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Surgical & Cosmetic Dermatology

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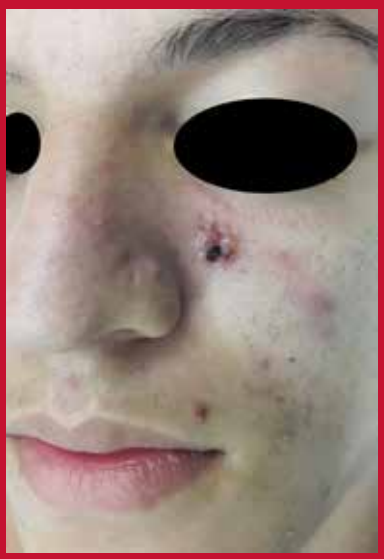
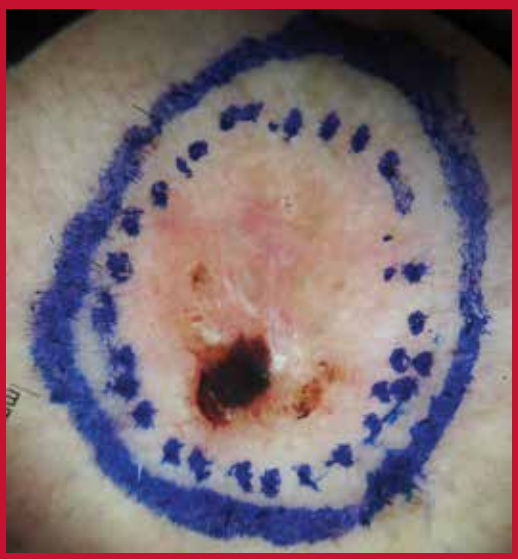
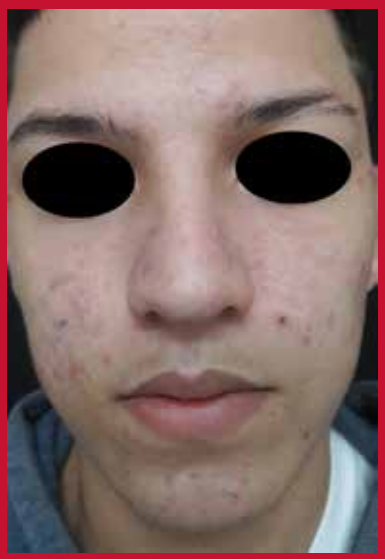
Basal Cell Carcinoma in the Face of Non-Syndromic Adolescents: From Rarity to a New Reality?

Deaths related to liposuction in Brazil

Basal cell carcinoma originating in a tattoo: report of two cases

Case Report: Persistent, Intermittent Delayed Swelling (PIDS) of Hyaluronic Acid filler, triggered by COVID-19

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Av. Rio Branco, 39 18º andar
Cep: 20.090-003
Rio de Janeiro-RJ, Brasil.
Fone: 55 (21) 2253-6747
E-mail: surgicalcosmetic@sbd.org.br
website: www.surgicalcosmetic.org.br

A *Surgical & Cosmetic Dermatology* é uma publicação oficial da Sociedade Brasileira de Dermatologia (SBD) em parceria com a Sociedade Brasileira de Cirurgia Dermatológica. O conteúdo técnico-científico apresentado nesta publicação é de co-propriedade da Sociedade Brasileira de Dermatologia.

Editada por: Sociedade Brasileira de Dermatologia.

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Equipe Técnica
Nazareno Nogueira de Souza

Bibliotecária
Vanessa Mafra

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INSTRUÇÕES AOS Autors

A Surgical & Cosmetic Dermatology (S&CD), editada em 2009, constitui publicação médica destinada a difundir conhecimento e experiência nas áreas de Cirurgia Dermatológica, Oncologia Cutânea, Estudo de Imagens, Tecnologia em Dermatologia e Cosmiatria. É uma publicação trimestral da Sociedade Brasileira de Dermatologia (SBD) que conta com o apoio científico da Sociedade Brasileira de Cirurgia Dermatológica e do Colégio Íbero Latino de Dermatologia, que baseia sua política ética e editorial nas regras emitidas pelo The International Committee of Medical Journal Editors (ICMJE), www.icmje.org. A revista está disponível na íntegra online e adota a política de acesso aberto. A S&CD não cobra aos Autors para que submetam ou publiquem manuscritos, não havendo qualquer tipo de custo ou taxas aos Autors. A revista adota também a licença de uso da Creative Commons CC BY, https://creativecommons.org/licenses/by/3.0/br/.

Os manuscritos devem estar de acordo com os padrões editoriais para artigos submetidos a periódicos biomédicos estabelecidos na Convenção de Vancouver (Requisitos Uniformes para Manuscritos Submetidos a Revistas Biomédicas), regras para relatos de ensaios clínicos e revisões sistemáticas (metanálises). A inclusão em um registro público de ensaios clínicos é uma condição para a publicação de ensaios clínicos nesta revista, de acordo com as recomendações do ICMJE.

Serão produzidos exemplares impressos da versão em língua portuguesa, com resumos e títulos em inglês. A versão da língua inglesa estará disponível nos websites da SBD e da S&CD, no link: www.surgicalcosmetic.org.br.

Nomes de Autors e de pareceristas são mantidos em sigilo; a revista adota o sistema de double blind review. Todos os artigos propostos à publicação serão previamente submetidos à revisão anônima e confidencial de no mínimo dois membros do Conselho Editorial ou dos Conselhos Nacional e Internacional de Revisores, seguindo as diretrizes do COPE (Committee on Publication Ethics).

Quando aceitos, estarão sujeitos a pequenas correções ou modificações que não alterem o estilo do autor.

A S&CD segue o Guia para o registro e publicação de retratação e também o Guia para registro e publicação de errata elaborados pela SciELO, disponível no endereço eletrônico http://www.scielo.org/php/level.php?lang=p-t&component=56&item=57

Os Autors ao submeterem manuscrito para avaliação da revista devem garantir que o mesmo não contém Nonea violação de quaisquer direitos autorais ou outro direito de terceiro. A S&CD utiliza software antiplágio para combater o plágio acadêmico e profissional, verificando a originalidade de artigos.

