24]. The Tyndall effect may result from either traces of hemosiderin after vascular lesion and/or visual distortion of light through the skin due to refraction caused by the filler[25]. Fillers should only be injected after the needle has reached the appropriate depth and injection should be stopped before the needle is withdrawn. Also, placement in the correct plane is crucial. For example, semi-permanent fillers, such as poly-L-lactic acid (PLLA) or calcium hydroxyapatite (CaOH), cannot be placed too superficially and need to be injected in the subcutaneous or supra-periosteal planes[6].

Local massage, incision and drainage, and, in case of HA, hyaluronidase (HYAL), are treatment options. Also, the use of Q-switched 1,064nm laser has been reported[26].

Calcium hydroxyapatite is ideally placed in the subcutaneous and may present product migration if the product is placed superficially or in highly mobile areas, such as the lips. Treatment options are intra-lesional steroid injection, saline injection followed by massage, incision and expression or surgical removal[7]. Also superficial filler placement can lead to lumps and nodule formation. Please, refer to the Nodules and the Lumps sections.

E) Herpes activation

The risk of herpes activation following dermal filler injection due to direct damage to the axon caused by the needle, with subsequent tissue manipulation and inflammatory reaction[27] is estimated to be less than 1.45%. Since there are no defined guidelines, a systemic antiviral prophylaxis can be performed in patients with personal history of recurrent facial herpes (>3 epi-

sodes/year). Acyclovir 400mg three times per day for 10 days or valacyclovir 500mg twice per day for 7 days can be employed, starting 2 days before the procedure (28).

F) Infection

Early-onset infections arise with induration, erythema, tenderness and pruritus, and might be indistinguishable from transient post-procedure response. Fluctuating nodules and systemic symptoms (fever, chills) can occur later on. Skin infections are usually related to resident flora (*Staphylococcus* or *Streptococcus* spp.) introduced through injection. Microbiological culture should be performed and culture-appropriate antibiotic treatment installed. Abscess should be drained. In longer lasting infections or poor response to antibiotics, atypical infection (i.e. *Mycobacterium* spp.) and biofilms should be considered. In these cases alternative antibiotic may be necessary.

G) Acute hypersensitivity

Foreign body fillers can trigger immune response. Hypersensitivity reactions can range from mild redness to anaphylaxis. The incidence of hypersensitivity reaction related to HA is around 0.6%. About 50% (4) of these cases are transient and resolve within 3 weeks. In a prospective, randomized study, 433 patients injected with NASHA HA were evaluated using skin testing, IgE and IgG antibody serology, and histopathology studies. No detectable allergenicity (Type 1) or delayed hypersensitivity (Type IV) was reported (29). Use of anti-histamines, non-steroidal anti-inflammatory drugs (NSAIDs), intralesional or systemic steroids, minocycline and hydroxychloroquine have been reported. Hyaluronidase may help removing the core of the inflammation (30).

H) Lumps

Lumps are caused by excessive HA, superficial product placement, areas of thin skin (i.e. eyelids) or migration due to muscle movement (i.e. lips) (22). Treatment options comprise aspiration, incision and drainage or removal by HYAL injection in case of HA (24). It is important to note that this reversion ability of HA is unique (6). Previously diluted HYAL and lidocaine can be used to dissolve the lump (31).

In a retrospective study conducted in Brazil, 50 patients who underwent HYAL injections to treat complications or unaesthetic results following HA injections were given doses of this enzyme ranging from 40 to 160 Units per anatomic area (32).

I) Vascular complications

The most feared complication among those caused by the use of dermal fillers is injection-induced necrosis, which is caused by vascular occlusion or trauma. Impending necrosis was described with different filling materials with an estimated frequency of 0.001% of total procedures performed (33).

First and foremost, a thorough knowledge of the facial vascular network is crucial, especially when treating areas with terminal blood vessels, such as the glabella and the nose. Among risk factors for intra-arterial injection are related to: 1) the injected areas: high-risk areas include areas near the facial artery, angular artery along the nasolabial fold, nose and glabella. The glabella has tenuous blood supply, originating in branches of internal and external arteries, having a close connection with the eye's vascular system. The facial artery becomes superficial close to the pyriform fossa at the apex of the nasolabial fold. Therefore in this area, the filler placement should be carried out deeply in the supra-periosteal area with a needle, or more superficially, with a blunt cannula; 2) large volume of injection; 3) small sharp needles, that are more likely to penetrate the vascular lumen, as compared to larger bore needles and cannulas. Nevertheless blunt cannulas may reduce – but not eliminate – the risk of vascular lesion; 4) previous scarring, which stabilize and immobilize arteries in place, making them easier to penetrate with needles; 5) composition of the filling material: permanent fillers cannot be dissolved and can obstruct the lumen (34). The filling material primarily implicated in blindness is fat. Nonetheless, other substances, such as collagen, CaOH and HA, have also been reported to have caused blindness (30).

The typical clinical appearance following HA filling caused ischemia is transient blanching (duration of a few seconds), followed by a livid pattern or reactive hyperemia (minutes), black-bluish discoloration (ten minutes to hours), blister formation (hours to days), and cutaneous necrosis and ulceration (days to weeks).

Preventative measures include the use of small volumes, greater than 27G blunt cannulas, and slow injection. Aspiration prior to injection does not ensure vascular safety, but should be performed.

Clinical symptoms that should prompt the physician to immediately stop injecting are: pain, skin blanching or color changes (livedo, blue or gray color) in the distribution of the regional blood vessels. Another cue is observing the blood return after digital compression of the area. Return to normal color takes 1-2 seconds. Slower capillary blood return may be a sign of arterial insufficiency (35). Ice and epinephrine may mask the signs and symptoms of arterial insufficiency.

Hyaluronidase is considered the backbone of vascular occlusion treatment (5, 34). It consists of a soluble protein enzyme that hydrolyzes both natural and cross-linked HA. Even tough actual need of intravascular injection has been reported (34), diffuse injection of HYAL into the tissues affected by ischemia seems to be enough in most cases, for HYAL can easily cross facial planes and tissue structures by affecting the HA of the dermal matrix (35, 36).

A recent consensus recommendation for impending necrosis treatment included (33):

1) The use of significant amount of HYAL in the area of necrosis. It is important to flood the area, as soon as possible. A minimum of 200UI is recommended. No test is needed to assess impending necrosis. Early HYAL injection reduced the size of necrosis in animal experiments, when compared to late injection (24hs) (33). Also, the nature and quality of the dermal filler are important considerations for HYAL effectiveness. Hyaluronidase hydrolyzes Restylane® more quickly and with smaller volumes when compared to other HAs (Juvederm®,Volbella®, Prevelle® and Belotero®) (11, 33, 36-38). If no improvement is seen in 60 min, the injection should be repeated.

2) Vigorous massage and warm compress (for 5-10min, every 30-60 min).

3) Massaging topical 2% nitroglycerin (NTG) paste on the area immediately on suspicion of necrosis and up to 2-3 times daily is an option[39]. The patient should be lying down during the application of NTG to prevent syncope by fall of blood pressure due to systemic vasodilation. In addition, nitroglycerin paste is contra-indicated in patients taking PGE2 medications such as Viagra® (Pfizer, NY, USA). Alternative protocol[39]: nitroglycerin paste under occlusion for 12hs, followed by a 12-hour interval before applying again.

It is important to highlight that the use of topical NTG is controversial, since according to the preliminary data in animal models, topical NTG was not effective and, in theory, could worsen the picture with dilation of the arterioles, further propagating the product into the smaller capillaries, causing increased dermal ischemia[40].

Nitroglycerin is not available in Brazil.

4) Introduce oral aspirin regimen: two 325mg pills per day, usually for 1 week to prevent further clot formation[33]. Since in Brazil available aspirin dosages are 100mg and 500mg, patients can take 500-600mg daily for 1 week.

5) Daily patient follow-up: HYAL and NTG can be continued as needed for the following few days. If improvement is observed, NTG massages can be stopped. If there is no improvement or progression, HYAL, NTG and aspirin should be repeated daily.

6) Daily low-molecular weight heparin, prostaglandin E1, systemic anticoagulation, hyperbaric oxygen therapy, and sildenafil have been recommended as other treatment options [41].

7) Patient aftercare should ensure: proper wound care with daily dressings and wound coverage with ointment to prevent crusting, skin hydration, debridement of necrotic skin and secondary infection prevention.

Even though the use of HYAL for the reversal of vascular complications is "off-label", the prompt diagnosis and immediate treatment with this enzyme is crucial[33].

II) Late onset reactions (from weeks to years)

A) Nodules

In a 5-year retrospective review, 14 complications were reported out of 2,089 injectable soft-tissue filler treatments (PLLA, HA and CaOH), with nodule or granuloma formation being the most common. Calcium hydroxyapatite was the filling substance that was most associated with complications in this series (2.6% of treated cases)[42]. Delayed reactions to HA-based fillers are estimated to occur in approximately 0.02% of treatments[43]. More recently, the authors of a retrospective study reported an exceptionally high rate of late-onset recurrent and resistant inflammatory nodules (4.25% vs expected 0.02%) after HA injection using Vycross technology[38].

Nodules can occur due to the misdistribution of the filling material, reaction to the product (including inflammation, hypersensitivity or granulomatous reaction) or infection[25]. Most are palpable and not visible, and can be noticed immediately after the procedure or several months later (late-onset).

Nodules may be asymptomatic or inflammatory, and can present erythema, tenderness and swelling. These are denominated *angry red bumps* by some authors[9,30]. The role of biofilms in late-onset nodule formation has been discussed recently. Biopsy should be considered to differentiate infectious and inflammatory processes. The authors of the present study propose an algorithm for the management of nodules (Figure 1).

A1) Nodules caused by misdistribution of fillers (non-inflammatory)

Superficial placement of CaOH can lead to white nodules, especially in the lips. These nodules might resolve spontaneously or become permanent[4]. Incision with a number 11 blade or needle, and expression or surgical excision is recommended (24). Injection of saline can be performed in an attempt to dilute the material[11].

Poly-L-lactic acid: palpable non-inflammatory nodules with sizes greater than or equal to 5mm can occur due to incorrect reconstitution, uneven product distribution in the suspension, superficial injection, product placement in contraindicated areas (such as perioral region and eyelids), or lack of post treatment massage[4]. Recommendations of 8ml sterile water for injection dilution, at least 24hs before the procedure and deep plane placement (subcutaneous or supra-periosteal fat) reduce nodule formation to <1% [7,42,44]. These lesions might resolve spontaneously, otherwise they need to be injected with saline.

A2) Inflammatory nodules

The histopathology examination inflammatory nodules may reveal foreign body reaction, infection, sterile abscess or granuloma[30]. Given that slow growing bacteria are thought to play a role in formation of nodules, some authors suggest that inflammatory nodules should be treated empirically as an infection. Empiric antibiotics such as clarithromycin 500mg 12/12 and/or a tetracycline should be administered for 7-10 days. If no improvement is observed, punch biopsy, microbiological culture and prolonged antibiotics should be considered[30]. Hyaluronidase has been used successfully.

A3) Granuloma

The term nodule is used generically when no pathological diagnosis is available. The term granuloma should only be used when the pathologic criteria of granuloma have been fulfilled[11]. Granuloma occurs in 0.01-1% of the treated population and is a distinctive form of chronic inflammation[25,45], consisting of a nodular or more prolonged inflammation, with modified macrophages (epithelioid cells) and multinucleated cells. It typically appears months to years after injection and remains in the injection site. Many triggering factors have been proposed, such as systemic infection, intense exposure to sunlight and systemic drugs, however the pathogenesis of inflammatory granuloma remains unknown[45-47]. The inflammatory reaction may be caused by a hypersensitivity to the filling material or immunologic response to the protein contaminants in the preparations[5].

Considering that subclinical granulomatous inflammation is normal and in case of some injected materials, the desired tissular response, the clinical significance of granulomatous in-

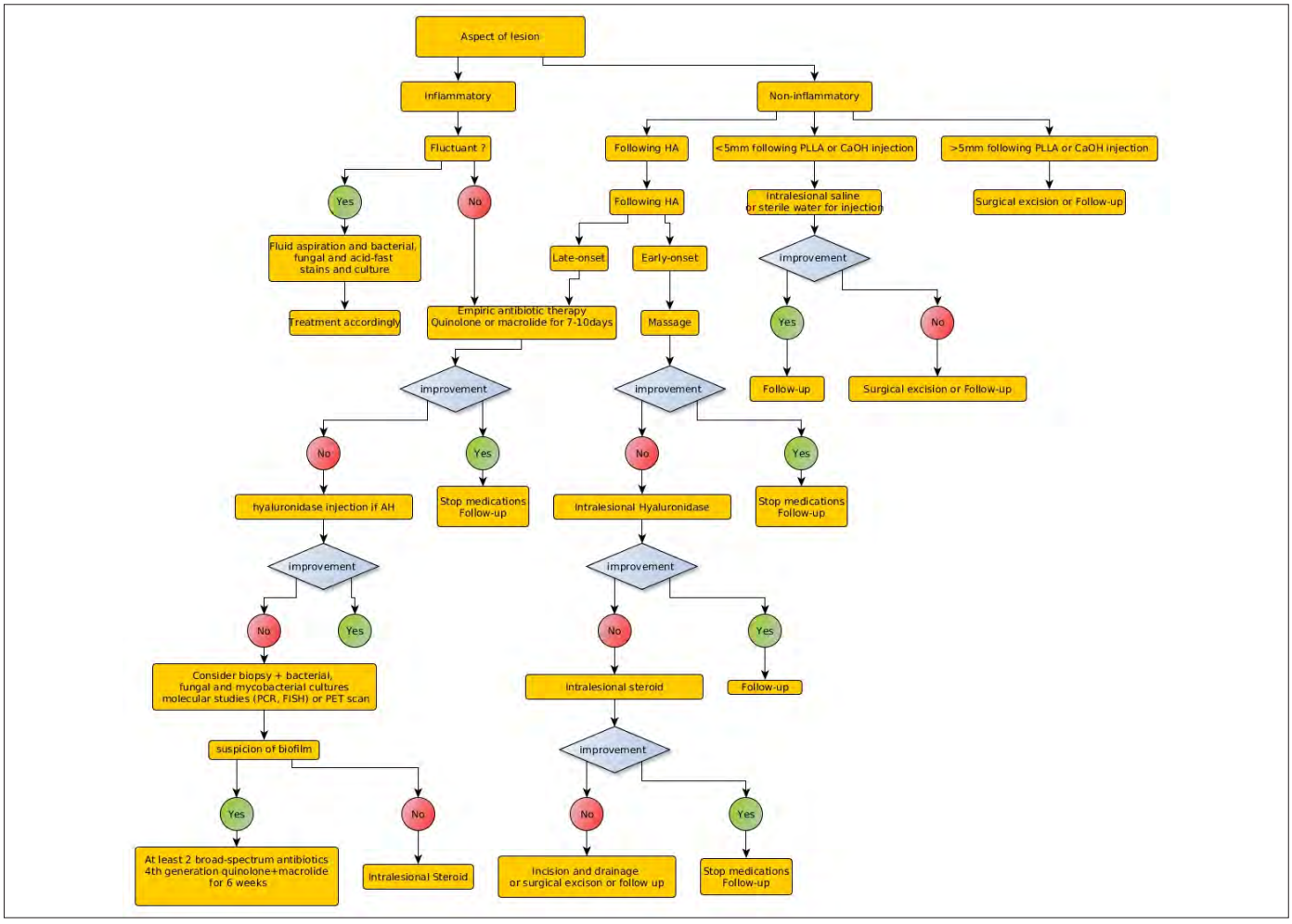


FIGURE 1: Complications with fillers – algorithm for the management of nodules

Management of nodules according to clinical inflammation, size and type of filler used

flammation should be based on its extent, severity and long-term progression of the response[25]. Clinically, granulomas may be accompanied by discomfort, persistent or transient edema, erythema and periods of crisis and regressions. Also, when all implantation sites develop a similar scenario, the differentiation from a nodule caused by filler misdistribution is easier (45).

In the absence of fluctuation and systemic symptoms, histologic and/or microbiologic examination is required to rule out infection. Histopathology is useful not only for the diagnosis of granuloma, but also for the recognition of the implant's nature (48). Permanent fillers present higher risk of granulomatous reaction (49). Less frequently, granulomatous reactions have been described after CaOH (50, 51), PLLA, and HA injections (45).

Intralesional steroid is the recommended treatment for granuloma (6). Usual dosage would be 5-10mg/cc, repeated 4-6 weeks later, according to necessity (9). In case of HA, HYAL injection may be a therapeutic option. Massage, oral steroids (0.5-1mg/kg/day up to 60mg/day), oral minocycline (anti-inflammatory, immunomodulating and anti-granulomatous properties), pulsed dye laser, intralesional bleomycin and intralesional 5-fluoracil have been reported as additional therapeutic tools. Antimalarials (hydroxychloroquine 4-6.6mg/kg/day) have anti-inflammatory and immunoregulatory properties, inhibiting phospholipase activity and blocking several pro-inflammatory cytokines (52). Retina evaluation should be performed periodically. Anecdotic reports have suggested colchicine, anti-histamines and cyclosporine A use in refractory cases. Surgical excision should be avoided during active inflammatory processes or in patients with multiple and/or extensive lesions, due to the risk of filler migration, fistulae formation, scars and persistent granulation tissue (52). The prognosis is usually good for temporary filler granulomas (49).

B) Infection

Late infection typically manifests as tingling sensation followed by swelling 8-12 days after injection. Usually common skin pathogens, such as *S. aureus* are associated. Symptoms are usually described as abscesses, abscess-like nodules, foreign-body nodules or delayed-onset reactions. Fluctuation and systemic symptoms help diagnose infection (25). Nevertheless, in face of a firm, tender mass or nodule, which develops from 2 weeks after the procedure, atypical infection and mycobacteria should be

considered in the differential diagnosis (53). Biological material from biopsy or fluid aspiration should be sent for staining, and for alcohol-acid resistant bacterial, fungal and bacilli culture[25].

B1) Biofilms

One factor is a common denominator for all biofilm implants: a bacterium or infective microorganism is necessary to contaminate the injection for the formation of a biofilm to begin. Biofilm is a glue-like matrix secreted by bacteria, forming a medium in which other bacteria thrive, while evading antibiotics and the immune system[11]. The colony-biofilm becomes antibiotic-resistant by lowering its metabolism, also being protected from phagocytosis by an extra-polymeric system membrane[54]. Chronicity and recurrence of infection are hallmarks of biofilms[42].

Implanted foreign bodies can become infected with skin contaminants during a procedure, or be colonized by direct or hematological spread of an infectious agent[55]. Biofilm may exist in a dormant state and be activated by local trauma, manipulation and injections. Once the biofilm is activated, it can become an acute purulent or a sub-acute course infection, with granulomatous response to the activated biofilm. The active infection can be controlled with antibiotic therapy, however the underlying biofilm can generate recurrence.[54]

In addition to being difficult to treat, biofilms can be involved in delayed-onset skin reactions to fillers, such as granulomatous inflammation, abscesses, nodules or recurrent infection[7,9,11]. A review of hypersensitivity reactions reports suggested that most of the reactions described were due to infectious processes[56].

Biofilms are difficult to diagnose, due to the fact that most microbiological cultures from biofilm-infected tissues are negative. Some bacteria are difficult to grow using traditional methodology, given that their slow-growing nature is often overgrown by faster growing bacteria. Molecular studies, such as PCR and fluorescent *in situ* hybridization (FISH) are more accurate methods[55,57]. Finding the location of the material for biopsy or HYAL injection in case of HA, can be performed by ultrasonography, computed tomography scan (radiopaque material), MRI (non radiopaque implant)[55]. Positron emission tomography scans may help identify foci of infection. Sufficient tissue from biopsy should be obtained for bacterial, fungal and mycobacterial cultures.

Some authors suggest avoiding additional injections in the region of the implant, as well as dental procedures and facial trauma for 2 weeks following dermal filler injection[42]. Even tough, the use of prophylactic antibiotics is debatable and it may be reasonable for certain large-volume filler injections[54].

Since the risk of biofilm should be considered in late-onset reactions, the use of oral steroids and NSAIDs should be avoided. Biofilms may require a 32 times higher amount of antibiotics than that required for killing planktonic bacteria. The recommended treatment should consider the association of at least 2 broad-spectrum antibiotics such as a quinolone (i.e. ciprofloxacin) and a third-generation macrolide (i.e. clarithromycin) for up to 6 weeks[7,21]. Macrolides have superior efficacy in treating biofilms, since they accumulate in the subcutaneous fat[21]. In addition, since bacteria are bound to the foreign material, complete resolution is difficult without its complete removal[42]. Therefore use of HYAL should be considered in case of HA or excision (11). Another reported option is the use of intralesional 5-FU, which has been shown to interact with a bacteria regulatory gene (*AriR*) that inhibits biofilm formation[55].