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Estudos em seres humanos e animais

Se o trabalho envolver seres humanos, o autor deve cerificar que o trabalho descrito foi realizado de acordo com a Declaração de Helsinque para experimentos envolvendo seres humanos. O manuscrito também deve estar de acordo com as Recomendações para a Elaboração e Publicação de Trabalhos Acadêmicos em Periódicos Médicos e incluir populações humanas representativas (sexo, idade e etnia) de acordo com essas recomendações.

O manuscrito deve conter a informação de que o consentimento informado foi obtido em experimentos envolvendo seres humanos. Os direitos de privacidade dos envolvidos na pesquisa devem sempre ser observados.

Todos os experimentos com animais devem estar em conformidade com as diretrizes ARRIVE e devem ser realizados de acordo com a Lei dos Animais (Procedimentos Científicos) do Reino Unido, 1986 e diretrizes associadas, com a Diretiva 2010/63/EU para experimentos em animais, ou com as orientações do National Institutes of Health para cuidado e uso de animais de laboratório (NIH Publications No. 8023, revisada em 1978).

Estudos em pacientes ou voluntários exigem termos de consentimento de aprovação do comitê de ética e o número de protocolo deve ser informado à revista. Os consentimentos, permissões e liberações apropriados devem ser obtidos sempre que um autor desejar incluir detalhes do caso, informações pessoais ou imagens de pacientes e quaisquer outros indivíduos em uma publicação.

Preprint

A revista S&CD procura manter suas normas em constante atualização, caminhando em conjunto com as tendências da publicação científica. Aceitamos os Preprints como forma de incentivo à comunicação entre os Autors e para dar agilidade à ciência.Preprint é um manuscrito científico previamente depositado pelos Autors em repositórios, afim de disseminar os dados de pesquisa mais rapidamente. Depositar um manuscrito em plataforma de Preprints não é considerado publicação duplicada. No entanto, a S&CD não aceita ma- nuscritos já publicados anteriormente em outro periódico.

PROCESSO DE AVALIAÇÃO

O processo de avaliação dos artigos submetidos à S&CD ocorre nas seguintes etapas:

- Verificação preliminar: a secretaria editorial verifica a consistência dos dados cadastrais e observância das normas de submissão. Se aprovados os manuscritos são direcionados para a próxima fase, o desk-review.

- Desk-review: nesta fase o Editor analisa o formato científico do manuscrito quanto aos objetivos, marco teórico, linguagem e metodologia, verificando o enquadramento do artigo ao escopo editorial da revista e o potencial de contribuição da pesquisa. Essa tarefa é dividida entre o editor geral e os editores adjuntos, cada qual em sua área de especialidade. Se aprovados pelos editores os artigos são direcio- nados para o double blind review.

- Double blind review: o artigo e demais documentos suplementares são encaminhados a pelo menos dois avaliadores,

especialistas nacionais ou estrangeiros reconhecidos no assunto dos manuscritos que avaliam, e que não possuam qualquer espécie de vinculação com o trabalho em revisão.

- Após o trabalho receber os pareceres oriundos do estágio double blind review, o editor envia aos Autors o resultado pelo sistema de submissão, que poderá referir-se a uma das três situações seguintes:

• Aprovação: o artigo quando aprovado, o autor correspondente será comunicado sobre a aprovação e depois sobre a publicação, também receberá uma prova final para aprovação e correções.

• Revisão: os Autors deverão realizar as adequações sugeridas, ou apresentarem as devidas argumentações para não procederem. As versões dos Autors visando atender as revisões solicitadas pelos pareceristas deverão sempre ser acompanhadas de uma respectiva minuta esclarecendo as alterações atendidas e explicando as razões das não atendidas. O prazo de entrega do artigo revisado é determinado pelo editor e informado aos Autors em função da revisão solicitada. Após a entrega do artigo revisado, o mesmo é novamente submetido aos pareceristas para verificação das alterações. A revisão poderá envolver várias rodadas até que se chegue ao parecer final de aprovação ou rejeição do manuscrito.

• Rejeição: o artigo não foi aceito para publicação conforme justificativa apresentada pelo editor embasada na avaliação dos pareceristas, que refletem as melhorias a se- rem realizadas no texto.

- Cabe ao Editor, após o parecer dos avaliadores, revisar e aprovar ou recusar a versão final do trabalho. O editor e editores associados também poderão recusar os manuscritos em avaliação prévia assim que submetidos por não se encaixarem no perfil editorial da revista.

- Durante todo o processo editorial os Autors podem acompanhar o *status* da avaliação, podendo inclusive recorrer de decisões.

*****_Os casos não previstos nestas diretrizes serão tratados pelo Editor-Chefe da S&CD, e pelo Conselho Editorial quando as- sim se fizer necessário_.

ORIENTAÇÕES PARA O PREPARO DOS ARTIGOS

A preparação correta do manuscrito torna os processos de revisão e publicação mais eficientes. Assim, recomendamos alguns cuidados que podem facilitar significativamente a preparação dos manuscritos.

1. Os artigos devem ser inéditos e redigidos no idioma de origem do autor (português, espanhol ou inglês): a equipe editorial providenciará as versões necessárias. A escolha da fonte deve ser Times New Roman ou Arial, de número 12.

2. O título do trabalho deve ser curto e conciso, informado em português e inglês, com até 150 caracteres sem espaços, acompanhado de um título resumido.

3. Os resumos em português e inglês devem acompanhar o formato adequado ao tipo de artigo.

4. Os Autors devem informar o nome com suas abreviaturas, e as suas afiliações institucionais, seguidos de cidade, estado e país. Os vínculos às instituições devem ser citados em ordem hierárquica (ex.1º Departamento, 2º Universidade) e não são permitidas a inclusão dos mini-currículos. Quando um autor é afiliado a mais de uma instituição, cada uma deve ser identificada separadamente. Quando dois ou mais Autors estão afiliados à mesma instituição, a sua identificação é feita uma única vez. É obrigatório mencionar o número ORCID, utilizado para a identificação de pesquisadores. O autor deve assumir pelo menos uma responsabilidade na elaboração do trabalho e deverá informar a contribuição de cada um na submissão. Um dos Autors deve ser designado como autor correspondente, com endereço de e-mail. Deve também ser citado o local de realização do trabalho.

5. Os Autors devem informar claramente se houve conflitos de interesse e suporte financeiro.A

6. s palavras-chave devem ser citadas em português e em inglês (Keywords), totalizando 3 a 10 por idio- ma, devendo ser incluídas em todos os tipos de artigos. É recomendável que estas palavras deverão estar contidas no DeCS (Descritores em Ciências da Saúde) e MeSH (Medical Subject Headings) que podem ser acessados na internet.

7. O número limite de palavras para os textos deve ser obedecido segundo o tipo de artigo, e computado excluindo as REFERENCES e os resumos em português e inglês.

8. Devem ser evitadas informações introdutórias extensas e repetitivas, dando-se preferência às mais recentes, ainda não publicadas. Evite textos com repetição da mesma informação no resumo, introdução e discussão.

9. Pesos e medidas devem ser expressos no sistema métrico decimal, e temperaturas em graus centígrados.

10. Drogas devem ser mencionadas por seus nomes genéricos, seguidos da dosagem e posologia empregadas, evitando-se a citação de termos comerciais ou marcas. Descrições de quaisquer equipamentos, instrumentos, testes e reagentes devem conter o nome do fabricante e o local de fabricação.

11. De acordo com o ICMJE, apenas podem ser designados como Autors, aqueles que participaram ativamente no trabalho, podendo assim assumir a responsabilidade pública pelo seu conteúdo. Os créditos de autoria devem se basear exclusivamente em contribuições substanciais para:

a- discussão e planejamento do tema e protocolo, análise ou interpretação de dados;

b- redação do artigo ou sua crítica;

c- responsabilidade pela aprovação final para a publicação.

Outras contribuições menores como sugestões de literatura, coleta e análise de dados, obtenção de financiamento, auxílio técnico na execução de rotinas, encaminhamento de pacientes, interpretação de exames de rotina e chefia de serviço ou departamento que não estejam envolvidas no estudo, não constituem critérios para autoria. e podem ser reconhecidas separadamente sob a forma de "agradecimentos", de acordo com a decisão dos Autors.

12. As REFERENCES bibliográficas devem ser listadas nas últimas páginas do artigo, e numeradas de acordo com a

citação no texto (em ordem numérica seqüencial), seguindo o estilo Vancouver, como indicado pelo International Committee of Medical Journal Editors (ICMJE). REFERENCES citadas em legendas de tabelas e Figures devem manter a seqüência com as citações no texto. Todos os Autors devem ser citados se forem até seis; acima disso, devem ser mencio- nados os seis primeiros e "*et al.*". Seguem-se exemplos dos tipos mais comuns de REFERENCES. Exemplos de citações no texto retirados do ICMJE:

a- Artigo em periódico:

Hallal AH, Amortegui JD, Jeroukhimov IM, Casillas J, Schulman CI, Manning RJ, *et al.* Magnetic resonance cholangiopancreatography accurately detects common bile duct stones in resolving gallstone pancreatitis. J Am Coll Surg. 2005;200(6):869-75.

b- Capítulo de livro:

Reppert SM. Circadian rhythms: basic aspects and pediatric implications. In: Styne DM, Brook CGD, editors. Current concepts in pediatric endocrinology. New York: Elsevier; 1987. p .91-125.

c- Texto na Internet:

Ex. com autor indicado:

Fugh-Berman A. PharmedOUT [Internet]. Washington: Georgetown University, Department of Physiology and Biophysics; c2006 [cited 2007 Mar 23]. Available from: https://www.pharmedout.org/. Ex. quando o autor é uma organização: International Union of Biochemistry and Molecular Biology. Recommendations on Biochemical & Organic Nomenclature, Symbols & Terminology etc. [Internet]. London: University of London, Queen Mary, Department of Chemis- try; [updated 2006 Jul 24; cited 2007 Feb 22]. Available from: https://www.chem.qmul.ac.uk/iubmb/.

d- Apresentação prévia em eventos:

Bruhat M, Silva Carvalho JL, Campo R, Fradique A, Dequesne J, Setubal A, editors. Proceedings of the 10th Congress of the European Society for Gynaecological Endoscopy; 2001 Nov 22-24; Lisbon, Portugal. Bologna (Italy): Monduzzi Editore, International Proceedings Division; c2001. 474 p.

13. Ilustrações (Figures, quadros, gráficos e tabelas) devem ser referidas em ordem numérica sequencial no texto em números arábicos (exemplo: Figure 3, Gráfico 7), cabendo ao Editor suprimir as redundantes. As legendas das Figures e gráficos e os títulos e notas de rodapé das tabelas devem descrever precisamente seu conteúdo com frases cur- tas, porém suficientes para a compreensão ainda que o arti- go não seja totalmente lido. Todos devem ser inseridos no passo correspondente a ilustrações no sistema, evitando que use o campo destinado ao texto para que não contabilizem as palavras dentro das ilustrações.

14. As Figures deverão ter resolução mínima de 300 DPI, largura mínima de 1.200 pixels com altura proporcional, e serem gravadas nos formatos JPG ou TIF. Podem ser colocadas setas ou linhas para localizar as áreas de interesse. As legendas das imagens histológicas devem especificar a coloração e o aumento. Se uma Figure já foi publicada anteriormente, deverá citar a fonte original abaixo da mesma e constar nas REFERENCES. Deverão enviar à revista a permissão do detentor dos direitos autorais para a sua reprodução. No uso de Figures que identifiquem a face de pacientes será preciso autorização por escrito para divulgação (ver no site da revista o documento Autorização para uso de fotografias).

15. Quanto aos vídeos é necessário inserir legendas contendo informações como título do manuscrito, autoria, instituição e outros comentários pertinentes. No uso de imagens de pacientes, a identidade deverá ser resguardada, do contrário, será preciso anexar-lhes permissão por escrito para divulgação.

16. Os gráficos deverão ser elaborados em Microsoft Excel. As tabelas dispensam sua descrição no texto tendo a finalidade de suplementá-lo e não a de aumentá-lo. As unidades utilizadas para exprimir os resultados (m, g, g/100, mL etc.) Figurerão no alto de cada coluna. Os pacientes devem ser identificados por números ou letras, e nunca pelos nomes, iniciais ou número de registro hospitalar.