C) Filling material migration

Filler migration can occur early or late, regardless of the type of the filling substance. Several mechanisms, such as poor technique, high volume of filler injected, filler injected under pressure, massaging after filler injection, muscle activity, gravity, pressure-induced displacement (i.e. injection of additional filler), lymphatic and intravascular spread (more related to permanent fillers) have been related[22,46]. Imaging and histopathology techniques are of assistance in the correct diagnosis.

Hyaluronidase (HYAL)

It is important to point out that HYAL is not commercially available in Brazil. The dosage is highly variable, depending on the treated area and volume of HA placed, ranging from 25UI (in tear though) to 1,500UI (in the case of vascular occlusion)[11]. Hyaluronidase can be diluted in saline or local anesthetics, however the resulting pH may alter the efficiency of the enzyme. It may be injected slowly and directly into the site of HA injection[36]. Massaging is important for obtaining the therapeutic effect. Hyaluronidase treatment should be performed as soon as possible. In a review study, if HYAL were injected within 2 days, full recovery was expected. On the contrary, if injection of HYAL were delayed, there was an increase in the risk of scar and tissue defect formation[58].

Adverse reactions to HYAL are uncommon. Urticaria and angioedema are reported in less than 0.1% of patients and have occurred after retrobulbar or intravenous injections[5]. Therefore, some authors suggested that before applying HYAL, a sensitivity test should be performed injecting 3 units intradermally, with the patient being observed for at least 20 minutes. Local swelling indicates a positive reaction and may reflect sensitivity to animal protein or to preservative or cross-reaction with bee venom[5,24,36,41].

Hyaluronidase has a half-life of 2.1 minutes, caused by inactivation in the kidneys and liver. The most common drug interactions occur with furosemide, benzodiazepines, and phenytoin, which are incompatible with HYAL. Hyaluronidase should not be used to enhance the absorption and dispersion of dopamine and/or alpha agonist drugs. Also, HYAL may accelerate the onset, shorten the effect's duration, and increase the incidence of systemic reactions to local anesthetics. Large doses of salicylates, cortisone, ACTH, estrogens or antihistamines may require larger amounts of HYAL for an equivalent dispersing effect (31).

The dermal filler's nature and quality are important factors for the effectiveness of HYAL in case of an adverse effect. Hyaluronidase can more quickly hydrolyze Restylane® (Q-med) as compared to other HAs (Juvederm® - Allergan, Volbella® - Allergan, and Belotero®). Juvederm® takes significantly longer to disperse than Restylane®[11, 33, 36-38].

Hyaluronidase should not be used in case of infection, due to the risk of spreading the infected material diffusely[11].

CONCLUSION

Dermal fillers are among the most common aesthetic injectable procedures. Although considered very safe, adverse events may occur. Careful patient assessment, adequate therapeutic planning, and an accurate technique are crucial for achieving the best treatment outcomes. To be prepared to assess and handle possible adverse effects promptly is of paramount importance. ●

REFERENCES

1. Surgery.org [Internet]. New York: The American Society for Aesthetic Plastic Surgery; c2009-16 [acesso 2016 Nov 23]. Disponível em: http://www.surgery.org/sites/default/files/ASAPS-Stats2015.pdf
2. Isaps.org [Internet]. Hanover: International Society of Aesthetic Plastic Surgery; c2006-16 [acesso 2016 Nov 23]. Disponível em: http://www.isaps.org/Media/Default/global-statistics/2015 ISAPS Results.pdf
3. Ezra N, Peacock EA, Keele BJ, Kingsley M. Litigation arising from the use of soft-tissue fillers in the United States. J Am Acad Dermatol. 2015 Oct;73(4):702-4
4. Luebberding S, Alexiades-Armenakas M. Safety of dermal fillers. J Drugs Dermatol. 2012;11(9):1053-8.
5. Hirsch RJ, Stier M. Complications of soft tissue augmentation. J Drugs Dermatol. 2008;7(9):841-5.
6. Winslow CP. The management of dermal filler complications. Facial Plast Surg. 2009;25(2):124-8.
7. Bailey SH, Cohen JL, Kenkel JM. Etiology, prevention, and treatment of dermal filler complications. Aesthet Surg J. 2011;31(1):110-21.
8. Sánchez-Carpintero I, Candelas D, Ruiz-Rodríguez R. [Dermal fillers: types, indications, and complications]. Actas Dermosifiliogr. 2010;101(5):381-93.
9. Lafaille P, Benedetto A. Fillers: contraindications, side effects and precautions. Journal of cutaneous and aesthetic surgery. 2010;3(1):16-9.
10. Parahitiyawa NB, Jin LJ, Leung WK, Yam WC, Samaranayake LP. Microbiology of Odontogenic Bacteremia: beyond Endocarditis. Clin Microbiol Rev. 2009;22(1):46–64.

11. DeLorenzi C. Complications of injectable fillers, part I. Aesthet Surg J. 2013;33(4):561-75.
12. Wortsman X. Identification and complications of cosmetic fillers: sonography first. J Ultrasound Med. 2015;34(7):1163-72.
13. Singh M, Wang S, Yee RW, Larin KV. Optical coherence tomography as a tool for real-time visual feedback and biomechanical assessment of dermal filler injections: preliminary results in a pig skin model. Exp Dermatol. 2016;25(6):475-6.
14. Di Girolamo M, Mattei M, Signore A, Grippaudo FR. MRI in the evaluation of facial dermal fillers in normal and complicated cases. Eur Radiol. 2015;25(5):1431-42.
15. Grippaudo FR, Di Girolamo M, Mattei M, Pucci E, Grippaudo C. Diagnosis and management of dermal filler complications in the perioral region. J Cosmet Laser Ther. 2014;16(5):246-52.
16. Jones JK. Patient safety considerations regarding dermal filler injections. Plast Surg Nurs. 2006;26(3):156-63.
17. Soothill JS, Bravery K, Ho A, Macqueen S, Collins J, Lock P. A fall in bloodstream infections followed a change to 2% chlorhexidine in 70% isopropanol for catheter connection antisepsis: a pediatric single center before/after study on a hemopoietic stem cell transplant ward. Am J Infect Control. 2009;37(8):626-30.
18. Mouchrek Junior JC, Nunes LH, Arruda CS, Rizzi Cde C, Mouchrek AQ, Tavarez RR, et al. Effectiveness of oral antiseptics on tooth biofilm: a study in vivo. J Contemp Dent Pract. 2015;16(8):674-8.
19. Quintas V, Prada-López I, Donos N, Suárez-Quintanilla D, Tomás I. Antiplaque effect of essential oils and 0.2% chlorhexidine on an in situ model of oral biofilm growth: a randomised clinical trial. PLoS One. 2015;10(2):e0117177.
20. Glogau RG, Kane MA. Effect of injection techniques on the rate of local adverse events in patients implanted with nonanimal hyaluronic acid gel dermal fillers. Dermatol Surg. 2008;34 Suppl 1:S105-9.
21. Gilbert E, Hui A, Meehan S, Waldorf HA. The basic science of dermal fillers: past and present Part II: adverse effects. J Drugs Dermatol. 2012;11(9):1069-77.
22. Kim JH, Ahn DK, Jeong HS, Suh IS. Treatment algorithm of complications after filler injection: based on wound healing process. J Korean Med Sci. 2014;29 Suppl 3:S176-182.
23. Calderhead RG, Kim WS, Ohshiro T, Trelles MA, Vasily DB. Adjunctive 830 nm light-emitting diode therapy can improve the results following aesthetic procedures. Laser Ther. 2015;24(4):277-89.
24. Cohen JL. Understanding, avoiding, and managing dermal filler complications. Dermatologic Surg. 2008;34 Suppl 1:S92-9.
25. Lowe NJ, Maxwell CA, Patnaik R. Adverse reactions to dermal fillers: review. Dermatol Surg. 2005;31(11 Pt 2):1616-25.
26. Hirsch RJ, Narurkar V, Carruthers J. Management of injected hyaluronic acid induced Tyndall effects. Lasers Surg Med. 2006;38(3):202-4.
27. Kim B, Somia N. Herpes reactivation after injection of dermal fillers. ANZ J Surg. 2013;83(12):998.
28. Gazzola R, Pasini L, Cavallini M. Herpes virus outbreaks after dermal hyaluronic acid filler injections. Aesthet Surg J. 2012;32(6):770-2.
29. Hamilton RG, Strobos J, Adkinson NF Jr. Immunogenicity studies of cosmetically administered nonanimal-stabilized hyaluronic acid particles. Dermatol Surg. 2007 Dec;33 Suppl 2:S176-85.
30. Sorensen EP, Urman C. Cosmetic complications: rare and serious events following botulinum toxin and soft tissue filler administration. J Drugs Dermatol. 2015;14(5):486-91.
31. Cavallini M, Gazzola R, Metalla M, Vaienti L. The role of hyaluronidase in the treatment of complications from hyaluronic acid dermal fillers. Aesthet Surg J. 2013;33(8):1167-74.
32. Balassiano LKA, Bravo BSF. Hialuronidase: uma necessidade de todo dermatologista que aplica ácido hialurônico injetável. Surg Cosmet Dermatol. 2014;6(4):338-43.
33. Cohen JL, Biesman BS, Dayan SH, DeLorenzi C, Lambros VS, Nestor MS, et al. Treatment of hyaluronic acid filler-induced impending necrosis with hyaluronidase: consensus recommendations. Aesthet Surg J. 2015;35(7):844-9.
34. DeLorenzi C. Complications of injectable fillers, part 2: vascular complications. Aesthet Surg J. 2014;34(4):584-600.
35. DeLorenzi C. Transarterial degradation of hyaluronic acid filler by hyaluronidase. Dermatol Surg. 2014;40(8):832-41.
36. Landau M. Hyaluronidase caveats in treating filler complications. Dermatol Surgery. 2015;41 Suppl 1:S347-53.
37. Rao V, Chi S, Woodward J. Reversing facial fillers: interactions between hyaluronidase and commercially available hyaluronic-acid based fillers. J Drugs Dermatol. 2014;13(9):1053-6.
38. Artzi O, Loizides C, Verner I, Landau M. Resistant and recurrent late reaction to hyaluronic acid-based gel. Dermatol Surg. 2016;42(1):31-7.
39. Glaich AS, Cohen JL, Goldberg LH. Injection necrosis of the glabella: protocol for prevention and treatment after use of dermal fillers. Dermatol Surg. 2006;32(2):276-81.
40. Hwang CJ, Morgan PV, Pimentel A, Sayre JW, Goldberg RA, Duckwiler G. Rethinking the role of nitroglycerin ointment in ischemic vascular filler complications: an animal model with icg imaging. Ophthal Plast Reconstr Surg. 2016;32(2):118-22.
41. Nettar K, Maas C. Facial filler and neurotoxin complications. Facial Plastic Surg. 2012;28(3):288-93.
42. Daines SM, Williams EF. Complications associated with injectable soft-tissue fillers: a 5-year retrospective review. JAMA Facial Plastic Surg. 2013;15(3):226-31.
43. Friedman PM, Mafong EA, Kauvar AN, Geronemus RG. Safety data of injectable nonanimal stabilized hyaluronic acid gel for soft tissue augmentation. Dermatol Surg. 2002;28(6):491-4.
44. Ballin AC, Brandt FS, Cazzaniga A. Dermal fillers: an update. Am J Clin Dermatol. 2015;16(4):271-83.
45. Lemperle G, Gauthier-Hazan N, Wolters M, Eisemann-Klein M, Zimmermann U, Duffy DM. Foreign body granulomas after all injectable dermal fillers: part 1. Possible causes. Plast Reconstr Surg. 2009;123(6):1842-63.
46. Jordan DR, Stoica B. Filler Migration: A Number of Mechanisms to Consider. Ophthal Plast Reconstr Surg. 2015;31(4):257-62.
47. Bisschop C, Bruijn MS, Stenekes MW, Diercks GF, Hospers GA. Foreign body reaction triggered by cytotoxic T lymphocyte-associated protein 4 blockade 25 years after dermal filler injection. Br J Dermatol. 2016 Apr 18. doi: 10.1111/bjd.14674. Pubmed PMID: 27086747.
48. Molina-Ruiz AM, Requena L. Foreign Body Granulomas. Dermatol Clin. 2015;33(3):497-523.

49. Rongioletti F, Atzori L, Ferreli C, Pau M, Pinna AL, Mercuri SR, et al. Granulomatous reactions after injections of multiple aesthetic micro-implants in temporal combinations: a complication of filler addiction. J Eur Acad Dermatol and Venereol. 2015;29(6):1188-92.
50. Shahrabi-Farahani S, Lerman MA, Noonan V, Kabani S, Woo SB. Granulomatous foreign body reaction to dermal cosmetic fillers with intraoral migration. Oral Surg Oral Med Oral Pathol Oral Radiol. 2014;117(1):105-10.
51. Sankar V, McGuff HS. Foreign body reaction to calcium hydroxylapatite after lip augmentation. J Am Dent Assoc. 2007;138(8):1093-6.
52. Alijotas-Reig J, Fernandez-Figueras MT, Puig L. Late-onset inflammatory adverse reactions related to soft tissue filler injections. Clin Rev Allergy Immunol. 2013;45(1):97-108.
53. Rodriguez JM, Xie YL, Winthrop KL, Schafer S, Sehdev P, Solomon J, et al. Mycobacterium chelonae facial infections following injection of dermal filler. Aesthet Surg J. 2013;33(2):265-9.
54. Monheit GD, Rohrich RJ. The nature of long-term fillers and the risk of complications. Dermatol Surg. 2009;35 Suppl 2:1598-604.
55. Beer K, Avelar R. Relationship between delayed reactions to dermal fillers and biofilms: facts and considerations. Dermatol Surg. 2014;40(11):1175-9.
56. Dayan SH, Ellis DA, Moran ML. Facial fillers: discussion and debate. Facial Plastic Surg Clin North Am. 2012;20(3):245-64.
57. Dumitrascu DI, Georgescu AV. The management of biofilm formation after hyaluronic acid gel filler injections: a review. Clujul Med. 2013;86(3):192-5.
58. Sun ZS, Zhu GZ, Wang HB, Xu X, Cai B, Zeng L, et al. Clinical outcomes of impending nasal skin necrosis related to nose and nasolabial fold augmentation with hyaluronic acid fillers. Plastic Reconstr Surg. 2015;136(4):434e-41e.

Diagnostic imaging

Authors:
Maria Victória Quaresma[1]
Luciana de Abreu[2]
Lara Braga Oliveira[3]
Bárbara Poggi[4]
Thalyta Valley de Rezende[5]
Bruna Souza Felix Bravo[6]

[1] Dermatologist Physician. Dermatopathology fellow and Doctoral degree student, Faculdade de Medicina, Universidade de São Paulo (FMUSP) - São Paulo (SP), Brazil.

[2] MSc student degree in Medical Clinic, Universidade Federal do Rio de Janeiro (UFRJ) and Preceptor at the Instituto de Dermatologia Professor Rubem David Azulay, Santa Casa de Misericórdia do Rio de Janeiro (IDPRDA / SCMRJ) - Rio de Janeiro (RJ), Brazil.

[3] Dermatology Postgraduate Student, Tropical Dermatology Service, Hospital Central do Exército - Rio de Janeiro (RJ), Brazil.

[4] Dermatology Fellow, Hospital Heliopolis - São Paulo (SP), Brazil.

[5] Dermatology Postgraduate Student, Universidade Federal do Estado do Rio de Janeiro (UNIRIO) - Rio de Janeiro (RJ), Brazil.

[6] MSc from the UFRJ. Head of the Cosmiatry Department, IDPRDA / SCMRJ.

Correspondence:
Maria Victória Quaresma
Al. Itu, 1030, 9B – Jardim Paulista
Cep 01421-001
e-mail: mavi@mavictoria.com.br

Received on: 26/03/2016
Approved on: 02/12/2016

This study was performed at the Instituto de Dermatologia Professor Rubem David Azulay - Santa Casa da Misericórdia do Rio de Janeiro – Rio de Janeiro (RJ), Brazil.

Financial support: None

Conflict of interests: None

Fixed drug eruption on the face associated with dipyrone: correlation of clinical, histopathological and dermatoscopic findings

Erupção medicamentosa fixa na face associada a dipirona: correlação dos achados clínicos, histopatológicos e dermatoscópicos

DOI: http://dx.doi.org/10.5935/scd1984-8773.201684800

ABSTRACT

Adverse reactions associated with drugs presenting cutaneous manifestations are among the most common, expressing itself with multiple clinical aspects and causing significant morbidity. The fixed drug eruption (FDE) is a common adverse reaction with cutaneous involvement and is associated with the use of numerous drugs. Dipyrone is a drug with analgesic and antipyretic effects prescribed widely used in Brazil, however, it is known for its potential to triggering adverse reactions, including the FDE. This report shows an EMF case related to the use of dipyrone, with unique clinical presentation and correlate the clinical, histopathological and dermatoscopic found.

Keywords: dermoscopy; face; pathology

RESUMO

As reações adversas associadas aos fármacos com manifestações cutâneas não são raras, expressando-se com múltiplos aspectos clínicos, podendo gerar morbidade significativa. A erupção medicamentosa fixa é uma reação adversa comum, com envolvimento cutâneo, associada ao uso de inúmeros medicamentos. A dipirona é fármaco com efeitos analgésicos e antitérmicos amplamente utilizada no Brasil, porém, sabe-se que é uma substância potencialmente desencadeadora de reações adversas, e a erupção medicamentosa fixa entre elas. Relata-se um caso de erupção medicamentosa fixa relacionada ao uso da dipirona, com apresentação clínica singular e correlacionam-se os achados clínicos, histopatológicos e dermatoscópicos encontrados.

Palavras-chave: *dermoscopia; face; patologia*

INTRODUCTION

Adverse reactions to drugs can be defined as any response elicited by a given drug that is harmful, unintentional and occurs at the doses used by individuals for prophylaxis, diagnosis and treatment of diseases. [1] Reactions involving the skin, known as pharmacodermy, are among the most common and can have many clinical appearances – from solitary lesions up until generalized pictures. [2] Fixed drug eruption (FDE) is a common pharmacodermy and can be associated with the use of countless medicaments. [3] It was first described by Brocq,[1] FDE clinically arises as a macular, erythematous-violaceous, oval lesion with recurrence in previously affected sites, triggered by the re-exposure to the involved drug. This eruption may occur in any body area, mainly affecting mucosal surfaces. [4, 5]

Dipyrone is a non-steroidal anti-inflammatory derived from pyrazolone, being widely used as an analgesic. Numerous adverse reactions secondary to dipyrone are known: interstitial nephritis, hepatitis, pneumonitis and severe skin drug eruptions, such as the Stevens-Johnson and Lyell syndromes. [2] Despite being known, the association of this drug with FDE has only occasionally been reported in the literature, often linked to lesions involving the trunk and extremities. [5, 6]

In light of these facts, the authors of the present paper report a FDE case triggered by dipyrone, a drug that is widely used in Brazil, however with few reports describing this association. In addition, the unique clinical appearance of the case stands out, with facial involvement (periorbital and nasal regions), correlating it with the relevant histological and dermoscopic findings.

CASE REPORT

A 30 year-old female patient originary from the Brazilian Southeast state of Rio de Janeiro, bore hyperchromic macules on the face for one month. The patient referred using dipyrone to treat a headache 7 hours before the cutaneous picture emerged. She denied any systemic symptomatology, comorbidities or local trauma. The dermatological examination evidenced hyperchromic, grayish-brown, oval in shape, well delimited macules, bilaterally symmetric in the periorbital regions (Figure 1). There were no lesions in other cutaneous or mucosal sites. The possibility of FDE associated with dipyrone was raised, and the patient was instructed to avoid using this drug.

Four months after the initial event, the patient had recurrence of the picture with the extension of the lesions up until the nasal dorsum (Figure 2). During the examination, she denied the use of dipyrone, however describing the use of a diverse medication that reportedly contained dipyrone in it formulation.

The dermoscopic examination of the bilateral periorbital lesion showed a granular annular pattern with pigmented blurs and multiple bluish-gray dots ("peppering"), evenly distributed around the follicular ostia, with accentuation of the grayish-brown facial pseudo network (Figure 3).