17. O limite máximo de Autors aceitável é de 5; só haverá exceção para trabalhos de maior complexidade (ex. Artigo Original, Revisão) mediante justificativa e aprovação dos editores.

18. As opiniões e declarações contidas na revista são de responsabilidade única e exclusiva de seus Autors, não sendo, necessariamente, coincidentes com as da Equipe Edi- torial, do Conselho de Revisores ou da Sociedade Brasileira de Dermatologia.Os Autors deverão submeter seu manuscrito para avaliação do Conselho Editorial da revista no endereço eletrônico que se segue: https://www.sgponline.com.br/scd/ sgp/.

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CONTATO DA REVISTA:

A/C Surgical & Cosmetic Dermatology Av. Rio Branco, nº 39, 18º andar.
Rio de Janeiro – RJ, Brasil. CEP: 20090-003.
surgicalcosmetic@sbd.org.br

A revista aceita trabalhos inéditos e não publicados das seguintes categorias:

1– ARTIGOS DE REVISÃO

Poderão ser aprofundados os temas específicos nas áreas de interesse da S&CD, algoritmos, compilações e estatísticas. Estes trabalhos têm formato livre, porem devem conter resumo não estruturado de até 100 palavras e conclusões ou considerações finais. Limite: texto até 6000 palavras, 10 ilustrações e 60 REFERENCES. Os artigos de revisão sistemática ou metanálises devem seguir orientações pertinentes (https://www.cochrane.org/)

2– ARTIGO ORIGINAL

É o relato de uma pesquisa investigativa original nas áreas de Cirurgia Dermatológica, Oncologia Cutânea, Tecnologia em Dermatologia e Cosmiatria. Exemplos: estudos experimentais, estudos clínicos, comparações e descrições de técnicas ou de métodos de avaliação, estudos de áreas afins (ex: estudos farmacêuticos em cosmiatria). O texto deverá conter até 4000 palavras, 10 ilustrações e 35 REFERENCES e seguir o formato IMRDC (Introdução e objetivo, Métodos, Resultados, Discussão, Conclusão)

Resumo: deverá conter no máximo 200 palavras e ser estruturado seguindo os itens: Introdução, Objetivo, Métodos, Resultados e Conclusões. Não é permitido afirmar que os resultados ou outros dados serão apresentados ou discutidos.

Introdução: citar as razões que motivaram o estudo, descrevendo o estado atual do conhecimento sobre o tema. Utilizar o último parágrafo para especificar a principal pergunta ou objetivo do estudo, e a principal hipótese testada, se houver.

Métodos: Explicar como o estudo foi feito:

a- Tipo de estudo: descrever o seu desenho especificando a direção temporal (retrospectivo ou prospectivo), o tipo de randomização quando utilizada (pareamento, sorteio, sequenciamento, etc), se o estudo foi cego, comparativo, controlado por placebo, etc.

b- Local: indicar onde o estudo foi realizado (instituição privada ou pública), citar que a pesquisa foi aprovada pelo Comitê de Ética em Pesquisa de sua instituição, os procedimentos de seleção, os critérios de inclusão e exclusão, e o número inicial de pacientes.

c- Procedimentos: descrever as principais características das intervenções realizadas, detalhando a técnica e lembrando que o estudo de investigação deverá ser reprodutível.

d- Descrição dos métodos utilizados para avaliação dos resultados.

e- Inclusão da análise estatística descritiva e/ou comparativa com descrição do planejamento da amostra

(representativa do universo a ser estudado), a análise e os testes estatísticos e apresentação dos níveis de significância adotados. A utilização de análises estatísticas não usuais é incentivada, porém neste caso, deve-se fazer uma descrição mais detalhada da mesma.

Resultados: descrever os principais resultados que devem ser acompanhados de estimativas pontuais e medidas de dispersão (p.ex., média e erro padrão) ou de estimativas intervalares (p.ex., intervalos de confiança), bem como os níveis descritivos dos testes estatísticos utilizados (p.ex. "p-value"). Os achados também devem ser interpretados sob o ponto de vista clínico.

Discussão: enfatizar os novos e importantes resultados encontrados pelo estudo e que farão parte da conclusão. Relatar observações de outros estudos relevantes. Mencionar as limitações dos achados e as implicações para pesqui- sas futuras.

Conclusões: devem ser concisas e responder apenas aos objetivos propostos. A mesma ênfase deve ser dada para estudos com resultados positivos ou negativos.

3- COMUNICAÇÕES

Artigos originais, breves, abordando resultados preliminares de novos achados de interesse nas áreas focadas pela revista. Texto com formatação semelhante ao artigo original, resumo estruturado de até 200 palavras. Limite: texto até 2000 palavras, 8 ilustrações e 15 REFERENCES.

4– DIAGNÓSTICO POR IMAGEM

Abordagem de temas ou casos clínicos, em que os exames de imagens (dermatoscopia, microscopia confocal, ultrassom e outros métodos) são fundamentais no diagnóstico ou tratamento. Resumo não estruturado de até 100 palavras, texto até 1200 palavras, 6 ilustrações e 5 REFERENCES.

5– COMO EU FAÇO?

Descrição de novas técnicas ou detalhes de técnicas. Resumo não estruturado de até 100 palavras, introdução com revisão de literatura, métodos, resultados, discussão e conclusão. Limite: 1200 palavras, 8 ilustrações e 30 REFERENCES.

6– RELATO DE CASO

Descrição de casos ou serie de casos de relevância nas áreas de interesse da S&CD, com descrição de tratamentos, complicações, etc. Resumo não estruturado de até 100 palavras, introdução com revisão de literatura, métodos, resultados, discussão e conclusão, sempre que pertinentes. Limite: texto até 1200 palavras, 8 ilustrações e 30 REFERENCES.

7– CARTAS

Comentários objetivos e construtivos sobre matérias publicadas. Texto até 600 palavras, e no máximo 5 REFERENCES.

Surgical & Cosmetic Dermatology

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Axillary bromhidrosis surgical treatment

Tratamento cirúrgico da bromidrose axilar

Review

Authors:
Flávio Barbosa Luz [1]
Lara Assunção Kriger[1]

[1] Universidade Federal Fluminense, Niterói (RJ), Brazil.

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ABSTRACT

Introduction: Axillary bromhidrosis is a disease of significant psychosocial impact characterized by bad odor in the armpits. The cause of bromhidrosis is multifactorial, and studies indicate that it is related to the bacterial transformation of substances secreted by the apocrine glands. Some cases of bromhidrosis are difficult to control by clinical therapies, and surgical therapies are well indicated. Surgical treatments for the disease aim to remove the axillary sweat glands and range from more aggressive to minimally invasive procedures. This review aims to list and compare all surgical alternatives described in the medical literature.
Keywords: Surgical Procedures, Operative; Sweat Glands; Hyperhidrosis; Apocrine Glands

RESUMO

Introdução: *A bromidrose axilar é uma doença de impacto psicossocial relevante caracterizada por mau odor nas axilas. A causa da bromidrose é multifatorial, e os estudos apontam que está relacionada à transformação bacteriana das substâncias secretadas pelas glândulas apócrinas. Alguns casos de bromidrose são de difícil controle pelas terapêuticas clínicas, estando bem indicadas as terapias cirúrgicas. Os tratamentos cirúrgicos da doença visam à remoção das glândulas sudoríparas axilares e variam de procedimentos mais agressivos aos minimamente invasivos. Esta revisão objetiva elencar e comparar todas as alternativas cirúrgicas descritas na literatura médica.*
Palavras-chave: *Glândulas Apócrinas; Hiperidrose; Procedimentos Médicos e Cirúrgicos de Sangue; Glândulas Sudoríparas*

Correspondence:
Flávio Barbosa Luz
R. Guapiara, 78
Tijuca
20521-180 Rio de Janeiro (RJ)
E-mail: luzflavio@gmail.com

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INTRODUCTION

Axillary bromhidrosis is a common condition that can cause severe social obstacles to the individual.[1] Osmidrosis is characterized by the foul odor produced by the bacterial decomposition of the secretion emitted mainly by the apocrine glands. Hyperhidrosis is a condition of excessive sweat linked to the eccrine glands. Bromhidrosis is the sum of hyperhidrosis and osmidosis.[1]

There are three types of sweat glands: apocrine, eccrine, and apoeccrine.[2] Apocrine glands are present in specific areas of the body, such as the armpits, genitalia, scalp, periorbital area, and ear canals. They secrete a small amount of odorless fluid that undergoes bacterial decomposition upon reaching the skin, which makes it odorous. Eccrine glands have their own characteristic. The re-absorbent duct opens directly to the skin surface, and its secretory portion produces a solution rich in NaCl, directly related to axillary hyperhidrosis. Apoeccrine glands become apparent in the 8-14 age range and appear to be closely associated with excessive sweating (hyperhidrosis).[1]

METHODS

We collected the scientific articles in the PubMed and Web of Science databases using the terms "axillary bromhidrosis" and "surgery". We selected articles published between 1972 and 2019 (the oldest ones are related to the surgical technique of axillary skin with the adjacent subcutaneous tissue resection) in English and Spanish.

All abstracts were read, and the articles to be inserted contained relevant information on surgical therapies and bromhidrosis etiopathogenesis. As bromhidrosis's surgical treatment is very similar to hyperhidrosis, this review also used articles on the latter condition. Some articles were discarded for not bringing any novelty compared to the others already selected.

JUSTIFICATION

Axillary bromhidrosis is a common disease, underdiagnosed and undertreated, affecting social interactions too much and reducing patients' quality of life. According to the conception that clinical treatments usually have satisfactory effects only in mild cases, surgical approaches are of paramount therapeutic importance. Due to the low number of studies that standardize these interventions, the present review aims to list such techniques, reinforcing the positive and negative aspects for a better possibility of therapeutic choice.

RELEVANCE

Axillary bromhidrosis is a disease with severe psychosocial impacts on the individual, interfering with their daily activities. Patients with more severe symptoms consider it intolerable or almost intolerable. The Dermatology Life Quality Index (DLQI) of patients with axillary hyperhidrosis was analyzed, and the result was compared with other dermatological problems, such as acne, birthmarks, pruritus, psoriasis, and eczema. The results indicated that hyperhidrosis was associated with a lower quality of life when compared to other diseases.[3] It is believed that bromhidrosis can often be an even more embarrassing condition when compared to hyperhidrosis, in addition to the frequent overlap between the two entities.

ETIOLOGY

The etiology of bromhidrosis is multifactorial, but the leading causes are its intimate relationship with axillary hyperhidrosis, the composition of the sweat secreted by the apocrine glands, and the degradation of these components by microorganisms present in the axillary skin, in addition to genetic and dietary factors.

SWEAT COMPOSITION

The foul odor comes from transforming non-odorous substances secreted by the apocrine, eccrine, and sebaceous glands into volatile and odorous substances. The axillary microbiota consists mainly of gram-positive bacteria of the genera *Staphylococcus*, *Micrococcus*, *Propionibacterium*, and *Corynebacterium*, which is the primary cause of the foul odor, whose substrate originates from the apocrine glands.[4]

Volatile fatty acids and thioalcohols are mainly responsible for the foul axillary odor, while steroids, although they contribute, are not so relevant in this process. Medium-chain volatile fatty acids (C6-C10), in particular the trans (E) isomer of 3-methylhex-2-enoic acid (3M2H), have a significant contribution to axillary foul odor. It is linked to the amino acid L-glutamine in the secretion of apocrine glands, and the action of a Corynebacterium enzyme releases it.[5] It was later discovered that an ABCC11 gene allele is essential for the secretion of L-glutamine conjugated to E-3M2H.[6]

The volatile fatty acids that cause the foul axillary odor are short-chain (C2-C5) and medium-chain (C6-C10). Propionibacterium and Staphylococcus ferment glycerol from the hydrolysis of triacylglycerol, and lactic acid present in the skin, transforming them into acetic and propionic acid. Regarding steroids, 16-androstenes, 5α-androstenol, and 5α-androstenone are present in the sweat of the apocrine glands and have already been significantly associated with a foul odor. However, it is known today that axillary bacteria can only produce 16-androstenes from precursors containing C16 with a double bond.[4]