The biopsy of the skin with the lesion was assisted by the dermoscopic examination, being performed where there was greater concentration of the blue-grayish granularity, known as peppering. [7]

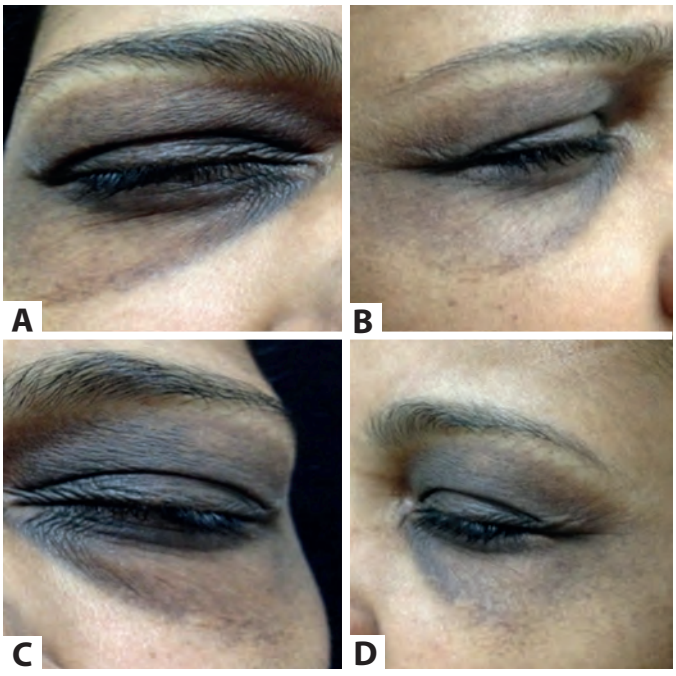


Figure 1: Fixed drug eruption. **A** and **B.** Hyperchromic, grayish-brown macula located in the right periorbital region. **C** and **D.** Macular lesion located in the left periorbital region

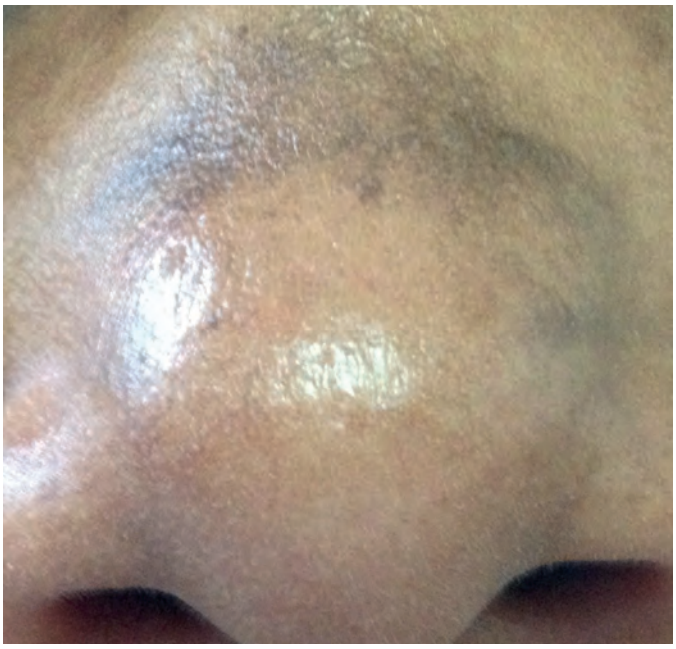


Figure 2: Hyperchromic, grayish-brown macula located in the nasal dorsum

The histological examination revealed: lymphocytic exocytosis, vacuolar degeneration of the basal layer, perivascular and superficial interstitial lymphocytic infiltrate, and melanophages in the papillary dermis, corroborating the diagnosis of FDE (Figure 4). In addition, melanophages were regularly distributed in the superficial dermis among the hair follicles (Figure 5).

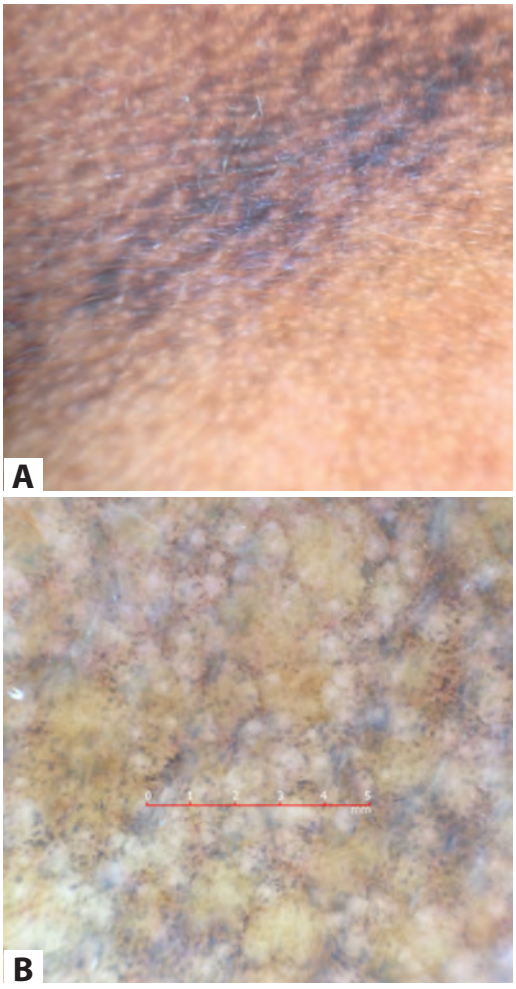


Figure 3: A: Dermoscopic findings - Accentuation of the grayish-brown facial pseudo network with presence of bluish-gray blurs evenly distributed around the follicular ostia (DermLite II PRO HR, 3Gen, California, USA, 10x); **B:** Dermoscopic findings – The rough peppering around the follicular ostia and hypochromia can be observed in detail after the treatment with Nd-YAG Q-Switched laser (Handyscope, Fotofinder Systems, Bad Birnbach, Germany, 20x).

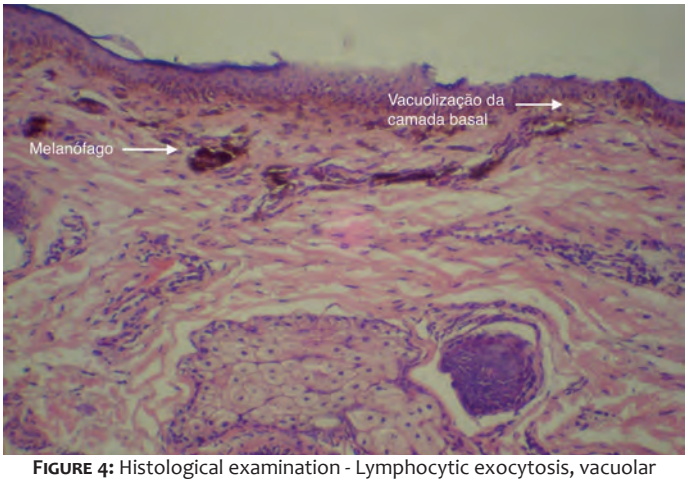


Figure 4: Histological examination - Lymphocytic exocytosis, vacuolar degeneration of the basal layer, perivascular lymphocytic and interstitial superficial infiltrate, and evidence of melanophages in the papillary dermis (hematoxylin-eosin)

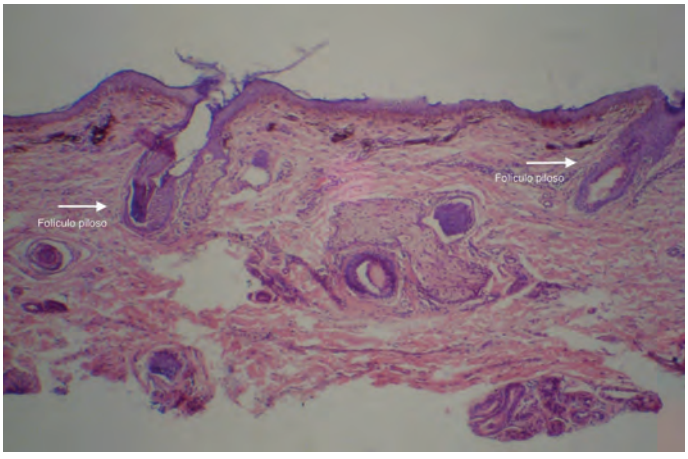


Figure 5: Histology - The presence of melanophages in the papillary dermis, sparing the hair follicles regions, stand out (hematoxylin-eosin)

DISCUSSION

Fixed drug eruption is a drug-related reaction linked to the use of numerous drugs (Table 1), [3-5,8,9] with no gender prevalence, predominantly occurring in the third decade of life. [3,4] Patients with family history of drug allergy or atopy have increased susceptibility to develop this pharmacodermy. [3]

The picture usually arises between 30 minutes and 8 hours after the use of the medication; however, manifestations within 24 hours have already been described. Classically, it has the appearance of a single erythematous or violaceous-erythematous, oval-shaped, well demarcated macula, with up to 10cm in diameter, which may progress with residual hyperpigmentation. It rarely emerges with multiple lesions. The more frequently involved regions are the mucous membranes and, in special, the genital and lip regions. [4]

The association of dipyrone with FDE is recognized by the literature, however there are few reports describing this relationship. [2,6] According to Sharma et al., [8] FDE triggered by this drug arises as a single lesion, affecting mainly the trunk and extremities. [5,6]

In the histological evaluation, FDE in its initial phase shows hydropic degeneration of the basal layer's cells, with apoptotic keratinocytes, lymphocytic perivascular infiltrate in the superior dermis, and may show sparse neutrophils, eosinophils and edema in the superficial dermis. [9] In its late stage, the presence of melanophages in the papillary dermis is remarkable – which can be the only finding in lesions with long development. [5,9]

Dermoscopy is an auxiliary diagnosis method that has been standing out for its practicality and clinical applicability, due

Chart 1: Main drugs associated to Fixed Drug Eruption

Antibiotics	Ampicillin
	Cephalosporins
	Clindamycin
	Dapsone
	Doxycycline
	Erythromycin
	Metronidazole
	Penicillin
	Sulfas
	Tetracycline
Antifungals	Griseofulvin
	Tinidazole
Non-opioid analgesics and anti-inflammatories	Acetylsalicylic acid
	Mefenamic Acid
	Diclofenac
	Dipyrone
	Eterocoxib
	Ibuprofen
	Indomethacin
	Naproxen
	Oxicans
	Paracetamol
Antiepileptics / Sedative and Hypnotic	Barbiturates
Antihistamines	Cetirizine
	Hydroxyzine
	Orfenadine
Laxative	Phenolphthalein
Chemotherapy	Paclitaxel

to its ability to recognize specific standards and criteria established for various dermatoses. The dermoscopic examination has peculiar patterns when performed on the face, since the epidermis presents attenuation and flattening of interpapillary cones and abundance of cutaneous adnexa, such as hair follicles' and eccrine glands' ostia. However, in the adult face, the conventional pigmented network usually seen at dermoscopy cannot be observed, for the epidermal crests are flat or absent; in the face, therefore, the pigmentation is described as a pseudo network, being characterized by brown pigmentation interspersed with circular spaces represented by follicular openings and glandular orifices. [10]

In the present case, dermoscopy evidenced a granular annular pattern, with bluish-gray blurs and dots (peppering), predominantly around the follicular ostia, corresponding to the melanophages aggregates in the papillary dermis observed in the histology. The pattern's bluish-gray color is attributed to the depth and extension of the melanin deposit in the papillary dermis. These melanin deposits are the result of the vacuolization of the epidermal basal layer associated with an inflammatory process, with the subsequent "fall" of the melanin pigment into the papillary dermis and phagocytosis by macrophages (melanophages). [7,10]

The case's dermoscopic characteristics suggest it is an underlying inflammatory condition. [7] On the other hand, the asymmetric pigmentation, when more pronounced at the edges of the follicular openings, with progressive obliteration of the ostia, is a criterion for suspicion in favor of melanocytic malignant lesions, such as lentigo maligna melanoma type. [10]

As a conclusion, recognizing the drug causing the FDE allows the proper management of the treatment, avoiding recurrences. The association of this disease with dipyrone is sparsely reported, especially when linked to the emergence of facial lesions. The use of dermoscopy allows the recognition of typical patterns, such as the observation of the granular, rough peppering as the preponderant dermoscopic criterion in the present case. The pigmentation's symmetrical and regular distribution was key to the suspicion of inflammatory dermatosis, since in most cases this finding corresponds to intradermal melanophages. [7] In this manner, despite the fact that histological analysis is considered the gold standard method for the diagnosis of FDE, in the present case dermoscopy was effective in assisting in the choice of an ideal site for performing the cutaneous biopsy. ∗

REFERENCES

1. Brocq L. Eruption erythemato-pigmentee fixe due a l'antipyrine. Ann Dermatol Venereol. 1894;5:308-313.
2. Bentur Y, Cohen O. Dipyrone overdose. J Toxicol Clin Toxicol. 2004;42(3):261-5.
3. Mahboob A, Haroon TS. Drugs causing fixed eruptions: a study of 450 cases. Int J Dermatol. 1998;37(11):833-8.
4. Heng YK, Yew YW, Lim DS, Lim YL. An update of fixed drug eruptions in Singapore. J Eur Acad Dermatol Venereol. 2015;29(8):1539-44.
5. Justiniano H, Berlingeri-Ramos AC, Sánchez JL. Pattern analysis of drug--induced skin diseases. Am J Dermatopathol. 2008;30(4):352-69.
6. Ozkaya-Bayazit E. Specific site involvement in fixed drug eruption. J Am Acad Dermatol. 2003;49(6):1003-7.
7. Bugatti L, Filosa G. Dermoscopy of lichen planus-like keratosis: a model of inflammatory regression. J Eur Acad Dermatol Venereol. 2007;21(10):1392-7.
8. Sharma VK, Dhar S, Gill AN. Drug related involvement of specific sites in fixed eruptions: a statistical evaluation. J Dermatol. 1996; 23(8):530-4.
9. Joshi R. Interface dermatitis. Indian J Dermatol Venereol Leprol. 2013;79(3):349-59.
10. Stolz W, Schiffner R, Burgdorf WH. Dermatoscopy for facial pigmented skin lesions. Clin Dermatol. 2002;20(3):276-8.

Reconstructing surgical defects of the nasal tip in a single-stage procedure

Reconstrução de defeitos cirúrgicos da ponta nasal em único tempo cirúrgico

DOI: http://dx.doi.org/10.5935/scd1984-8773.201684884

ABSTRACT

Repairing surgical defects of the nasal tip is challenging, mainly because of the lack of freely mobile skin available peripherally. The Peng flap is a one-stage cutaneous flap that circumvents this difficulty by recruiting skin from the nasal dorsum and sidewall regions. The design produces a tridimensional shape perfectly adapted to the conFiguretion of the nasal tip and allows for an inconspicuous closure of the defect. Herein, we describe a modified version of a Peng flap in a single-stage procedure, performed in three patients subjected to excison of basal cell carcinomas.

Keywords: nose; nose neoplasms; carcinoma, basal cell; surgical flaps

RESUMO

A reconstrução de defeitos cirúrgicos envolvendo a subunidade da ponta nasal coloca desafios particulares já que essa região é rodeada de pele de difícil mobilização. O retalho de Peng é retalho cutâneo passível de ser executado num único tempo cirúrgico que ultrapassa essa dificuldade mobilizando pele do dorso e das vertentes laterais do nariz. O seu desenho permite alcançar forma tridimensional adaptada à conFigureção da ponta nasal e produz excelentes resultados estéticos. Descreve-se a realização de uma modificação do retalho de Peng em único tempo cirúrgico, em três pacientes submetidos a excisão de carcinomas basocelulares.

Palavras-chave: *retalhos cirúrgicos; carcinoma basocelular; nariz; neoplasias nasais*

Authors:
Artur Jorge Fernandes César[1]
Ana Margarida Barros[2]
Paulo Henrique Santos[2]
Filomena Maria Azevedo[3]

[1] Resident Physician, Dermatology and Venereology Service, Centro Hospitalar São João EPE, Portugal. Visiting Assistant Physician, Faculdade de Medicina, Universidade do Porto - Porto, Portugal.

[2] Garduate Hospital Assistant, Dermatology and Venereology Service, Centro Hospitalar São João EPE.

[3] Head of Dermatology and Venereology Service, Centro Hospitalar São João EPE.

Correspondence:
Artur Jorge Fernandes César
Serviço de Dermatologia e Venereologia
Centro Hospitalar São João EPE
Alameda Prof. Hernani Monteiro
4200-319 Porto, Portugal.
e-mail: arturjfc@gmail.com

Received on: 09/08/2016
Approved on: 10/11/2016

This study was performed in the Centro Hospitalar São João EPE - Porto, Portugal.

Financial support: None
Conflict of interests: None

INTRODUCTION

Basal cell carcinoma (BCC) is the most common non-melanoma skin cancer affecting the head and neck regions. [1] Nearly 80% of all BCCs arise in the facial region, with up until 30% of these, occurring in the nose. [2] Surgical excision is the treatment of choice; however, it is often challenging to close the surgical defects when they are located in the nasal tip, mainly due to the lack of elastic and mobile skin at the defect's periphery so that direct suture can be performed.

METHODS

This paper describes 3 cases of women with full thickness surgical defects located in the nasal tip, resulting from the excision

of BCCs, in which the used reconstructive technique was a modified version of the Peng flap.

The purpose of the present article is to describe this reconstruction technique, demonstrate its aesthetic results and discuss its surgical applicability in light of the literature and the authors' experience.

Three patients bearing BCCs in the nasal tip (nodular, micronodular and morpheaform types, respectively) underwent wide excision of the tumors. In two of the cases the removal of the BCC and the closure of the surgical wound were performed in one surgical time. In the other case, due to the morpheaform lesion's poor delimitation, the BCC was excised in the first surgical time, with the closure being performed in a second surgical time, after margins free of neoplasia were histologically confirmed.

The post-excisional defects measured between 1.6cm and 2.0cm horizontally and between 1.6cm and 2.2cm vertically (Figures 1A, B and C). The intraoperative steps of the closure technique were as follows (Figure 2):

- The flap was demarcated with the incision beginning in the surgical defect's distal margins, continuing laterally and superiorly, along the ala nasi folds and the transition between the nose's lateral region and the malar region;
- Local with 1% lidocaine was performed in the nasal pyramid;
- After the incision of the skin was carried out, the flap and the surrounding skin were separated from the subcutaneous plan. Meticulous hemostasis was performed at this moment aimed at avoiding any bleeding or hematoma that might compromise the flap's survival;
- The distal extremities of each of the flap's "arms" were trimmed (in order that a thickness adequate to the defect could be obtained) and sutured in place using resorbable subcutaneous sutures 4-0;
- The excess of triangular skin in the center of the flap's "arms" were removed later on. (Note: in midline defects, the triangle's direction should be vertical, while in eccentric defects it must be directed obliquely towards the wider "arm" of the flap);
- Once the deep resorbable sutures are completely put in place along the flap's limits, the removal of the redundant tissue in the eye's medial epicanthus area is sometimes necessary in order to prevent "dog ear" deformities;
- Finally, the epidermis was approximated using non-resorbable sutures 5-0 with the proper eversion of the wound's edges;
- The non-resorbable sutures were removed between 8 and 10 days after the procedure, and the patients re-evaluated monthly for the first 4 months.

RESULTS

The postoperative recovery was uneventful. Figures 1D, 1E and 1F depict the outcomes 4 months after the reconstructive surgery, with absence of any distortion of the nasal anatomy and with excellent aesthetic results.

DISCUSSION

The reconstruction of surgical defects in the nasal tip poses particular difficulties given the three-dimensional shape form the latter and the limited area from which to mobilize skin with similar characteristics (thickness, color and adnexa composition). The more frequently used closure methods in this location are: the primary closure (small defects), cutaneous flaps (bilobed flap, dorsal-nasal glabellar flap, Rintala flap, bilateral rotation flap and frontal paramedian flap), and skin grafts.