Laboratory studies have identified four thioalcohols involved in foul axillary odor. These represented two groups of isomers, molecular weight 120-u, and 134-u. The first isomer has an unpleasant smell, comparable to meat or onion, characteristic of the foul axillary odor. The other is a less pronounced odor occasionally related to fruits. The less foul odor of the 134-u isomer was identified as 3-mercaptohexan-1-ol. The odor compared to meat or onion (120-u) was confirmed as 2-methyl-3-mercaptobutan-1-ol. Later, other thioalcohols were also identified, such as 3-mercaptopentan-1-ol (probably equivalent to the least odorous, isomer 120-u), and 3-methyl-3-mercaptohexan-1-ol (molecular weight 148-u), identified and associated with the foul odor. In conclusion, there is vast evidence that, together with medium-chain fatty acids, such as 3M2H and 3-hydroxy-3-methylhexanoic acid, the primary molecules cause axillary odor.[4]

GENETICS

The starting point for understanding human odor came from the study of cerumen (ear wax), which is a product of the ceruminous apocrine glands. The study investigates the polymorphism of a nucleotide of the ABCC11 gene, which encodes an ATP-driven pump and is responsible for determining the cerumen (the AA genotype corresponds to the dry cerumen and the GA and GG genotype to the wet cerumen, which is dominant over the other). Thus, the study proposed that wet cerumen relates to a strong axillary odor and dry cerumen to a less pronounced aroma.[7]

MICROBIOTA

The apocrine glands secrete long-chain fatty acids, fatty acids linked to amino acids, sulfur compounds, and hormones, which have too long chains to be volatile. The bacteria (mainly Staphylococcus and Corynebacterium spp.) break down these compounds into smaller ones, which become volatile and have a noticeable odor.[8] These bacteria are distributed both on the skin and below the surface, mainly in the glandular structures, hair follicles, and ducts of these glands. It seems to explain why topical treatments of bromhidrosis that interfere with bacterial colonization tend to be ineffective since they only affect bacteria present on the axillary surface, with rapid recolonization, especially of the attachments.

SURGICAL TREATMENT OF BROMIDROSIS

Often, the use of deodorants and antiperspirants by individuals who have bromhidrosis can be harmful since it can increase bacteria's diversity and select those primarily responsible for the foul odor. It subsequently leads to intense colonization by such bacteria.[8] When clinical treatments do not show satisfactory results, there are options for local surgery with the main objective of removing the apocrine.

Local surgeries for axillary hyperhidrosis (also applicable to bromhidrosis) can be divided into three main groups:[9]

1. Resection of glandular tissue without excision of the skin (only surgical incision to access the subcutaneous glandular tissue);
2. Axillary skin with adjacent subcutaneous tissue resection;
3. Combination of the two methods resulting in a partial resection of the skin associated with the subcutaneous tissue and adjacent tissues excision.

We will approach these three major groups in chronological order.

Axillary skin with adjacent subcutaneous tissue resection

They are more invasive techniques and with higher morbidity and risk of complications.

It is the most radical surgical technique and, consequently, the one with a higher chance of complications, mainly related to healing and arm movement limitation. Based on the cases in which this technique was performed, high rates of complications were observed, such as infection, bleeding, poor healing, and necrosis, the most common being: wound dehiscence, partial necrosis, and prolonged healing with subsequent formation of adhesions.[10]

A less invasive alternative to this surgical technique consists of an elliptical excision removing the skin and subcutaneous tissue, containing the sweat glands only in the axillary dome. This method decreases sweating caused by the eccrine glands by up to 80%.[11]

Combination of the two methods resulting in a partial resection of the skin associated with the subcutaneous tissue and adjacent tissues excision

The primary surgical method used to perform this combination of methods is the famous Shelley technique,[12] which consists of a central elliptical excision in the armpit until reaching the fat portion. The lesion margins are everted, and the glandular tissue (containing the eccrine and apocrine glands - Figure 1) is removed along with the dermis and subcutaneous tissue using surgical scissors (Figure 2). The wound is closed using subcutaneous sutures attached to the underlying axillary fascia to obliterate spaces with high chances of bruising (it is also possible that the suture is superficial, as preferred by the surgeon). Occlusive dressing is usually left for 24 hours. Due to the higher infection rates of this surgical technique compared to the others, chlorhexidine solution can be applied before and after the procedure, in addition to prophylactic antibiotics, which the surgeon must evaluate according to the needs of each patient.[12]

It is important to note that there are several variations of the standard technique. For example, a study conducted with 63 patients to assess the surgical procedure's effectiveness to treat axillary bromhidrosis used a method similar to that described

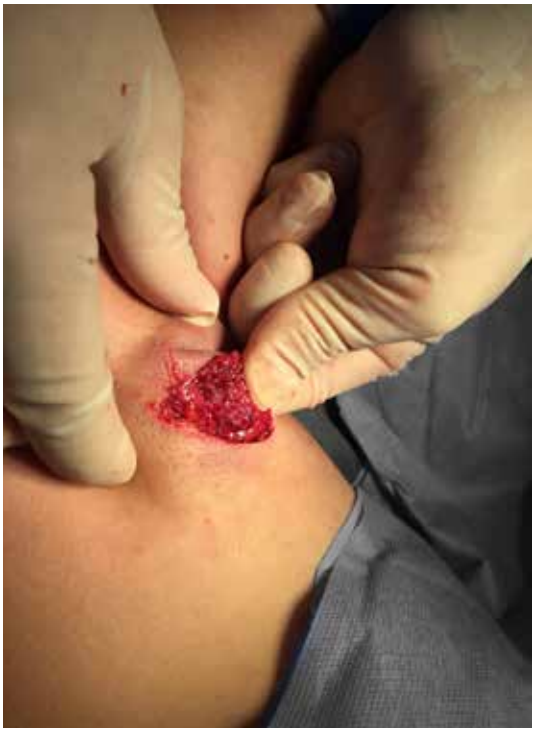

Figure 1: Visualization of glandular tissue after skin incision using the Shelley technique