The Peng cutaneous flap is seen as an advancement and rotation flap that was initially described by Peng et al. in 1987. [3] This flap's fundamental concept is a "pincer-like" modification applied to the Rintala flap (linear advancement flap starting in the glabella and dorsum of the nose), classically used to repair defects on the nasal dorsum and tip. [3] This modification allows the closure of larger defects in the nasal tip, taking advantage of the skin excess in the lateral wall of the nose, and improves the

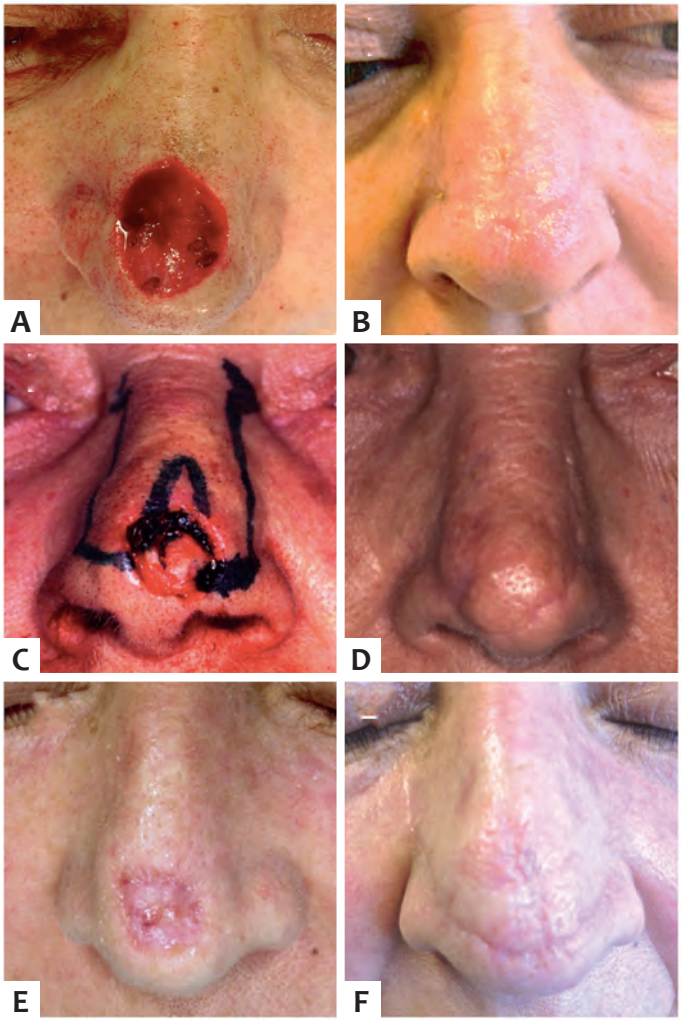


Figure 1: A, B and C – Surgical defects after the excision of the BCCs in the nose (Note: the image of last BCC was recorded 2 weeks after the excision of a morpheaform BCC aimed at obtaining histological confirmation of the free margins). **D, E and F -** outcomes 4 months after the surgery

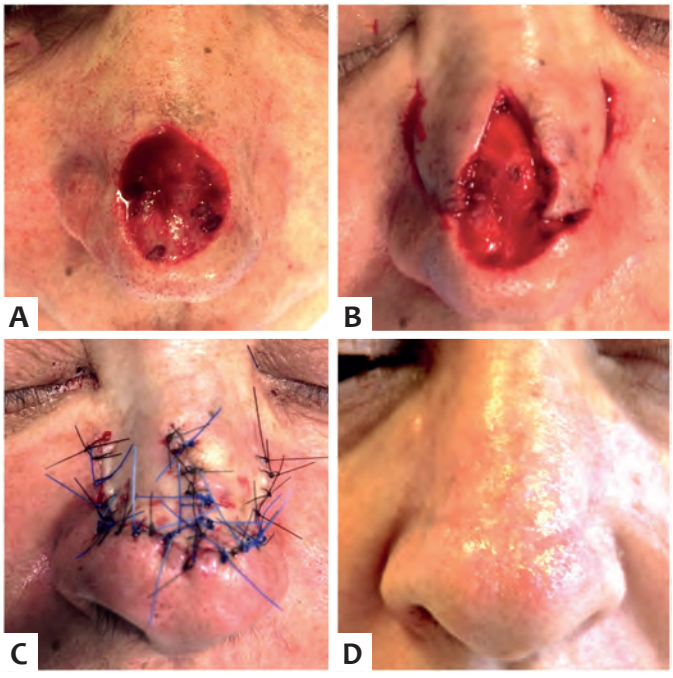


Figure 2: A - Surgical defect in the nasal tip after widened excision of the BCC; **B -** Once the incisions were carried out, the flap is elevated in the subcutaneous plane. Meticulous hemostasis should to be performed n this phase; **C -** After the suture of the flap's ends, the excess of central tissue is removed, and once the deep resorbable sutures are put in place, the epidermis is closed with non-resorbable sutures. **D -** Outcomes 4 months after surgery

flap's survival, since it reduces the length and widens the pedicle's base. Furthermore, the medial rotation movement in its two "arms" produces a convex configuration that perfectly adapts to the nasal tip's three-dimensional shape. [4]

In 1995, Rowe et al. proposed to begin the incisions of the flap's two "arms" more distally regarding the defect, thus reducing the extent of the flap's advancement. [4] More recently, Ryan et al. added another modification, placing the incisions more laterally along the transition between the nose and the cheek. In most of the total thickness defects in the nasal tip that the authors have performed in their care service practice, they have implemented the last version of the modified Peng flap. This is not only due to the fact that the pedicle's base is larger therefore improving the flap's survival, but also because it produces better aesthetic outcomes since the incisions are placed along the junctions between different facial aesthetic units. [5] Moreover, this flap's symmetrical shape minimizes the risk of asymmetrical distortion of the nose, especially of the nasal ala, a complication sometimes observed in other flaps used in the nasal tip. [4]

In the authors' experience with more than 20 patients who underwent this procedure, the Peng flap led to excellent results in medium/large nasal tip defects, whether paramedian or located in the midline. It still leads to good outcomes in defects simultaneously involving the distal portion of the nasal dorsum and the tip of the nose. However, the authors' opinion is in line with that of others, who advocate that this flap is not suitable for most defects affecting more than 50% of the nasal tip subunit or deep defects involving cartilage. In these cases, the additional volume of frontal paramedian flaps, skin grafts or composite techniques, should be considered. The authors of the present paper did not observe cases of distortion or complications with this technique; nonetheless, this flap is not exempt from possible complications. In addition to cases of partial necrosis and infection, cases of elevation of the nasal alae have been described in larger defects, as well as asymmetries in eccentric defects, corrected by this technique. [4,5]

CONCLUSIONS

In conclusion, this modification of the Peng flap is a reconstructive technique for defects in the nasal tip, even when they extend up until the nasal dorsum, being capable to be executed in a single surgical time. This flap usually leads to excellent matching of color and texture with the perilesional skin, preserves the nasal architecture and results in minimum surgical scars, which are camouflaged in the transition lines between facial aesthetical subunits. Thus, the authors of the present paper are of the opinion that this is an essential tool for the dermatologic surgeons' armamentarium for reconstructing defects in the nasal tip.

REFERENCES

1. McGuire JF, Ge NN, Dyson S. Nonmelanoma skin cancer of the head and neck I: histopathology and clinical behavior. Am J Otolaryngol. 2009;30(2):121-33.
2. Choi JH, Kim YJ, Kim H, Nam SH, Choi YW. Distribution of Basal cell carcinoma and squamous cell carcinoma by facial esthetic unit. Arch Plast Surg. 2013;40(4):387-91.
3. Peng VT, Sturm RL, Marsh TW. "Pinch modification" of the linear advancement flap. J Dermatol Surg Oncol. 1987;13(3):251-3.
4. Rowe D, Warshawski L, Carruthers A. The Peng flap. The flap of choice for the convex curve of the central nasal tip. Dermatol Surg. 1995;21(2):149-52.
5. Ahern RW, Lawrence N. The Peng flap: reviewed and refined. Dermatol Surg. 2008;34(2):232-7.

New Techniques

Basal Cell Carcinoma with unusual location in the ear - surgical reconstruction

Carcinoma basocelular de localização inusitada na orelha - reconstrução cirúrgica

Authors:
Cibele Conceição dos Apóstolos Pereira[1]
Vando Barbosa de Sousa[1]
Solange Cardoso Maciel Costa Silva[2]
Candida Naira Lima and Lima Santana[3]
Mario Chaves Loureiro do Carmo[4]
Paula Renaux Wanderley Caratta Macedo[5]

[1] Dermatology Resident Physician, Hospital Universitário Pedro Ernesto – Universidade do Estado do Rio de Janeiro (Hupe/Uerj) - Rio de Janeiro (RJ), Brazil.

[2] Head of the Dermatologic Surgery Service, Hupe/Uerj.

[3] Dermatology Post-graduate Student, Hupe/Uerj.

[4] Dermatologist Physician and Research Assistant, Hupe/Uerj.

[5] Collaborating Dermatologist Physician, Dermatology Service, Hupe/Uerj.

Correspondence:
Cibele Conceição dos Apóstolos Pereira
Boulevard 28 de Setembro, 77 - Vila Isabel
Cep 20551-030 Rio de Janeiro (RJ), Brazil
Email: cibelecap@hotmail.com

Received on: 11/06/2016
Approved on: 12/08/2016

This study was performed Hospital Universitário Pedro Ernesto – Universidade do Estado do Rio de Janeiro (Hupe/Uerj) - Rio de Janeiro (RJ), Brazil.

Financial support: None
Conflict of interests: None

DOI: http://dx.doi.org/10.5935/scd1984-8773.201684836

ABSTRACT

The skin flaps are surgical techniques particularly useful to aesthetic repair in cases of extended excision and/or unusual sites, as in the ear. Many skin flaps options were already reported, resulting in variable results of the theoretical knowledge and practical experience of the surgeon. This article aims to describe two successful cases of ear reconstruction with the use of anterior and posterior flaps and to review the current literature.
Keywords: surgical flaps; ear; carcinoma, basal cell

RESUMO

Retalhos cutâneos constituem técnica cirúrgica particularmente útil para reparos estéticos nos casos de excisões extensas e/ou lesões de localizações peculiares, como a orelha. Diversas opções de retalhos cutâneos já foram descritas, determinando resultados variáveis que dependem do conhecimento teórico e da experiência prática do cirurgião. O objetivo deste artigo é relatar dois casos de sucesso com a utilização das técnicas de retalhos anterior e posterior para reparação da orelha e revisar a literatura afim.
Palavras-chave: *retalhos cirúrgicos; orelha; carcinoma basocelular*

INTRODUCTION

Cutaneous flaps constitute an important reconstructive technique in dermatologic surgery. They are characterized by the maintenance of the original vascular pedicle in the tissue to be transplanted and, for didactic purposes, can be classified into: advancement, rotation, transposition, interpolation, island and subcutaneous flaps. [1] Aiming at obtaining the best aesthetic outcome, the choice of the surgical technique for reconstructing facial areas must consider items such as vascularization, tension caused by the suture, skin redundancy, tension lines, the surgeon's experience with a certain technique and the base condition, among other factors.[1,2] The ear is comprised by the auricle (formed by cartilage with convexities and concavities covered with thin skin), the lobe (fibroadipose tissue) and the external auditory meatus.[1] Due to the small amount of skin available and restricted vascularization, in addition to the fact that the ear is an

area difficult to manipulate, the surgical reconstruction in that region is challenging.

Basal cell carcinoma (BCC) is a common cutaneous neoplasm whose excision does not always allow primary closure of the surgical incision, especially in the ear. In this paper, the authors describe their experience with the reconstruction of the triangular fossa – a branch of the anti-helix and concha – after excision of BCC, employing flaps originated from similar cosmetic units using two different techniques.

METHODS

Case 1

A 46 year-old male patient who did not have comorbidities bore a lesion in the auricular anti-helix with approximately 3cm in diameter in its longest axis and that was clinically suggestive of BCC.

Anterior auricular flap surgical technique

After both the lesion to be excised (Figure 1) and the pre-auricular flap were marked, local anesthesia and regional block were carried out with 2% lidocaine, epinephrine and 8.4% sodium bicarbonate solution.

The removal of the nodular lesion located in the triangular fossa was performed using curettage followed by spindle excision up until the cartilage was exposed (Figure 2).

Next, the flap was prepared in the pre-auricular region (Figure 3). The transection of the helix by the flap's pedicle and subsequent positioning on the open area was performed via an incision in the helix's skin and cartilage (Figure 4). Suture with 5.0mm mononylon thread for internal stitches was then carried out, followed by a simple suture for attaching the flap to the receiver area.

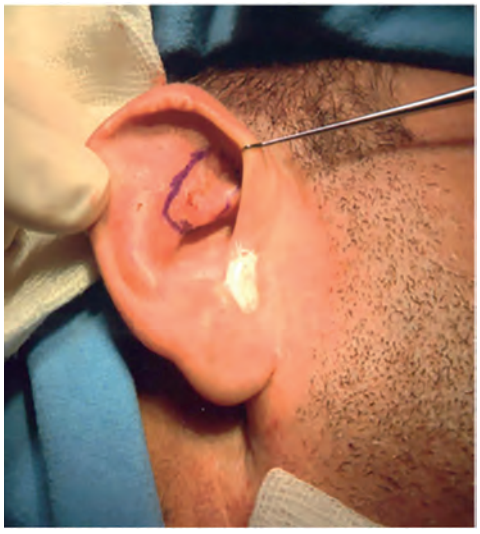


Figure 1: Marking of the area corresponding to the basal cell carcinoma

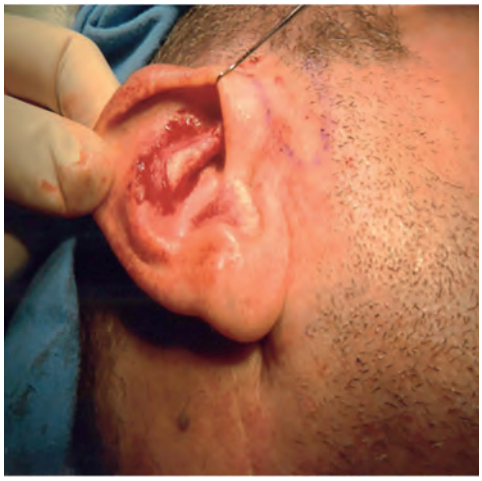


Figure 2: Surgical defect after the removal of the tumor

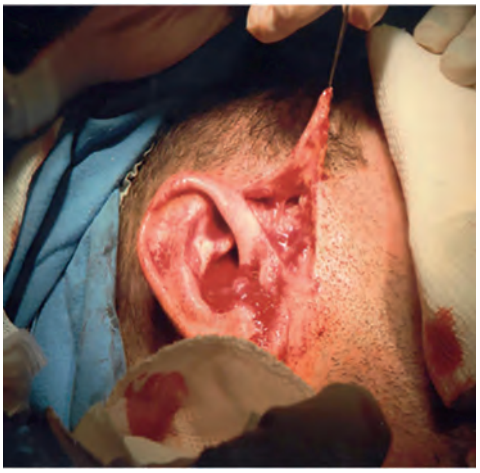


Figure 3: Excision of the interpolation flap aimed at filling the triangular fossa's and scapha's defects

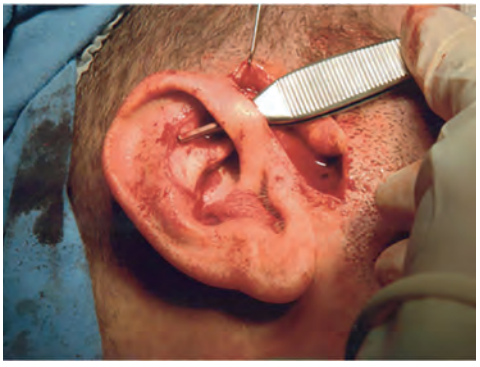


Figure 4: Detail: opening in the cartilage for sliding the flap

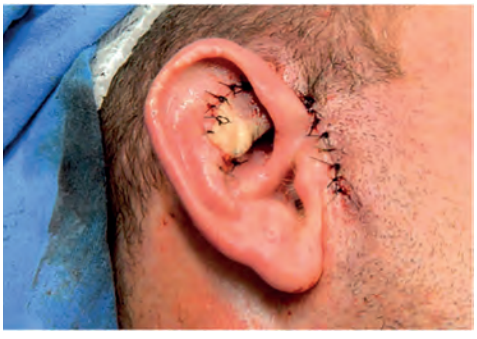


Figure 5: Flap positioned and sutured

The surgery was completed with the primary closure of the donor area in the anterior auricular region (Figure 5).

The pedicle resection and the defect closure was carried out in a second surgical time using 5.0 mononylon thread.

Case 2

A 83-year-old male patient with chronic obstructive pulmonary disease had been bearing a pruriginous ulcerated lesion located at the auricular concha for 8 months. The lesion had progressively grown in the previous 4 months. Clinical examination evidenced an ulcerated lesion with pearly border, as well as telangiectasias, suggesting the clinical diagnosis of BCC.

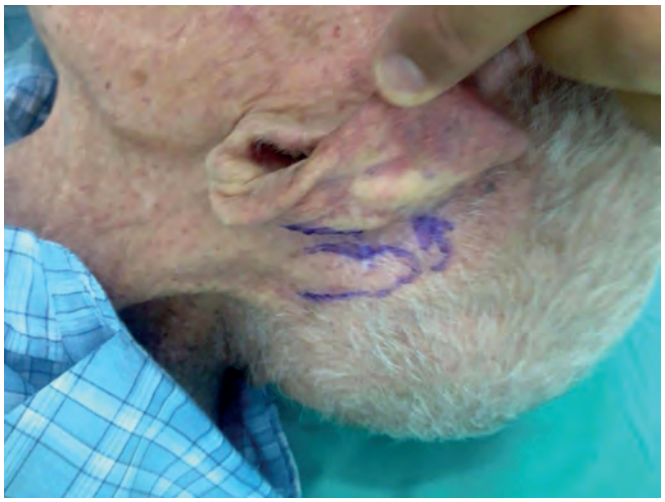


Figure 6: Marking of the retroauricular flap

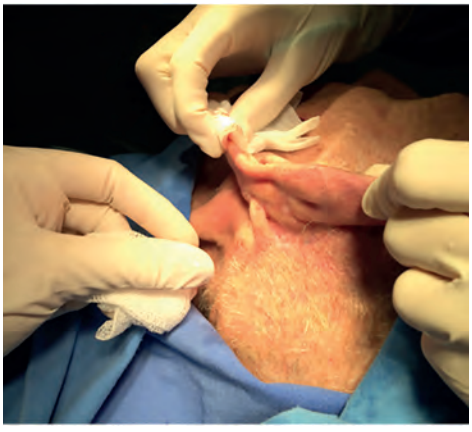


Figure 7: Pedicle before resection

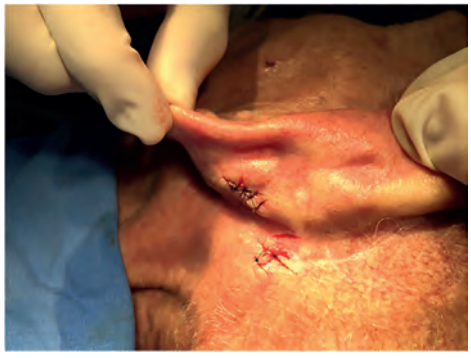


Figure 8: Outcome after resection of the pedicle

Posterior auricular flap surgical technique

The excision of the lesion located in the auricular concha was performed similarly to that described in Case 1.

In Case 2, however, the flap was originated from the retroauricular region, having been transfixed through the concha's cartilage, aimed at accommodating the flap in the receiving area (Figure 6). The suture was the carried out for attaching the flap in the receiving bed and primarily closing the donor area. The resection of the pedicle and closure of the defect were performed in the second surgical time (Figures 7 and 8).

RESULTS

Both ear reconstruction techniques were successfully performed with absence of complications, leading to excellent aesthetic and functional outcomes, based on the use of flaps prepared using both the anterior and posterior regions.

In both cases, the pathological examination's result of the surgical specimen evidenced BCC with free margins.

DISCUSSION

The use of flaps for reconstructing the ear after the excision of tumors is the most indicated technique, for direct closure is not feasible and grafts are difficult to adhere to this region. [1,2] Sites with adequate similarity and rich vascularity should be used as donor areas. [2-4] Among the sites compatible for ear reconstruction, the pre-auricular [5] and posterior auricular areas, as well as the retroauricular sulcus and the mastoid region stand out. [3,4]

Interpolation flaps are performed by shifting the tissue to a nearby – but not contiguous – receiver area. [1] This technique was chosen due to the possibility of better local vascularization and aesthetic outcome, as compared to the second-intention closure. [2,6]

Despite being the first choice in the reconstruction of the concha, the posterior flap's interpolation technique (or Masson's flap), firstly described in 1972, is a high-risk procedure. [6] The tissue tends to allow only a narrow pedicle, and performing the rotation inside the ear hampers local blood circulation. [6] Stemming from these characteristics, complications, such as necrosis, might arise. [7] Nevertheless, the literature does not highlight the need to preserve the posterior auricular artery's pedicle and suggests that the preservation of 50% of the flap's vascular pedicle is sufficient for its viability. [7]

In this flap type, special attention should be given to the second surgical time 3 weeks after the primary approach, making possible proper revascularization, adhesion and viability of the transferred tissue. [2] This caution was observed in the reported cases. The need for the second surgical time is however a limiting factor for patients with low adherence to the treatment, with the risk of loss of follow-up. [8] As a consequence, the need for an additional intervention after the first surgery should be explained to the patient.

The pre-auricular region's flap was initially described by Pennisi and is also an option when it is not feasible to use retroauricular flaps (for instance, when there is a tumor in this region). [9] While thin, the flap originating from this area has the advantage that it can be used in the reconstruction of the upper and lower regions of the ear, [10] as well as being a better option than closure by second intention (associated with increased risk of infection and retraction as compared to covering the cartilage with flaps). [2,9]

Due to the use of similar aesthetic units (skin with similar color and texture), this technique leads to a good aesthetic outcome and preserves the anatomy of the ear pavilion by maintaining its natural curvature. [8, 10]

CONCLUSION

The anterior and posterior ear flaps techniques should be part of the therapeutic armamentarium for the correction of larger surgical defects arising from the removal of extensive tumoral lesions, preserving the site's anatomy, functionality and aesthetics.

REFERENCES

1. Silva, SCMC. Técnica Avançada de Excisão. In: Cirurgia Dermatológica Teoria e Prática. Rio de Janeiro: DiLivros; 2008. p. 173 – 256.
2. Cordova A, D'Arpa S, Pirrello R, Giambona C, Moschella F. Retroauricular skin: a flaps bank for ear reconstruction. J Plast Reconstr Aesthet Surg. 2008;61(Suppl 1): S44-51.
3. Lynch J, Mahajan AL, Regan P. The trap door flap for reconstructing defects of the concha. Br J Plast Surg. 2003;56(7):709-11.
4. Johnson TM, Fader DJ. The staged retroauricular to auricular direct pedicle (interpolation) flap for helical ear reconstruction. J Am Acad Dermatol.1997;37(6): 975-8.
5. Sánchez-Sambucety P, Alonso-Alonso T, Rodríguez-Prieto MA. Tunnelized Preauricular Transposition Flap for Reconstruction of Anterior Auricular Defects. Actas Dermo-Sifiliográficas. 2008,99(2):161-162.
6. Masson, JK. A simple island flap for reconstruction of concha-helix defects. Br J Plast Surg. 1972;25(4):399-403.
7. Talmi YP, Horowitz Z, Bedrin L, Kronenberg J. Auricular Reconstruction with a Postauricular Myocutaneous Island Flap: Flip-Flop Flap. Plast Reconstr Surg. 1996; 98(7):1191-9.
8. Suchin KR, Greenbaum SS. Preauricular Tubed Pedicle Flap Repair of a Superior Antihelical Defect. Dermatol Surg. 2004;30(2 Pt 1):239-41.
9. Braga AR, Pereira LC, Grave M, Resende JH, Lima DA, De Souza AP, et al. Tunnelised inferiorly based preauricular flap repair of antitragus and concha after basal cell carcinoma excision: Case report. J Plast Reconstr Aesthet Surg. 2011;64(3): e73-5.
10. Pennise VR, Klabunde EH, Pierce GW. The Preauricular Flap. Plast Reconstr Surg. 1965;35:552-6.

Case Reports

Surgical approach to multiple foreign body granulomas (PMMA)

Tratamento cirúrgico seriado de múltiplos granulomas por PMMA

Authors:
Guillermo Loda[1]
Francine Papaiordanou[2]
Joaquim José Teixeira de Mesquita Filho[3]
Bruna Souza Félix Bravo[4]
Luciana de Abreu[5]
Tullia Cuzzi[6]

[1] Instructor, Dermatologic Surgery, Instituto de Dermatologia Prof. Rubem David Azulay – Santa Casa de Misericórdia do Rio de Janeiro – Rio de Janeiro (RJ), Brazil.

[2] Dermatology Resident Physician, Instituto de Dermatologia Prof. Rubem David Azulay.

[3] Head of the Dermatologic Surgery Sector, Instituto de Dermatologia Prof. Rubem David Azulay.

[4] MSc in Medicine from the Universiade Federal do Rio de Janeiro (UFRJ). Head of the Cosmiatry Sector, Instituto de Dermatologia Prof. Rubem David Azulay. Head of the Cosmiatry Sector, Hospital Federal da Lagoa - Rio de Janeiro (RJ), Brazil. Specialist member of the Brazilian Society of Dermatology (SBD) and the Brazilian Society of Dermatologic Surgery (SBCD).

[5] MSc Student in Clinical Medicine, UFRJ. Specialist member, SBD. Preceptor, Instituto de Dermatologia Prof. Rubem David Azulay.

[6] Associate Instructor, Pathology Department, UFRJ. Researcher at the Instituto Nacional de Infectologia, Fundação Oswaldo Cruz (Fiocruz) – Rio de Janeiro (RJ), Brazil.

Correspondence:
Francine Papaiordanou
R. Santa Luzia, 206 / Centro
Cep 20020-022 - Rio de Janeiro (RJ), Brazil
e-mail: francinepapaiordanou@gmail.com

Received on: 17/03/2016
Approved on: 20/07/2016

This study was performed at the Instituto de Dermatologia Prof. Rubem David Azulay – Santa Casa de Misericórdia do Rio de Janeiro – Rio de Janeiro (RJ), Brazil.

Financial support: None
Conflict of interests: None

DOI: http://dx.doi.org/10.5935/scd1984-8773.201684793

ABSTRACT

Injectable fillers have long been used for cosmetic purposes and in HIV induced lipodystrophy patients. A foreign body granuloma may be a side effect of the application of absorbable products/temporary and most often the nonabsorbable/permanent fillers. It is not possible to predict the formation of these granulomas, and it may occur regardless of the application technique. In this article we describe the surgical treatment of a patient with multiple granulomas caused by intradermal injection of PMMA in the face, with poor response to conservative treatments, and severe psychosocial impairment due to this unsightly and disfiguring complication.

Keywords: polymethyl methacrylate; granuloma; ambulatory surgical procedures

RESUMO

Substâncias para preenchimento têm sido muito utilizadas nos últimos anos em procedimentos estéticos e para correção de lipodistrofias em pacientes HIV-positivos. O granuloma de corpo estranho pode ser secundário à aplicação de produtos absorvíveis/temporários e mais frequentemente aos preenchedores inabsorvíveis/permanentes. Não é possível prever a formação desses granulomas que podem ocorrer independentemente da técnica utilizada. Neste artigo descreve-se o tratamento cirúrgico de uma paciente com múltiplos granulomas causados por preenchimento intradérmico prévio de PMMA na face, com resposta pobre a tratamentos conservadores, e com grave comprometimento psicossocial devido a essa complicação inestética e deformante.

Palavras-chave: *polimetil metacrilato; granuloma; procedimentos cirúrgicos ambulatoriais*

INTRODUCTION

In the few last years, filling substances have been widely used in aesthetic procedures and for the correction of lipodystrophy in HIV-positive patients. Products containing hyaluronic acid in different densities, bovine collagen, autologous fat, liquid silicone, poly-l-lactic acid and polymethyl methacrylate (PMMA), among others are widely used for this purpose. [1] According to the product's bioavailability and its chemical composition and degradation capacity, these substances can be classified as temporary or permanent, organic or inorganic and autologous or heterologous. [2,3]

In order for a substance to be considered safe, some important aspects should be taken into account: it must be biocompatible, phagocytosis resistant, stable, non-migratory, induce the least possible inflammatory response, not be carcinogenic or teratogenic [2].

Polymethyl methacrylate (PMMA) is a polymer composed of synthetic microspheres of 30μm to 40μm, with homogenous surface, conveyed suspended in a 1:3 solution (3.5% bovine collagen and lidocaine) or in carboxymethylcellulose colloid solution. [4] It should be strictly applied in the deeper layers of the dermis. [1,5] It initially promotes volumization, however has the capacity to stimulate neocollagenesis, with long-term effects.

The application of PMMA might be related to some adverse effects, such as nodules, inflammation, allergic reactions, dyschromias, necrosis, infection and foreign body granuloma formation. [6-8] Although described in the literature as rare, these complications are often permanent and very difficult to treat.

The foreign body granuloma can be secondary to absorbable/temporary products and, more often, to nonabsorbable/permanent fillers. It is not possible to foresee the formation of these granulomas, which can occur regardless of the used technique. Granulomas often form many years after the first application. [9]

The present paper describes the surgical treatment of a patient bearing multiple granulomas caused by a previous PMMA based intradermal filling in the face, with a poor response to conservative treatments and severe psychosocial compromise due to this unsightly and deforming complication.

CASE REPORT

A 63-year-old female patient reported having undergone facial filling 18 years before, observing the onset of palpable hardened cylindriform nodular lesions painful on palpation, located in the sites of prior application of the product. The nodules were not adhered to deep subcutaneous planes.

Ultrasonographic examination of the face showed heterogeneous elongated hypoechoic images, superficial and with defined limits, located between the skin and the subcutaneous tissue, bilaterally dispersed in the malar, periorbital, temporal and supralabial regions, in addition to the nasogenian sulcus. Dimensions varied from 3.2 x 0.8 x0.5cm in the left malar region to 3.6 x 2.4 x 0.5cm in the right malar region. Doppler examination evidenced avascular images. A new ultrasound examination was performed 1 year after the first, revealing poorly-defined nodular images with the following measures: 12mm in the left nasal region; 6.6mm in the left nasogenian sulcus; 8.1mm in the superior right labial region; 11.2mm in the right nasogenian sulcus; 14.0mm in the right temporal region; and 11.0mm in the left temporal region. The examinations were performed in diverse laboratories – note that the lesions were first measured in *cm* and then in *mm*.

Magnetic resonance imaging of the face (performed with contrast) showed multiple heterogeneous nodular formations, with lobular borders and isointense signal at t1 and predominantly intense in t2 and stir, showing slight contrast uptake, with confluent appearance in the subcutaneous of the malar and mandibular regions, nasogenian sulcus, bilaterally periorbicular, possibly corresponding to foreign bodies.

The histology of one of the lesions demonstrated it was a foreign body granuloma (Figure 1).

The patient underwent multiple facial surgeries aimed at correcting the unsightly defects secondary to PMMA filling.

Due to the fact that the zygomatic region's surfaces are convex and have multiple static rhytids, a decision was made to perform the w-plasty technique, aimed at obtaining a scar with a more irregular pattern, aligned with the skin's tension lines, thus being less apparent. The w-plasty consists of triangular advancement flaps uniformly interposed, parallel to the relaxed skin tension lines (RSTL). A scalpel blade n. 11 was used, observing a minimum of 60 degrees for the triangles' angles. The closure was performed with simple stitches and nylon thread 6.0.

The nasogenian and melomentonian grooves had lesions with clinical and histological characteristics similar to those in the zygomatic region.

A choice was made to perform long incisions positioned inside the grooves so that they could be hidden in the RSTL.

A "hockey stick" incision was used in the angle of the mouth's region, allowing a more cautious divulsion of the nodules located in that area.

Surgeries with the same characteristics were performed in four surgical times, with intervals of approximately 1 month, progressing with good cicatrization, without infectious complications and satisfactory aesthetic outcome, according to the patient's report (Figures 2 and 3).

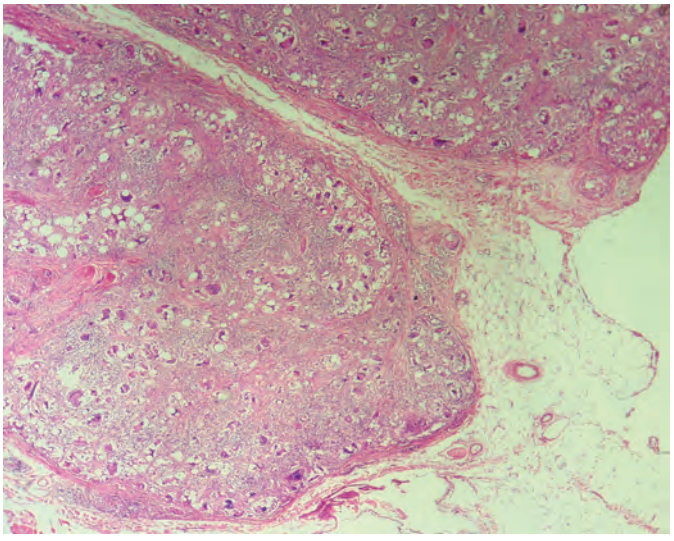


Figure 1 : Slide with 4x magnification reveals infiltrate with arrangement nodular and vacuoles, surrounded by fibrous tissue, characterizing a foreign body granuloma

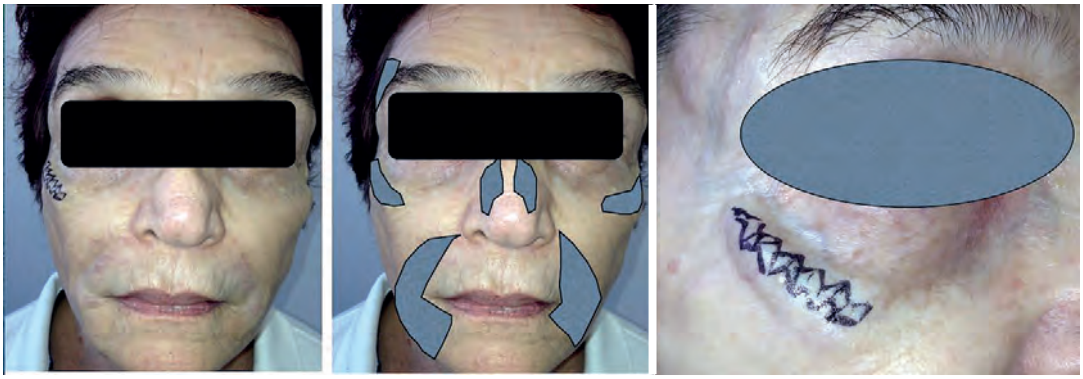


Figure 2: Areas marked in gray delimit sites with hardened subcutaneous nodules (nasogenian sulcus, temporal, zygomatic, lateral wall of the nose and melolabial sulcus, bilaterally). Preparing the W-shape or "broken lines" in the right zygomatic region

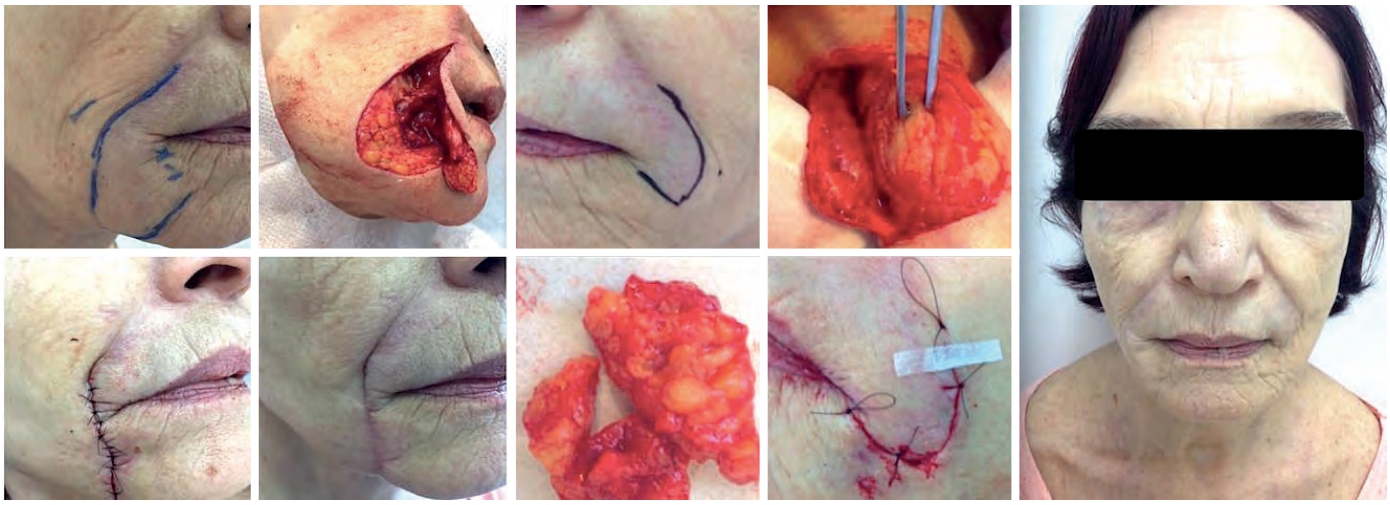


Figure 3: Surgical times: **A.** Marking of the hardened area, comprising the nasogenian and melolabial sulci to the right; **B.** Excised granuloma bed; **C.** Suture along the skin's tension lines; **D.** Seventh postoperative day; **E.** Arciform marking in the nasogenian sulcus region and left labial commissure; **F.** Divulsion of the area to be excised; **G.** Removal of the nodule with hardened consistency; **H.** Suture along the skin's tension lines; **I.** Final appearance after multiple interventions for correcting unsightly defects resulting from PMMA.

DISCUSSION

Applications of synthetic polymers in the skin generate some degree of inflammatory response, due to either the trauma caused by the application or the interaction of the receptor's tissue with the implant.

The particulate filler's biocompatibility varies according to the particles' size, shape and surface. When they are irregular, they cause greater inflammatory response, while varied sizes induce a higher degree of foreign body reaction. According to the recent literature, granuloma formation occurs in between 0.01% and 2.5% of applications. [2]

Three days after the PMMA injection, monocytes invade the implant, and on the sixth day they differentiate into fibroblasts. In two or three weeks the connective tissue infiltrates the material, forming clusters of the product, and the neovascularization becomes more evident. The autologous collagen fibers' density increases during the four months after the application, when the fibrosis and active vascularization. [2]

The presence of foreign body giant cells is evident after the first week after the application, reaching its maximum number around the third week and remaining at that level for two months. The late mass development of giant cells indicates the formation of foreign body granuloma formed by multinucleated giant cells and macrophages arranged in palisade with a lymphocytic halo. [1]

The reason that the host reacts with a granulomatous inflammatory response in these cases is still unknown. Some authors believe that a mild chronic inflammation may occur due to improper location of the filler or even to the displacement of the material to more superficial skin layers. There are some therapeutic options for the management of this complication: intralesional corticosteroids injections, corticosteroid therapy and oral antibiotics, in addition to allopurinol. In cases that are more severe or resistant to other therapies, surgical excision is mandatory. [1,2,5]

Several treatments, such as oral and intralesional corticosteroids were tried in the reported case, however with absence of satisfactory response. In addition, the patient described constant pain and dissatisfaction with the lesions' aesthetic appearance. For that reason surgery was proposed to remove the greatest possible number of the most evident granulomas.

The aesthetic result of the removal of granulomas was very satisfactory, since it progressed without unsightly scars, significantly improving the nodular appearance of the analyzed regions, with a high degree of patient satisfaction. The patient continues under ambulatory follow-up, and therapy with allopurinol has been initiated to reduce small residual granulomas. [4]

CONCLUSION

There is not a filling substance that can be deemed as ideal since all materials can cause early or late adverse effects. Although PMMA is relatively safe, the host's immunology is primarily responsible for the different reactions that might arise.

It is crucial that the patient be informed beforehand of the possible complications in advance of undergoing any procedure.

Currently, the trend points towards a choice for absorbable fillers, which have a lower incidence of adverse reactions and do not lead to permanent outcomes. ●

REFERENCES

1. Reisberger EM, Landthaler M, Wiest L, Schröder J, Stolz W. Foreign Body Granulomas Caused by Polymethylmethacrylate Microspheres: Successful Treatment With Allopurinol. Arch Dermatol. 2003;139(1):17-20.
2. Campos DLP, Proto RS, Santos DC, Ruiz RO, Brancaccio N, Gonella HA. Avaliação histopatológica do polimetilmetacrilato em ratos ao longo de um ano. Rev Bras Cir Plast. 2011;26(2):189-193.
3. Thaler MP. Foreign body granulomas caused by polymethylmethacrylate microspheres: an added perspective. Arch Dermatol. 2003;139(11):1505-6.
4. de Barros Silveira LK, de Oliveira FL, Alves T de B, Rambaldi ML, de Andrade FC, Kelmer S de C, Barbosa FC. The therapeutic benefit of allopurinol in the treatment of foreign body granulomas caused by polymethylmethacrylate microspheres. Case Rep Dermatol Med. 2012; 2012: 1-3.
5. Ledon JA, Savas JA, Yang S, Franca K, Camacho I, Nouri K. Inflammatory Nodules Following Soft Tissue Filler Use: A Review of Causative Agents, Pathology and Treatment Options. Am J Clin Dermatol. 2013;14(5):401-411.
6. Park TH, Seo SW, Kim JK, Chang CH. Clinical experience with polymethylmethacrylate microsphere filler complications. Aesthetic Plast Surg. 2012;36(2):421-6.
7. da Costa Miguel MC, Nonaka CF, dos Santos JN, Germano AR, de Souza LB. Oral foreign body granuloma: unusual presentation of a rare adverse reaction to permanent injectable cosmetic filler. Int J Oral Maxillofac Surg. 2009;38(4):385-7.
8. Salles AG, Lotierzo PH, Gemperli R, Besteiro JM, Ishida LC, Gimenez RP, et al. Complications after polymethylmethacrylate injections: report of 32 cases. Plast Reconstr Surg. 2008;121(5):1811-20.
9. Rongioletti F. Granulomatous reactions from aesthetic dermal micro-implants. Ann Dermatol Venereol. 2008;135(1 Pt 2):1S59-65.