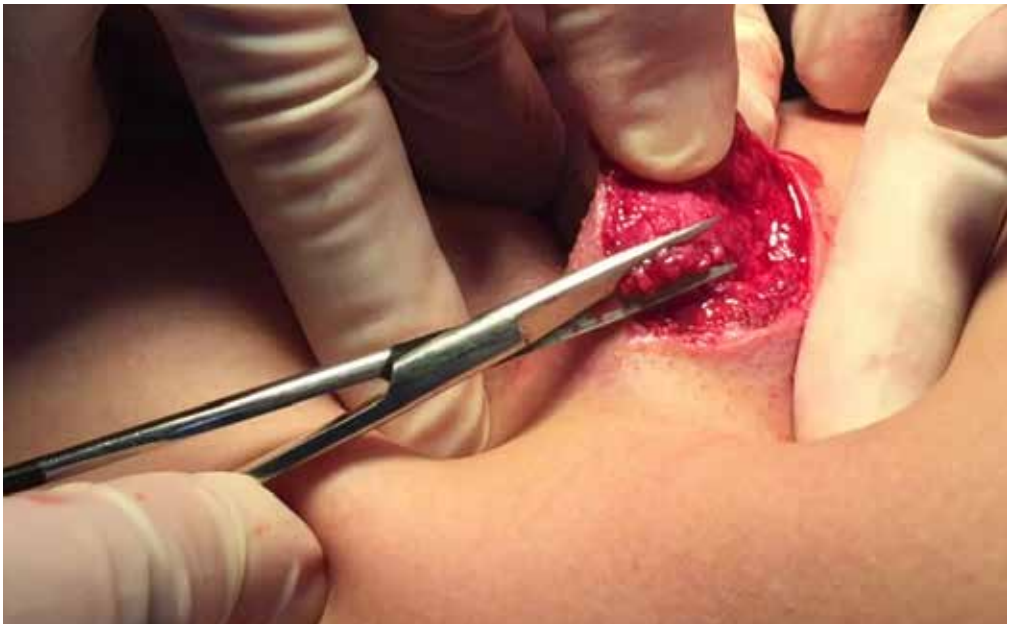

Figure 2: Removal using scissors of the glandular tissue after skin incision using the Shelley technique

above. Still, the superficial fascia was also dissected and removed. Of the 126 operated armpits, bromhidrosis was eradicated in 112 and markedly reduced in 14, with necrosis in only three operated armpits.[13]

Another study with 15 patients[14] operated the armpits using another technique slightly modified from the Shelley technique. The study delimited the sweat area by examining it in bright light to identify and mark the maximum sweat area's extent instead of using Minor's starch-iodine test. An average sweating reduction rate greater than 60% could be achieved.[14]

Another modification of the Shelley's method appears with the technique "pinch and turn-over" the exposed flap,[15] maneuver that significantly facilitates removing the glands. However, comparing the photos in this article with those by Lawrence et al. (2006), there seems to be no novelty in this technique.

Li et al., in 2015, modified the Shelley technique by making two parallel incisions in each armpit instead of one and excising the apocrine glands preserving the superficial axillary fascia. Its results in 115 patients were very encouraging, suggesting that this may be a surgical procedure with a lower recurrence rate, a significant odor reduction, and fewer complications. No necrosis was reported, 112 patients had eradication of bromhidrosis, and three achieved substantial reduction.[16]

A study conducted with 396 patients [17] used a technique similar to the Shelley's, presented that 87.1% of the patients achieved very satisfactory results, 7.8% obtained moderately satisfactory results, and 5.1 % were unsatisfactory due to complications and persistent underarm odor. The complications observed were hematomas, necrosis, infection, wound dehiscence, rippled skin, comedone, cyst, keloid. A possible explanation for the return of the foul odor is that, as the surgery removes only the most superficial tissue of fat and deep dermis, some portion of the apocrine glands may remain in the region and regenerate.[17]

Resection of glandular tissue without excision of the skin

With the emergence of new minimally invasive therapeutic options, this type of surgery can be subdivided into three: superficial liposuction, aspiration curettage, and simple curettage. The first one predominantly removes the subcutaneous tissue; the other two resects the subcutaneous tissue and deep dermal tissue.

When choosing the best technique to be performed, one must consider the difference between the eccrine glands' bromhidrosis). The eccrine glands are located more superficially in the dermis, while the apocrine glands extend from the deep dermis to the subcutaneous tissue. As the reticular dermis is composed of dense and irregular connective tissue, removing apocrine glands attached firmly to the deep dermis is technically more complicated than those located in the subcutaneous tissue.[18] Therefore, although there is no consensus, histological studies [19,20] demonstrate that the eccrine glands are dominant in the dermis, and most of the apocrine glands are located in the subcutaneous tissue.

1) Aspiration curettage

The procedure consists of two main parts: dissection of the dermis from the underlying subcutaneous tissue followed by removing the sweat glands from the dermo-hypodermic junction and the deep dermis. For surgical access, two or three small incisions are made outside the area to be curetted. The surgeon

can make the incision, according to their preference, in different locations: superomedial concerning the armpit, in the anterior and distal edges, in the upper internal region of the arm, and the central portion of the armpit.[21] Chart 1 describes in detail the technique, according to Rezende et al.[21]

According to Rezai, aspiration curettage has a sweating recurrence rate of 20% to 40%. However, with the innovation of surgical methods and instruments, the rates have decreased to less than 6%.[22]

2) Simple curettage

Unlike aspiration curettage, this surgical technique consists of curettage of the axillary region without aspiration. The purpose of this procedure is also the selective removal of the sweat glands. The anesthesia used is usually tumescent.