Case Reports

Exogenous ochronosis treated with CO2 Laser

Ocronose exógena tratada com laser de CO2

Authors:
Catarina Gonçalves da Silva Carvalho[1]
Vanessa da Nóbrega Vilela[1]
Amanda Eugênia Almeida Rocha[1]
Gustavo de Sá Menezes Carvalho[2]
Emmanuel Rodrigues de França[3]
Aldejane Gurgel de Amorim Rodrigues[4]

[1] Dermatology Resident Physician, Universidade de Pernambuco (UPE) - Recife (PE), Brazil.

[2] Medicine Student, UPE.

[3] Full Professor of Dermatology. Associate Professo and Head of the Dermatology Service, Faculdade de Ciências Médicas de Pernambuco, UPE.

[4] Dermatologist Physician, Associate Instructor, Dermatology Service, Faculdade de Ciências Médicas de Pernambuco, UPE.

Correspondence:
Catarina Gonçalves da Silva Carvalho
R. Arnóbio Marquês, 310 – Santo Amaro
Cep 50100-130 – Recife (PE), Brazil
e-mail: catarina.carvalho@yahoo.com

Received on: 16/07/2016
Approved on: 20/11/2016

This study was performed at Universitário Oswaldo Cruz – Universidade de Pernambuco (UPE) – Recife (PE), Brazil.

Financial support: None.
Conflict of interests: None

DOI: http://dx.doi.org/10.5935/scd1984-8773.201684863

ABSTRACT

Exogenous Ochronosis is a rare skin disease. It is usually associated with the topical use of hydroquinone, resulting in a grayish or bluish black hyperpigmentation due to dermal deposition of ocher pigment. There is no gold standard treatment and the therapeutic options are generally not effective. We report a case of a patient with exogenous achronosis after use of Hydroquinone, treated with CO_2 Laser and showing very good results.
Keywords: *hydroquinones; laser therapy; ochronosis*

RESUMO

Ocronose exógena é doença cutânea rara, geralmente associada ao uso tópico de hidroquinona. Leva à hiperpigmentação acinzentada ou preto-azulada, devido à deposição dérmica de pigmento ocre. Não existe tratamento padronizado, e as opções terapêuticas são em geral frustrantes. Relatamos o caso de uma paciente com ocronose exógena após uso de hidroquinona, tratada com laser fracionado de CO_2 e apresentando resultado bastante satisfatório.
Palavras-chave: *ocronose; hidroquinonas; terapia a laser*

INTRODUCTION

Exogenous ochronosis is a rare disease characterized by asymptomatic, bluish-black or grayish hyperpigmentation, typically located on the face, however it can involve the neck, dorsum and extensor surfaces. [1,2] It arises more commonly as a side effect of hydroquinone; nevertheless it may be associated with phenol, mercury, or antimalarial drugs or other medicaments. [3] There is microscopic dermal deposition of ocher colored pigment, histologically similar to the congenital endogenous phenomenon known as Alkaptonuria, when there is accumulation of homogentisic acid in the cartilage, cardiac valves and skin. [1,3]

The hydroquinone induced hyperpigmentation mechanism remains unclear. [1,2] There are reports of exogenous ochronosis in practically all ethnic groups, even with the use of low concentrations of the substance (2%) and for a short period of time (6 months). Nonetheless, this condition is in fact more frequent in higher phototypes after the prolonged use of hydroquinone in high concentrations. [2,3] Penneys has attributed the skin hyperpigmentation to the inhibition of the homogentisic acid oxidase enzyme by hydroquinone, resulting in homogentisic acid buildup that polymerizes to form the ochronotic pigment. [4]

There are three clinical phases: Phase I (presence of erythema and mild pigmentation), Phase II (pigmented papules with caviar-like appearance and atrophy) and Phase III (papulonodular lesions surrounded or not by inflammation). [1,5]

Several treatments have been used, however, there are in general high refractoriness rates and poor results. There is a report of an exogenous ochronosis case following the use of hydroquinone that was treated with CO_2 laser with quite satisfactory results.

CASE REPORT

A 46-year-old, Fitzpatrick phototype V patient sought care at the dermatology clinic reporting dark spots on the face (Figure 1). The patient was using a 4% hydroquinone formula for the treatment of melasma for approximately 5 years, with progressive worsening of the lesions. At the initial examination, the patient had poorly delimited papules and hyperchromic macules in the forehead, nasal dorsum and malar regions (Figures 2 and 3), and denied any other symptom or similar family history, altered urine color, hyperpigmentation of the sclera's, underarm's or joint's skin. The patient also denied the oral use of medication and comorbidities.

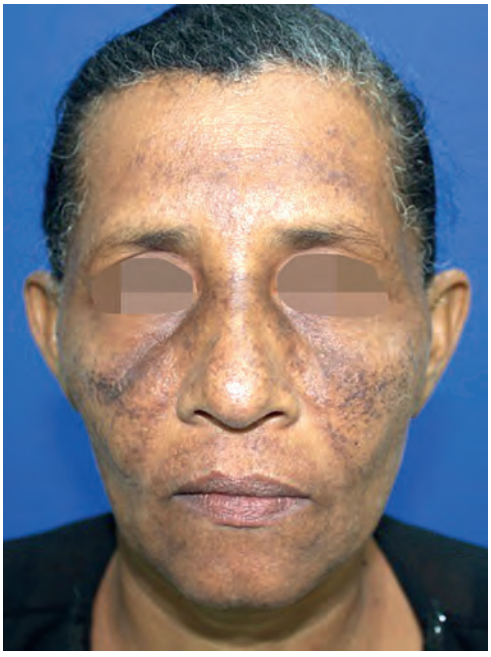


Figure 1: Patient at diagnosis

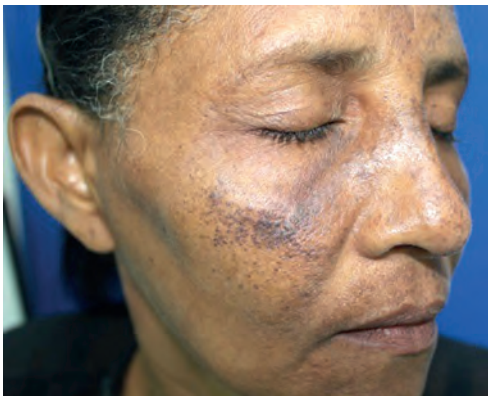


Figure 2: Right malar region before the treatment

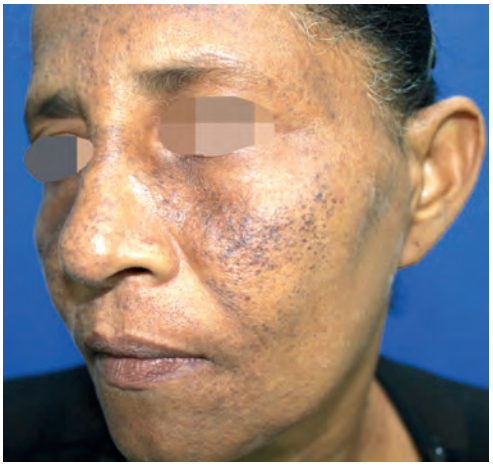


Figure 3: Left malar region before the treatment

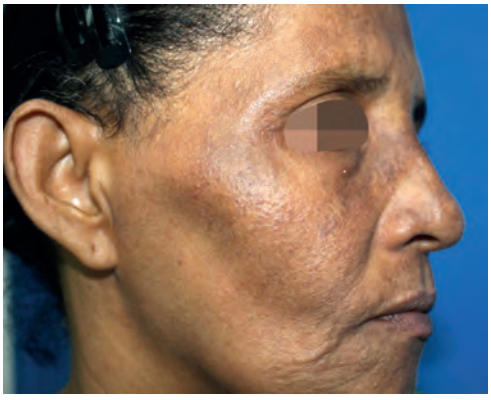


Figure 4: Right malar region after the treatment

Treatment with fractional CO_2 laser was initiated on the face using the device Dual Deep (Lutronics, Korea). A 120mm tip was used, with the parameters of energy and density set at 120mJ and 150 points per cm2, respectively. The treatment was repeated monthly during 1 year (12 sessions), with significant improvement of the clinical picture (Figures 4 and 5).

DISCUSSION

The treatment of exogenous ochronosis is deemed as difficult, meaning that prevention is therefore extremely important. The use of hydroquinone in lower concentrations, protection against the sun, early diagnosis of irritation and discontinuation of treatment in the absence of clinical response within 6 months

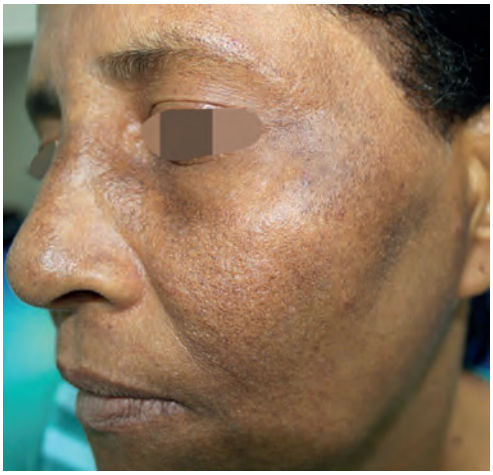


Figure 5: Left malar region after the treatment

are important preventive measures. [4,6] Avoiding the use of the triggering substance is beneficial, however several years might be required up until some degree of improvement is obtained.

The studied patient has Fitzpatrick's phototype V and has undergone prolonged treatment with hydroquinone – the main risk factors described in the literature.

Several treatments have been used, usually with frustrating outcomes. Treatment with trichloroacetic acid and cryotherapy are not effective. [7] In some cases tretinoin can improve lesions, however it may sometimes lead to transient hyperpigmentation. [4,7] Low strength corticosteroids associated with photoprotection showed good results. [7] Satisfactory results were also described with dermabrasion, CO_2 laser, glycolic acid peels and Q-switched lasers (694nm ruby and 755nm alexandrite). However, the outcomes are not homogeneous.[6,7]

The use of CO_2 laser for the treatment of exogenous ochronosis is scarcely described in the literature, mainly as an isolated therapy. Diven et al. employed a combination of dermabrasion and ablative CO_2 laser with satisfactory outcomes in the periorbital and nasal regions and partial improvement of cutaneous lesion, in a woman high Fitzpatrick phototype [7,8]

Exogenous ochronosis is a difficult to treat pathology, with several reports of ineffective therapies in the literature. [5,7] The studied patient had an excellent response to sessions of fractionated CO_2 laser, leading to the conclusion that it can be an effective option in some cases of refractoriness. ●

REFERENCES

1. Kindem S, Serra-Guillén C, Guillén C. Hiperpigmentación facial parcheada. Actas dermosifiliograficas 2015;106(4):317-8.
2. Martins VMR, Sousa AR, Portela NC, Tigre CA, Gonçalves LM, Castro Filho RJ. Exogenous ochronosis: case report and literature review. An Bras Dermatol 2012;87(4):633-6.
3. García García, C. Lesiones de la pigmentación cutânea. Medicine - Programa de Formación Médica Continuada acreditado. 2010;10(48):3195-3203.
4. O'Donoghue MN, Lynfield YL, Derbes V. Ochronosis due to hydroquinone. J Am Acad Dermatol. 1983;8(1):123.
5. França ER, Paiva V, Toscano LPN, Nunes GJB, Rodrigues TFA. Ocronose exógena: relato de caso. Surg Cosmet Dermatol. 2010;2(4):319-21.
6. Ribas J, Schettini APM, Cavalcante MSM. Ocronose exógena induzida por hidroquinona: relato de quatro casos. An. Bras. Dermatol 2010;85(5):699-703.
7. Bellew SG, Alster TS. Treatment of exogenous ochronosis with a Q-switched alexandrite (755 nm) laser. Dermatol Surg. 2004;30(4 Pt 1):555-8.
8. Diven DG, Smith EB, Pupo RA, Lee M. Hydroquinone-induced localized exogenous ochronosis treated with dermabrasion and CO2 laser. J Dermatol Surg Oncol.1990; 16(11):1018-22.

Atrophic Dermatofibrosarcoma: the importance of clinical suspicion

Dermatofibrossarcoma atrófico: a importância da suspeita clínica

DOI: http://dx.doi.org/10.5935/scd1984-8773.201684807

ABSTRACT

Dermatofibrosarcoma protuberans is an uncommon and relapsing fibrohistiocytic tumor of intermediate malignancy. Its rarest variant is known as atrophic, morphea type or dermatofibrosarcoma non protuberans and its clinical diagnose is difficult. There are not well established dermatoscopic criteria, so the diagnosis is histopathologic. There are advances in immunohistochemical and genetic that help the diagnosis and complete surgical excision. It is reported a case of atrophic dermatofibrosarcoma in a 27 years patient ant it is reviewed the clinical, dermoscopic, histological and genetic aspects.

Keywords: dermoscopy; neoplasms; dermatofibrosarcoma

RESUMO

Dermatofibrossarcoma protuberante é tumor fibro-histiocítico de malignidade intermediária, relativamente incomum e recidivante. Sua variante mais rara é conhecida como atrófica, tipo morfeia ou dermatofibrossarcoma não protuberante, sendo de difícil diagnóstico clínico. Não há critérios dermatoscópicos bem estabelecidos, portanto o diagnóstico é histopatológico. Existem avanços nas áreas da imuno-histoquímica e da genética que auxiliam no diagnóstico e excisão cirúrgica completa. Relatamos um caso de dermatofibrossarcoma atrófico em paciente de 27 anos, revisado na literatura quanto aos aspectos clínicos, dermatoscópicos, histopatológicos e genéticos.

Palavras-chave: *dermoscopia; neoplasias; dermatofibrossarcoma*

Case Reports

Authors:

Ticiana de Andrade Castelo Branco Diniz[1]
Maria Isabel Ramos Saraiva[2]
Marcella Amaral Horta Barbosa[3]
Larissa Karine Leite Portocarrero[4]
Priscila Kakizaki[5]
Neusa Yuriko Sakai Valente[6]

[1] Dermatology Resident Physician, Instituto de Assistência Médica ao Servidor Público Estadual (HSPE) – São Paulo (SP), Brazil.

[2] Dermatologist Physician. Cutaneous Oncology Specialist candidate, Hospital das Clínicas of the Faculdade de Medicina, Universidade de São Paulo (HCFMUSP) – São Paulo (SP), Brazil.

[3] Dermatologist Physician, private practice - Juiz de Fora (MG), Brazil.

[4] Dermatologist Physician, Pediatric Dermatology Specialist candidate, HCFMUSP.

[5] Dermatology Assistant Physician, Trichosis and Psoriasis Ambulatories, Instituto de Assistência Médica ao Servidor Público Estadual (HSPE-SP); Collaborating Physician, Trichosis Ambulatory, Hospital do Servidor Público Municipal (HSPM-SP) – São Paulo (SP), Brazil.

[6] Dermatology and Dermatopathology Assistant Physician, HSPE-SP. Dermatology Assistant Physician, HCFMUSP. Researcher Physician at the Dermatopathology, Medical Mycology (LIM 53) and Trichology Laboratory - São Paulo (SP), Brazil.

Correspondence:
Ticiana de Andrade Castelo Branco Diniz
R. Borges Lagoa, 1755. 4º andar – Vila Clementino
Cep 04038-034 - São Paulo (SP), Brazil
e-mail: ticidiniz@hotmail.com

Received on: 10/04/2016
Approved on: 30/09/2016

This study was performed at the Hospital Servidor Público Estadual (HSPE-SP) - São Paulo (SP), Brazil.

Financial support: None
Conflict of interests: None

INTRODUCTION

Dermatofibrosarcoma protuberans (DFSP) is a relatively uncommon fibro-histiocytic tumor of intermediate malignancy. It is often locally aggressive, with high-risk of recurrence and low risk of metastasis. [1] The initial clinical appearance is that of a hardened, violet or reddish-brown, keloid-like plaque. [2] Being asymptomatic and slow growing, there may be a delay in diagnosis. When the lesion is already established, the diagnosis is facilitated by its specific appearance. The initial lesion is rarely atrophic or depressed; however when this is the case it is called atrophic dermatofibrosarcoma (ADFSP) and diagnosis is difficult. [3,4]

CASE REPORT

A 27 year-old male patient had been bearing a lesion in the left infraclavicular region for 10 years. The examination revealed an atrophic hyperchromic lesion measuring 4x3cm (Figure 1). An incisional biopsy allowed to observe the presence of neoplastic infiltration in the superficial / deep dermis and hypodermis, with proliferation of fusiform cells with a mild degree of nuclear polymorphism and hyperchromasia forming multidirectional bundles, sometimes parallel to the epidermis, which had atrophy of the stratum spinosum (Figures 2,3 and 4). The immunohistochemistry's results were positive for CD34 and negative for XIIIa factor (Figure 5). The histological diagnosis was of dermatofibrosarcoma, however the final diagnosis after clinical correlation was that of ADFSP. The surgical excision of the lesion was performed with 5cm margins.

DISCUSSION

Sarcomas are soft tissue malignant tumors and contribute for the small percentage of cutaneous neoplasms. Dermatofibrosarcoma protuberans is most frequent cutaneous sarcoma, accounting for 1% of the conjunctive tissue sarcomas and any less

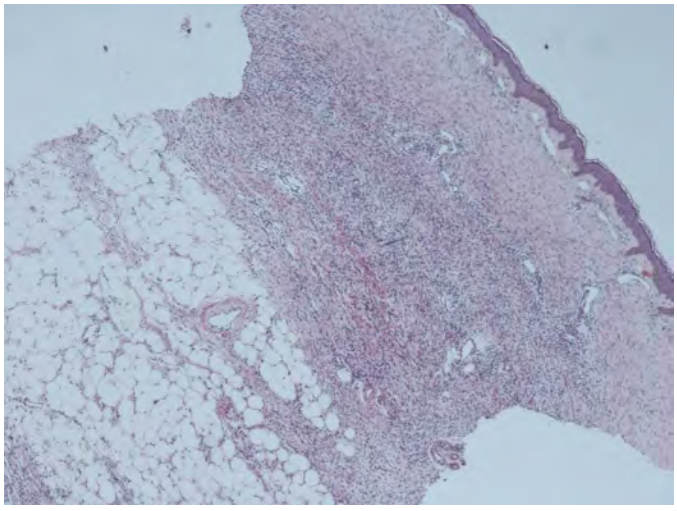


Figure 2: HE, 40x: Spindle cell infiltrate with low to medium cellularity in the dermis and hypodermis. Ectasiated vessels in the papillary dermis

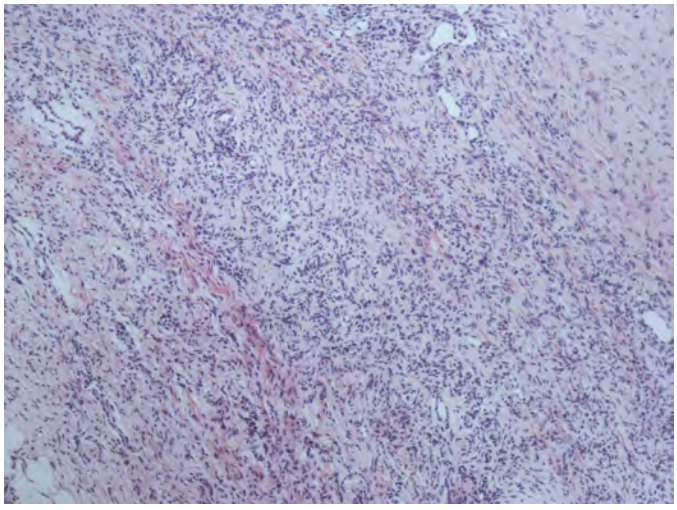


Figure 3: HE, 100x: The storiform arrangement characteristic of the protuberant form is not observed

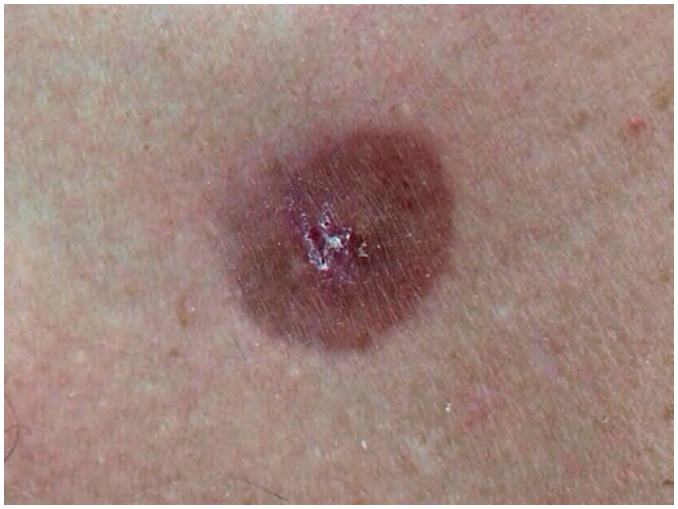


Figure 1: Atrophic hyperchromic lesion measuring 4cm x 3cm in the left infraclavicular region

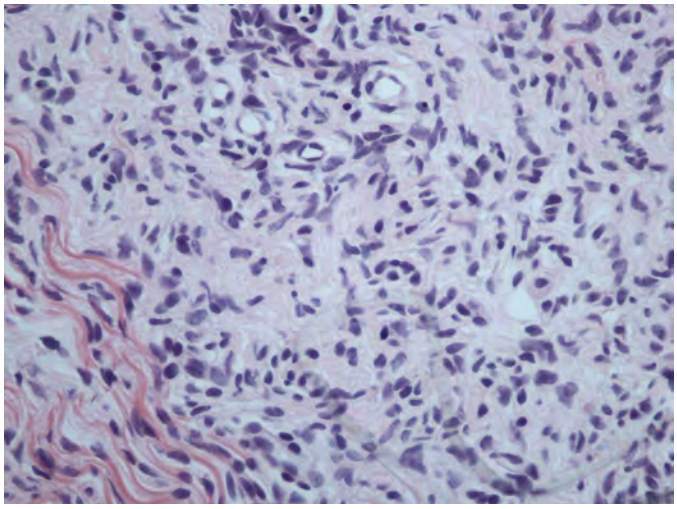


Figure 4: HE, 400x: Detail of spindle cells with mild atypias and medium cellularity

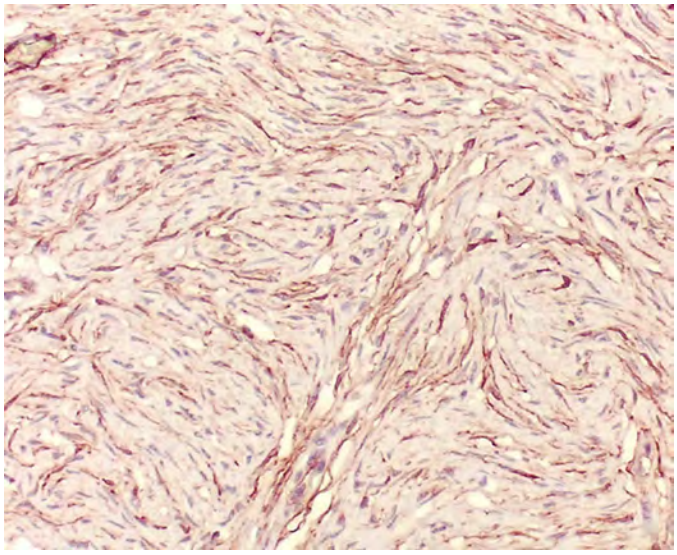


Figure 5: Immunohistochemistry: CD34-positive

than 0.1% of all malignant neoplasms [5] It is a slow growing tumor, usually asymptomatic, which might lead to late diagnosis. [2] The most common clinical development is a hardened, purplish or reddish-brown plaque, which develops into a nodule, [5] however possibly arising as an atrophic lesion. Initially described in 1985, this condition's rarest variant is known as ADFSP, a morphea-type variant of DFSP, or dermatofibrosarcoma non-protuberans. [3,4] It was once suggested that the term *protuberans* should be suppressed in favor of the designation *atrophic dermatofibrosarcoma*, since not all lesions have nodular aspect, [4] nevertheless, consensus has not been reached yet. The ADFSP has a difficult clinical diagnosis, as it may be misdiagnosed with morphea, idiopathic atrophodermia, atrophic scar, anetoderma or lipoatrophy. [6]

There are still no well-established dermoscopic criteria. Different patterns have been described in the literature. It can display branching vessels over a yellow background without pigmentary network, which might be due to skin atrophy,[7] or even brown regular reticular lines corresponding to melanin accumulation in basal keratinocytes over a purplish erythematous background, resulting from dilated vessels in the dermal plexus.[2] Specific findings or differentiation factors have not yet been found that would allow distinguishing ADFSP from other diagnoses. [2]

In a less intense way when compared to the protruding form, cells arranged in a storiform pattern over a fibrous stroma background characterize the ADFSP's anatomopathological examination. The infiltrate tends to extend up until the subcutaneous fat. In general, there is little nuclear pleomorphism. The epidermis is usually spared, and the dermis' thickness is reduced by roughly 50% (Figures 2 to 4). [1]

The use of immunohistochemistry can assist in the identification of the tumor, as well as in its delimitation for complete excision using Mohs micrographic surgery (MMS). The ADFSP is routinely CD34-positive and factor XIIIa-negative. Since the neoplasm can invade deeply along collagen bundles or connective tissue septa, the extent of the invasion might not be clinically apparent. This explains recurrence rates of 11% to 53% when 1cm to 3cm surgical margins are used (11% for 3cm margins in DFSP cases). [8,9] There is scant data available for the atrophic form. Mohs micrographic surgery using immunohistochemical staining with CD34 in frozen sections might allow the detection of the most asymmetrical tumors. [8,9]

Over the past decade, advances have shown that the mutation responsible for the ADFSP is a reciprocal translocation t(17; 22) (q22; q13.1) or, more often, the creation of a supernumerary ring chromosome derived from t(17; 22). These mutations cause the chromosome 17's type 1-alpha-1 collagen (COL1A1) to merger with chromosome 22's gene chain platelet-derived growth factor (PDGFB), forming a chimeric protein, COL1A1-PDGFB. [4]

After translocation, COL1A1 and its promoters replace the regulating elements that inhibit the PDGFB, allowing the production of high levels of COL1A1-PDGFB's messenger RNA. The cleavage of PDGFB by the COL1A1- PDGFB protein can lead to malignant transformation.[4] In the gene translocation process, variable lengths of COL1A1 are juxtaposed to the same PDGFB gene sequence. After the cleavage of COL1A1-PDGFB, fragments of COL1A1 become trimers associated to type 1-alpha-2 collagen (COL1A2), which is secreted in the extracellular medium. [4] It is proposed that the variety of COL1A1 and COL1A2 trimers may be responsible for different stroma present in a typical DFSP and its atrophic variant, given that each tumor can have a specific length of the COL1A1 fragment. Inhibition of the PDGFB receptor might explain the atrophic phenotype [4]

The treatment is similar to that used in the non-atrophic form. Mohs micrographic surgery is the first choice. The second choice is surgical excision with a margin of 3cm to 5cm, with chance of recurrence due to the possibility of invasion beyond the fascia and muscles.[10] Although recurrences often arise within the 3 first years after the surgery, they can take place several years after, justifying watchfulness in the long term. [1]

REFERENCES

1. Lee SJ, Mahoney MC, Shaughnessy E. Dermatofibrosarcoma protuberans of the breast: imaging features and review of the literature. AJR Am J Roentgenol. 2009;193(1):W64¬-69.
2. Akay BN, Unlu E, Erdem C, Heper AO. Dermatoscopic findings of atrophic dermatofibrosarcoma protuberans. Dermatol Pract Concept. 2015;5(1):71-¬3.
3. Lambert WC, Abramovits W, Gonzalez¬-Sevra A, Souchon E, Schwartz RA, Little WP Jr. Dermatofibrosarcoma non¬protuberans: description and report of five cases of a morpheaform variant of dermatofibrosarcoma. J Surg Oncol. 1985;28(1):7-¬11.
4. Young CR 3rd, Albertini MJ. Atrophic dermatofibrosarcoma protuberans: case report, review, and proposed molecular mechanisms. J Am Acad Dermatol. 2003;49(4): 761-¬764.
5. Fleury LFF Jr, Sanches JA Jr. Sarcomas cutâneos primários. An Bras Dermatol. 2006;81(3):207¬-21.
6. Bakry O, Attia A. Atrophic dermatofibrosarcoma protuberans. J Dermatol Case Rep. 2012;6(1):14-¬7.
7. Gungor S, Buyukbabani N, Buyuk M et al. Atrophic dermatofibrosarcoma protuberans: are there specific dermatoscopic features? J Dtsch Dermatol Ges. 2014;12(5):425-¬7.
8. Gloster HM Jr. Dermatofibrosarcoma protuberans. J Am Acad Dermatol.1996;35 (3 Pt 1):355¬-74.
9. Ratner D, Thomas CO, Johnson TM, Sondak VK, Hamilton TA, Nelson BR, et al. Mohs micrographic surgery for the treatment of dermatofibrosarcoma protuberans. Results of a multiinstitutional series with an analysis of the extent of microscopic spread. J Am Acad Dermatol. 1997;37(4):600-¬13.
10. Haycox CL, Odland PB, Olbricht SM, Casey B. Dermatofibrosarcoma protuberans (DFSP): growth characteristics based on tumor modeling and a review of cases treated with Mohs micrographic surgery. Ann Plast Surg. 1997;38(3):246-¬51.

Nevus sebaceous of Jadassohn of the scalp - reconstruction with bilateral rotational flap

Nevo sebáceo de Jadassohn no couro cabeludo - reconstrução com retalho de rotação bilateral

DOI: http://dx.doi.org/10.5935/scd1984-8773.201684835

ABSTRACT

The nevus sebaceous of Jadassohn is a congenital benign hamartoma of the skin that occurs more frequently in the scalp, but can also arise in the face. Due to its potential for malignization, exeresis is often required. Lesions located in the scalp are challenging to surgeons because of the anatomical characteristics of this body site, namely scarcity and inelasticity of the adjacent skin. In the present report, the authors describe a case of excision of a nevus sebaceous of Jadassohn located in the scalp, using a bilateral rotation flap – a very straightforward and versatile technique, excellent for reconstructing difficult topographies such as the scalp – for the closure of the surgical wound.

Keywords: *ambulatory surgical procedures; nevus, sebaceous of Jadassohn; surgical flaps*

RESUMO

O nevo sebáceo de Jadassohn é hamartoma benigno congênito da pele, mais incidente no couro cabeludo, podendo apresentar-se na face. Devido ao potencial de malignização, sua excisão muitas vezes se faz necessária. Lesões situadas no couro cabeludo constituem desafio ao cirurgião devido às características anatômicas do local, com escassez e inelasticidade da pele adjacente. Neste relato, apresentamos um caso de excisão de nevo sebáceo de Jadassohn no couro cabeludo, com fechamento da ferida operatória por retalho de rotação bilateral, técnica muito simples e versátil, excelente para topografias de difícil reconstrução, como o couro cabeludo.

Palavras-chave: procedimentos cirúrgicos ambulatoriais; nevo sebáceo de Jadassohn; retalhos cirúrgicos

Case Reports

Authors:

Marcela da Costa Pereira Cestari[1]
Andrea Penhalber Frange[1]
Bianca Pinheiro Bousquet Muylaert[1]
Anna Rita Ferrante Mitidieri de Oliveira[1]
Eduarda Braga Esteves[1]
Nátalie Schnaider Borelli[1]
Douglas Haddad Filho[2]

[1] Dermatology Resident Physician, Faculdade de Medicina da Universidade de Santo Amaro (Unisa) – São Paulo(SP), Brazil.

[2] Full Professor of Plastic Surgery, Unisa.

Correspondence:
Marcela da Costa Pereira Cestari
R. Professor Enéas de Siqueira Neto, 340 - Jd. Of Embuias
Cep 04829-300 – São Paulo (SP), Brazil
e-mail: marcelacestari@yahoo.com

Received on: 07/06/2016
Approved on: 10/10/2016

This study was performed at the Faculdade de Medicina da Universidade de Santo Amaro (Unisa) – São Paulo(SP), Brazil.

Financial support: None
Conflict of interests: None

INTRODUCTION

The sebaceous nevus of Jadassohn (SNJ) or organoid nevus is a congenital benign hamartoma of the skin, characterized by hyperplasia of the epidermis, degenerated hair follicles, sebaceous and ectopic apocrine glands. It occurs in approximately 0.3% of the individuals, with no gender prevalence. The lesion in general is present at birth and arises as a well-defined plaque composed of multiple confluent orangish-yellow or brownish-yellow colored papules, predominantly located on the scalp, where it courses with alopecia at the lesion's site.

Its surface becomes thickened and verrucous during puberty due to hormonal stimulation of the eccrine and apocrine components, with the possibility of the lesion becoming nodular in adulthood, with the occurrence of ulcerations and crusts. The probability of secondary neoplasms to emerge in this stage (mainly basal cell carcinoma, papillary syringocystadenoma and trichoblastoma) is of 10% to 30%. In a possible malignant transformation or in cases with presence of ulceration, surgical excision can be required. Large lesions located in the scalp are usually difficult to reconstruct due to local anatomical features. [1,2]

The cephalic segment's lining can be classified into soft parts and osseous tissues. The soft parts are responsible for covering and protecting the osseous structure, being sub-classified into skin, subcutaneous tissue, galea, loose areolar tissue and pericranium. The subcutaneous tissue is formed by dense connective tissue, fat and several fibrous septa resulting in inelastic structures. The main arteries and veins responsible for the region's irrigation and venous drainage are located in this layer. Among the most important are the superficial temporal, supraorbital, supratrochlear, posterior auricular and occipital vessels. This vast vascular network allows the use of various types of flaps, with considerable safety. The loose areolar tissue – or subaponeurotic tissue – is located between the galea and the pericranium. Its structural characteristics facilitate the surgical access and the elevation of the flaps, constituting a plane of easy dissection. It also has small arteries supplying the pericranium, and small emissary veins, which connect the intracranial venous sinuses with the superficial venous system. [3]

Reconstruction of surgical wounds on the scalp can be performed with the assistance of simple sutures, flaps and grafts, with the latter being used in very particular cases due to the difficulty of obtaining similar donor areas. Direct sutures are not always viable due to the scarcity of adjacent skin in the scalp, as well as its inelasticity. In this way, wounds with diameter greater than 3cm usually require reconstructions based rotation, advancement or transposition flaps. [3,4]

CASE REPORT

A 57-year-old male patient, originary from the Brazilian Southeast city of São Paulo sought assistance complaining of a lesion in the scalp, which had arisen in childhood and changed appearance in adulthood.

The dermatological examination showed a normochromic verrucous plaque with brownish and friable areas measuring 3.6 cm on their longest axis, in the left parietal region of the scalp (Figure 1). An incisional biopsy was performed with histological analysis, confirming the diagnosis of SNJ. Due to the patient's complaint and malignization risk, a decision was made for the exeresis of the lesion.

The patient underwent circular resection of the tumor, with a safety margin of 5mm (Figure 2), up until the galeal plane, followed by the reconstruction with the rotation of bilateral circular skin flaps, also prepared up until the galeal plane, based on branches of the occipital and superficial temporal vessels (Figures 3 and 4). The flaps were rotated towards the medial direction, and the suture was carried out with simple stitches and nylon 4.0 (Figure 5). The surgical specimen was sent for pathological examination, which verified free margins and absence of neoplasms.

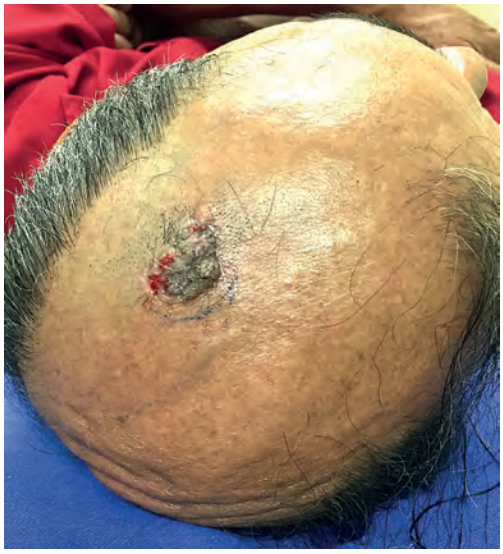


Figure 1: Sebaceous nevus of Jadassohn measuring 3.6cm in its greatest diameter

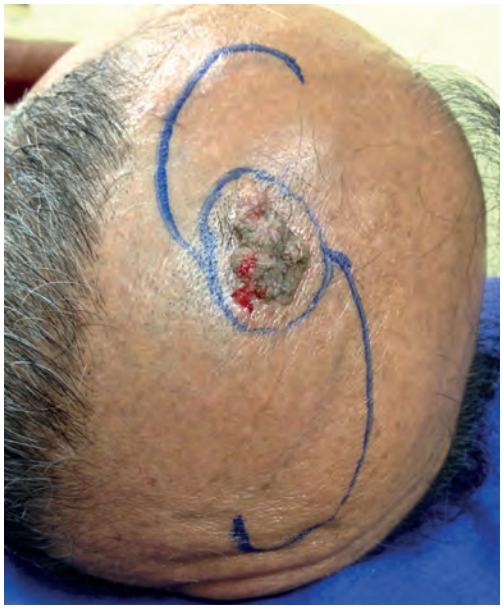


Figure 2: Tumor resection programming with safety margin and planning of cutaneous flaps

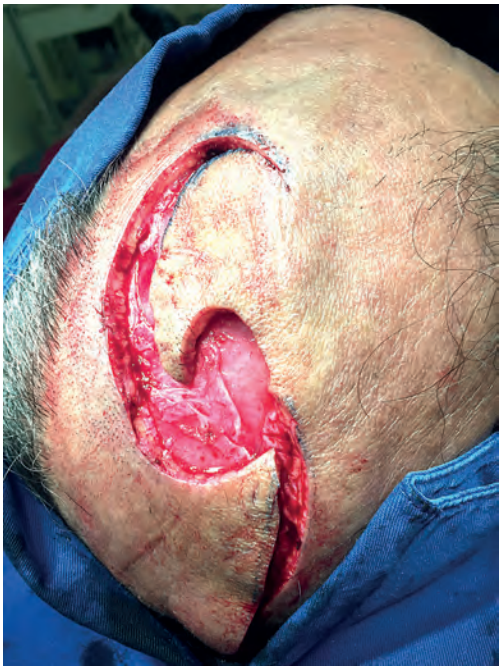


Figure 3: Preparation of the flaps

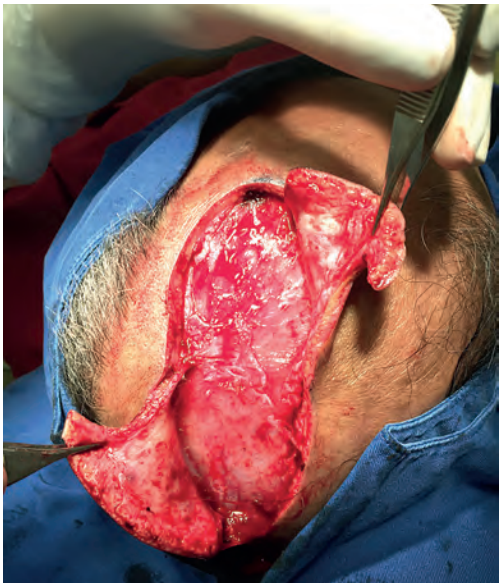


Figure 4: Elevation of the flaps and approaching movement towards the receiving area

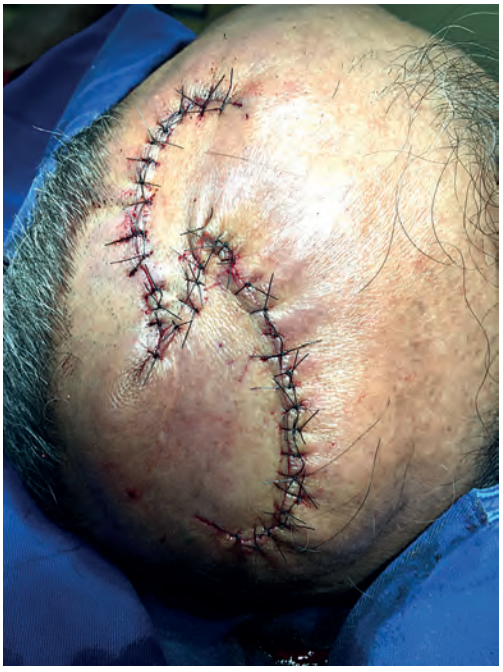


Figure 5: Complete suture of the flaps

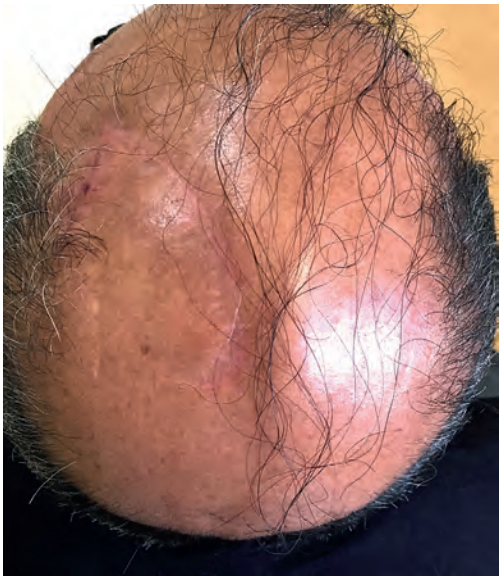


Figure 6: Outcome after two postoperative months

The patient had good postoperative development, with excellent healing and final aesthetic outcome (Figure 6).

DISCUSSION

Sebaceous nevus of Jadassohn occurs in approximately 0.3% of individuals, usually at birth, being more commonly located on the scalp. In adulthood, it may be associated with several tumors, most commonly with basal cell carcinoma, papillary syringocystadenoma, and trichoblastoma. Although initially arising as a benign lesion, surgical excision is indicated in most cases due to the risk of malignization, which increases over the years. Lesions located on the scalp can be difficult to approach due to the region's anatomical characteristics. [1, 2]

The scalp has little tissular expandability, which hampers the primary suture in larger lesions, very frequently entailing the necessity of more extensive undermining of tissues, which in turn leads to an inadequate tense approach of the borders, resulting in widened scars and / or alopecia [3, 4]

The alternative applied in such cases is the use of scalp skin flaps. The planning possibilities and options for these flaps are very diverse, given the extensive vascular network of the segment.

The scalp's irrigation network comprises – bilaterally – the supratrochlear, supraorbital, superficial temporal, occipital and posterior auricular vessels, forming a very extensive vascular network, mainly in the central region, where the branches of

these major vessels anastomose, [4] allowing large rotation arches for arterial flaps, as well as cutaneous transpositions in other aesthetic units (for instance the Washio flap for the reconstruction of facial regions). [4,5]

With this rich vascularity, the flap options for closure of tumor resections can be considerably varied: from small skin flaps to large reconstructions that require cutaneous expansions and microsurgical flaps.

Among the various possibilities for the use of scalp flaps, the rotation flap is a very safe and easy to implement option. In general, the reconstruction begins with the rotation of a unilateral flap and primary closure of the donor area. In cases where the unilateral rotation is not sufficient, it is possible to use another contralateral flap, similar in size and shape, in the same surgical time, demonstrating the great versatility of this proposal for rotation flaps.

REFERENCES

1. Quadros JM, Marques AS. Aspectos evolutivos do nevo sebáceo de Jadassohn. An Bras Dermatol. 1982;57(2):109-115.
2. Moody MN, Landau JM, Goldberg LH. Nevus sebaceous revisited. Pediatr Dermatol. 2012;29(1):15-23.
3. Leedy JE, Janis JE, Rohrich RJ. Reconstruction of acquired scalp defects: an algorithmic approach. Plast Reconstr Surg. 2005;116(4):54e-72e.
4. Washio H. Retroauricular-temporal flap. Plast Reconstr Surg. 1969;43(2):162-66 .
5. Washio H. Further experience with the retroauricular temporal flap. Plast Reconstr Surg. 1972;50(2):160-62.

Subcision and microneedling therapy: report of two cases

Subcisão e microagulhamento: relato de dois casos

DOI: http://dx.doi.org/10.5935/scd1984-8773.20168409

ABSTRACT

Inflammatory acne lesions may cause unaesthetic scars. Several treatments have been described to ameliorate its appearance. Will be described the treatment with subcision in two patients with acne and dystrophic crateriform facial scars. The female patient performed Microneedling in the same session of subcision. There was good clinical outcome in the treated areas of both patients after three monthly sessions.

Keywords: cicatrix; acne vulgaris; case reports

RESUMO

As lesões inflamatórias da acne podem resultar em cicatrizes permanentes, e vários tratamentos são propostos para reduzir sua aparência. Relatam-se os casos de dois pacientes, um homem e uma mulher com cicatrizes de acne distróficas, distensíveis retráteis e crateriformes na face, em que se optou pelo uso da subcisão nas áreas cicatriciais. Na paciente do sexo feminino foi associado na mesma sessão o microagulhamento. Houve bom resultado clínico nas áreas tratadas dos dois pacientes após três sessões mensais.

Palavras-chave: *cicatriz; acne vulgar; relatos de casos*

INTRODUCTION

Acne is a condition that affects more than 80% of the adolescent population in different degrees [1,2] and 12-51% of adults aged 20 to 49 years. [3,4] These inflammatory lesions might lead to permanent scarring, which usually occur early and can affect roughly 95% of patients, causing psychological stress for many individuals. [3,5] They are linked to the acne's severity and the delay in treatment. [1]

Acne scars can be classified into: elevated (subtypes: hypertrophic, keloid, papular and bridges), dystrophic and depressed (subtypes: distensible and non-distensible). The distensible subtype is sub-classified into: retractable and undulated; while the non-distensible subtype can be sub-classified into: superficial, medium, crateriform, deep (icepicks) and tunnels [6]

Several treatments are proposed for reducing the appearance of scars and should be individualized.[1] These therapies include: dermabrasion,[1] subcision [7], microneedling [8], punch techniques, [3] chemical peels, [3] fat grafting, [3] hyaluronic acid based cutaneous filling, [4] and ablative lasers, [2] such as 10,600nm CO_2.

This paper describes two cases of patients with acne scars: one who underwent subcision and microneedling and other,

Case Reports

Authors:

Heliana Freitas de Oliveira Góes[1]
Anangélica Rodrigues Virgens[1]
Alzinira Herênio Neta[1]
Caroline Coronado Cha[2]
Régia Celli Patricia de Sica[3]
Ana Paula Gomes Meski[4]

[1] Dermatologist Physician. Cosmiatry and Laser Specialist, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP) – São Paulo (SP), Brazil.

[2] Dermatologist Physician. Cosmiatry and Laser Assistant Physician, HCFMUSP.

[3] Dermatologist Physician. Head of the Cosmiatry and Laser Ambulatory, HCFMUSP - São Paulo (SP), Brazil.

[4] Dermatologist Physician. Coordinator, Cosmiatry Ambulatory, HCFMUSP.

Correspondence:
Heliana Freitas de Oliveira Góes
R. Itararé, 177, apt. 96 - Bela Vista
cep 01308-030 - São Paulo (SP), Brazil
e-mail: heliana_g@yahoo.com.br

Received on: 06/08/2016
Approved on: 12/11/2016

This study was performed at the Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HCFMUSP) – São Paulo (SP), Brazil.

Financial support: None
Conflict of interests: None

who only underwent subcision.

CASE REPORT

1.Thirty-seven year-old female patient with multiple acne scars (dystrophic, distensible retractable and crateriform) located bilaterally in the temporal, malar and mandibular regions (Figure 1).

2.Thirty-five year-old male patient with multiple acne scars (dystrophic, distensible retractable and crateriform) located bilaterally in the forehead and temporas, and in the malar, mandibular and mentonian regions (Figure 2).

METHODS

The subcision technique [9] was used in both patients, where a sterile aspiration needle (1.20 X 25mm, 18G) is inserted through transepidermal route, up until the dermis' and subcutaneous tissue's depth, producing linear paths in different directions in the areas with distensible retractable and crateriform scars, following regional blocks and local injection with 2% lidocaine and 1:100,000 epinephrine diluted in 0.9% saline solution (1:1).

In the female patient, microneedling with 1.5mm needles (Dermaroller System®, Ekai Electronic Technology co. Ltd, Guangzhou, China) was used in the whole face after the subcision. After the procedure, the patients were instructed to use healing cream (Cicaplast Baume B5® La Roche Posay, Rio de Janeiro, Brazil) once a day for seven days and sunscreen.

RESULTS

Three days after the procedure, the 2 patients showed good recovery. After 3 monthly sessions good outcomes could be observed in the treated areas, with elevation of the cars and satisfactory clinical response after each session, as well as in the first month after the three sessions (Figures 3 and 4).The patient who underwent the 2 procedures had a better response.

DISCUSSION

Microneedling corresponds to the application of a device with hundreds of needles, which inflict thousands of micro holes in the skin, at the papillary dermis' level.[1,8] The ideal scars to be treated with this method are the crateriform and deep types. [10] During the procedure, the device is usually rolled up continu-

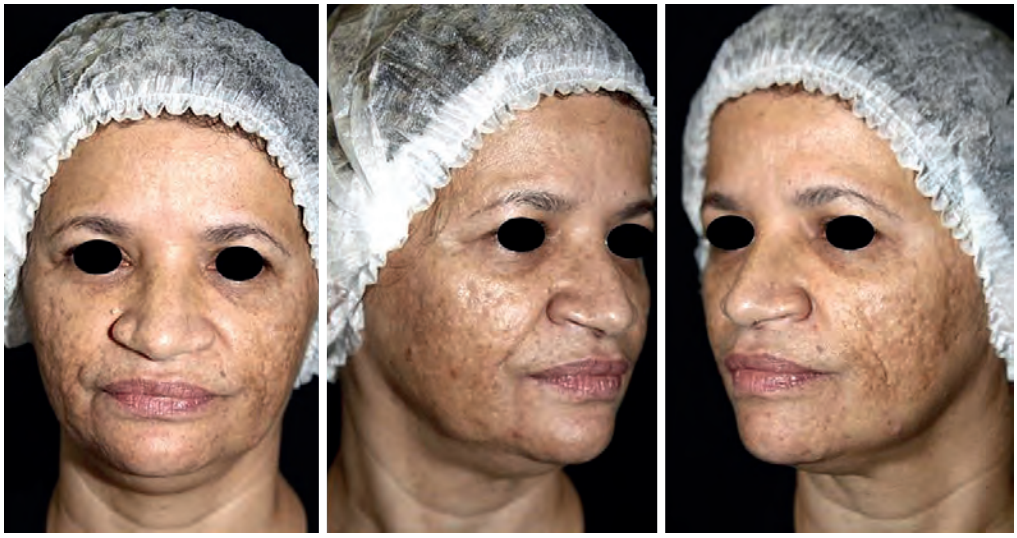


Figure 1:
Dystrophic and crateriform acne scars, Patient 1

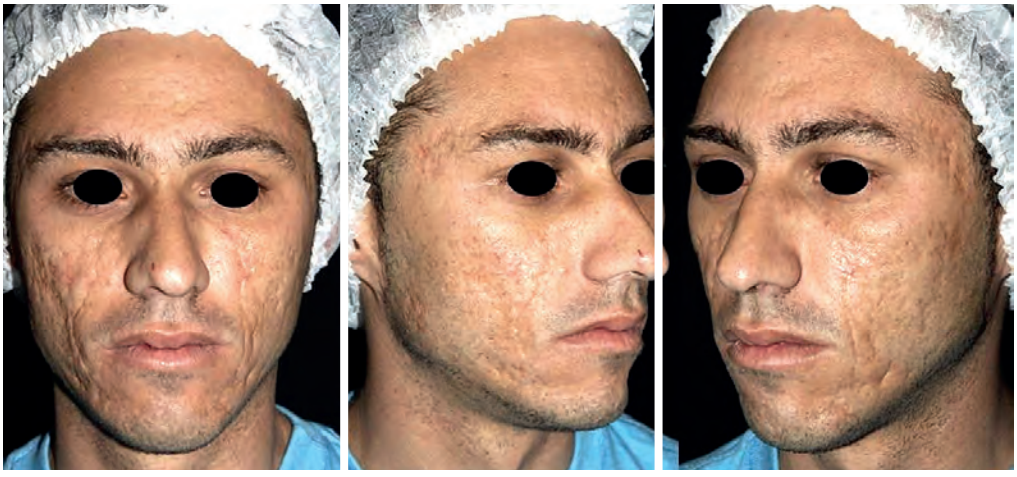


Figure 2:
Dystrophic and crateriform acne scars, Patient 2

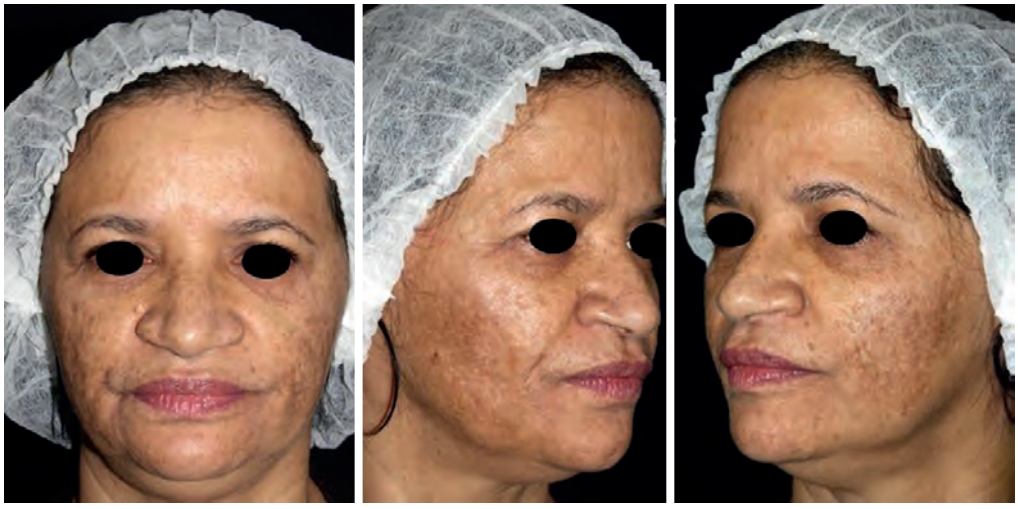


Figure 3:
One month after three monthly sessions of subcision and microneedling, Patient 1

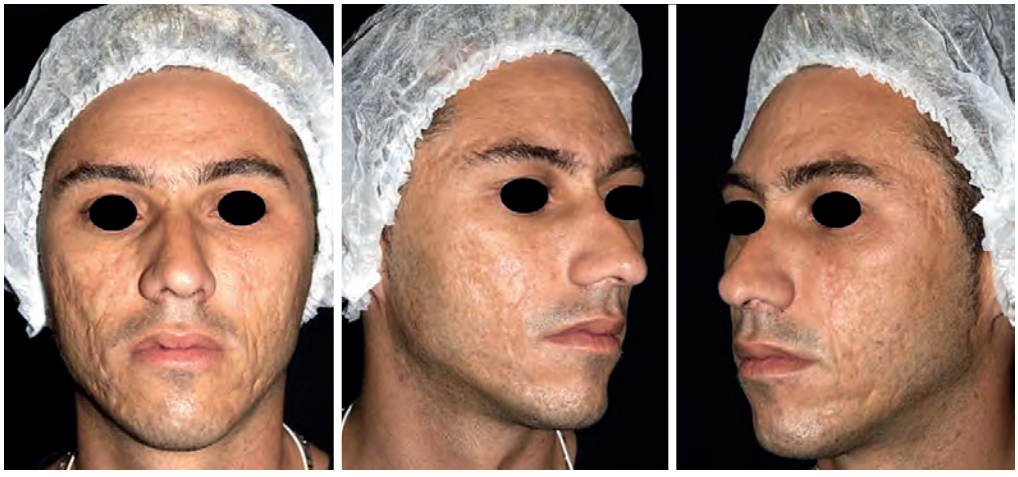


Figure 4:
One month after three subcision sessions, Patient 2

ously until bleeding takes place, triggering a complex cascade of release of growth factors that results in the production of collagen. Neocollagenesis usually starts after six weeks, but the full effect may take at least three months to manifest. In addition, as the deposition of this new collagen occurs slowly, the skin's texture will continue to improve over the following 12 months. [1,3,8]

Regarding the subcision technique – which was introduced in 1995 – it consists of a procedure in which a needle (in general hypodermic, 1.20 X 40mm) is inserted under the skin at the subcutaneous plane, being passed in multiple directions, aimed at breaking the fibrous components located beneath the scar. It is more effectively used in distensible retractable scars, and less efficacious in the treatment of crateriform and deep, icepick type scars.[1,7] This technique causes the rupture of underlying fibrotic bands, triggering an inflammatory response after the bleeding, which culminates in the production of underlying collagen with elevation and improvement of the scar. [7,9] Although subcision can be performed isolatedly, clinical results are usually better when there is association with other procedures, as was the case of the patient studied in this paper, when there was association of microneedling and subcision.

CONCLUSIONS

Subcision and microneedling have advantages – such as shorter recovery time (2 to 3 days), safety in all phototypes, decreased post-inflammatory hyperpigmentation risk and cost effectiveness – when compared to other techniques such as laser therapy, chemical peels or dermabrasion. ●

REFERENCES

1. Gozali MV, Zhou B. Effective treatments of atrophic acne scars. J Clin Aesthet Dermatol. 2015;8(5):33-40.
2. Petrov A, Pljakovska V. Fractional carbon dioxide laser in treatment of acne scars. Maced J Med Sci. 2016;4(1):38-42.
3. Hession MT, Graber EM. Atrophic acne scarring: a review of treatment options. J Clin Aesthet Dermatol. 2015;8(1):50-8.
4. Wollina U, Goldman A. Fillers for the improvement in acne scars. Clin Cosmet Investig Dermatol. 2015;8:493-9.
5. Al-Hammadi A, Al-Ismaily A, Al-Ali S, Ramadurai R, Jain R, McKinley--Grant L, Mughal TI. Topical, biological and clinical challenges in the management of patients with acne vulgaris. Sultan Qaboos Univ Med J. 2016;16(2):e152-e160.
6. Kadunc BV, Trindade de Almeida AR. Surgical treatment of facial acne scars based on morphologic classification: a Brazilian experience. Dermatol Surg. 2003;29(12): 1200-9.
7. Nilforoushzadeh M, Lotfi E, Nickkholgh E, Salehi B, Shokrani M. Can Subcision with the Cannula be an Acceptable Alternative Method in Treatment of Acne Scars? Med Arch. 2015;69(6):384-6.
8. El-Domyati M, Barakat M, Awad S, Medhat W, El-Fakahany H, Farag H. Microneedling Therapy for Atrophic Acne Scars: An Objective Evaluation. J Clin Aesthet Dermatol. 2015;8(7):36-42.
9. Barikbin B, Akbari Z, Yousefi M, Dowlati Y. Blunt Blade Subcision: An Evolution in the Treatment of Atrophic Acne Scars. Dermatol Surg. 2016. Epub 2016 Feb 15.
10. Fabbrocini G, Fardella N, Monfrecola A, Proietti I, Innocenzi D. Acne scarring treatment using skin needling. Clin Exp Dermatol. 2009;34(8):874-9.

Letter to the editor - Residual hansenomas: therapeutic alternatives

Carta ao editor -Hansenomas residuais: alternativas terapeuticas

DOI: http://dx.doi.org/10.5935/scd1984-8773.20168410

Autores:
Wladimir Fiori Bonilha Delanina[1]

[1] Dermatologist physician, Hansen's Disease Specialist. Director of the Dermatology Division and Clinical Director at Instituto Lauro de Souza Lima - Bauru (SP), Brazil.

To the Editors of Surgical & Cosmetic Dermatology

Firstly, we take pleasure in congratulating the Editors for the quality and excellence of the subjects addressed by the Journal.

Nevertheless, aiming at advising readers – especially those who are somehow involved with the field of the Hansen's disease – we would like to draw attention to the fact that regarding the Case Report published on Surgical & Cosmetic Dermatology 2015; 7 (3): 258-262 under the title "Therapeutic alternatives for the treatment of residual hansenoma in patients with cure criteria of leprosy ", the ROUTINE at the Instituto Lauro de Souza Lima is:

- not to recommend the injection of corticosteroids or other drugs into hansenomas
- to indicate surgical exeresis in hansenomas that cause aesthetic alterations
- the treatment of keloids does not depend on the patient's bearing (or not) leprosy

Kind Regards,
Wladimir Fiori Bonilha Delanina

Correspondence:
Wladimir Fiori Bonilha Delanina
Rodovia Comte João Ribeiro de Barros km 225/226
17034-971- Bauru - SP
Brazil
e-mail: dermatologia@ilsl.br

Received on: 28/03/2016
Approved on: 01/12/2016

This study was performed at the Instituto Lauro de Souza Lima, Bauru (SP), Brazil.

Suporte Financeiro: Nenhum
Conflito de interesse: Nenhum

REFERENCES

1. Wachholz PA, Masuda PY, Sette CS. Alternativas terapêuticas no tratamento de hansenomas residuais em paciente com critérios de cura de hanseníase. Surg Cosmet Dermatol. 2015;7(3):258-262.