This technique's main steps are the surgical incision made through the skin to the subcutaneous tissue. Subsequently, dermal tunneling can be done using a curette for scraping, with back and forth movements. This movement occurs until most of the tissue blocks containing the destroyed sweat glands, adipose tissue, and other skin attachments are eliminated.[18]

Curettage should be performed both on the superficial layer of the subcutaneous tissue and in the deep dermis to remove the sweat glands (Figure 3) and, inevitably, some other tissues, especially the hair follicles.[23]

According to Field, 2003, even though patients are informed about increased risks with a more invasive procedure, they prefer to undergo more aggressive surgery expecting a higher chance of curing their condition.[24]

However, surgeons should be alert to the fact that curettage should be performed in a way that generates the best possible results but with the least amount of complications. [21]

The interruption of curettage varies according to the perceptions of each author. However, the main parameters are skin thickness (Figures 4 and 5); skin color (a pale violet - Figure 6); complete elevation of the axillary skin of the subcutaneous tissue; "skin to skin" sliding, demonstrating that there is no more fat adhered to the dermis; palpable hair follicles during the "skin to skin" sliding; sound similar to sipping caused by the cannula; visualization of the curette by transparency (Figure 7); and easy removal of the axillary hair when pulled slightly by the surgeon.[21]

According to Bechara et al. (2008), the use of cannulas with sharp edges is more effective than other less aggressive or blunt cannulas. According to these authors, combining two types of cannulas can lead to extensive damage to the skin and the dermal vascular plexus.[25]

BOX 1: Aspiration curettage surgery technique	
1.	The patient is placed in a supine position with the arms abducted at a 90°-135 ° angle to expose the armpit. Excessive abduction should not occur to avoid injury to the brachial plexus
2.	Tumescent anesthesia is typically used in minimally invasive surgery to treat axillary bromhidrosis. After making the incisions, a volume of 100 ml to 500 ml per armpit of a tumescent solution is infiltrated into the pre-marked axillary area as superficially as possible, creating an "orange peel" effect on the overlying tissue. Although the standard formula of the tumescent solution is composed of 1,000 ml of saline, 50 ml to 100 ml of lidocaine1%, 1 ml of epinephrine 1:1,000, and 12.5 ml of sodium bicarbonate, different authors use numerous variations. The prolonged analgesic effect of tissue deposits of lidocaine guarantees an almost painless post-operative. The expansion of the soft tissues of the armpit minimizes the risk of injury to the brachial plexus. It also has the advantage of eliminating the risks involved in general anesthesia, intravenous sedation, and the use of narcotic analgesics. The use of small diameter infusion cannulas is essential for patient comfort.
3.	After bleaching the region, subcutaneous tunnels are created through a sudden dissection, in back and forth movements to separate the dermis from the subcutaneous tissue. The subcutaneous sweat glands are thus mobilized. Subsequently, the suction and curettage cannula of the Cassio type, or a curette, is inserted to perform dermal curettage.
4.	The aspiration of the removed tissue can be conducted using devices or manually. In manual vacuum suction, a syringe is attached to the cannula inserted into the tissue to be removed. A mechanical lock is required to keep the piston pulled. When a mechanical suction system is chosen, the cannulas are connected to a collection bottle via a tube. The tissue mobilized by the cannulas is taken to the receptacle using a collecting system, with negative pressure generated by a vacuum pump. The size of the cannula and its opening, in addition to the amount of vacuum applied and speed, directly affect the amount of tissue removed. The surgeon's non-dominant hand can assist in the procedure by compressing the overlying skin. Care should be taken when performing curettage around the skin incisions, as the subcutaneous tissue close to these areas may not be properly removed during aspiration. Irrigation and meticulous hemostasis are performed at the end of the procedure, and the surgical incisions are closed. It is suggested to use anchorage sutures where there were aggressive aspirations and curettage to reduce bruises' formation. The dressing can be done with antibiotic ointment.

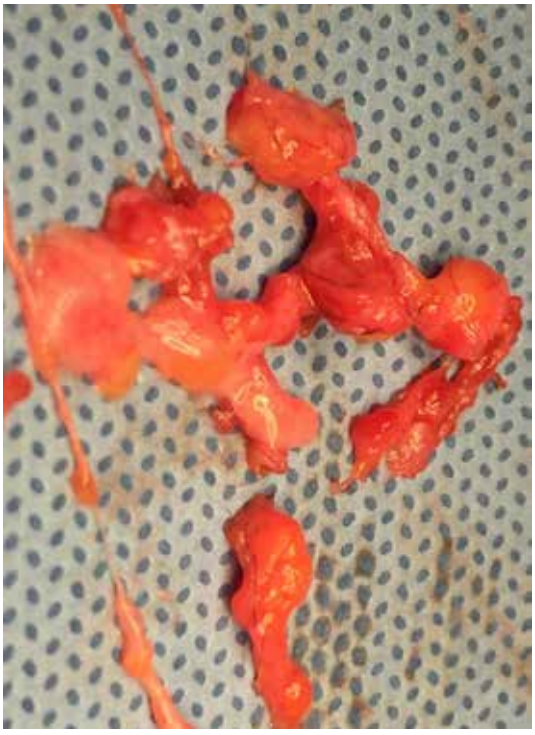

Figure 3: Macroscopic aspect of the tissue removed by curettage. Note the adipose tissue adhered to the glands and hair

Figure 4: Preoperative digital clamping of the axillary skin

3) Superficial liposuction

Usually, the technique consists of two small incisions (3 mm to 4 mm each). Dermal tunneling is performed, and the junction of the dermis with the subcutaneous tissue is aspirated with a cannula. There is the possibility of starting the procedure with a cannula and, after the subcutaneous tissue is very thin, one with an opening more suitable for subdermal scraping, for example, can replace it. A firm handgrip can stabilize the underlying skin and control the depth the cannula reaches. A thin axillary skin wholly separated from the underlying tissue characterizes the end of the procedure.[26-28]

DISCUSSION

The main element that leads to bromhidrosis is the bacterial degradation of compounds secreted by the apocrine glands. Also, dietary compounds can contribute to underarm odor, such as tomatoes.[29]

Also, contradicting the idea that only adults suffer from bromhidrosis, a study diagnosed six-year-old twin sisters with axillary bromhidrosis,[30] which brings an interesting discussion about the age group of the disease.

Regarding the treatments, there are conservative ones, such as topical agents and botulinum toxin, which have a temporary effect and need a periodic application, and those that are comparatively more permanent and radical, such as surgical techniques.[31]

Figure 5: Note the thickness of the skin after curettage in the same topography as the same patient as in the previous figure

The main objective of bromhidrosis's surgical treatment is the removal of apocrine glands and some local eccrine glands. Eccrine glands are dominant in the dermis, and apocrine glands are mostly located in the subcutaneous tissue.[18] The apocrine glands are composed of the secretory portion and the excretory duct.[1] These glandular segments are connected, and part of the secretory portion is firmly attached to the lower portion of the dermis.[32]

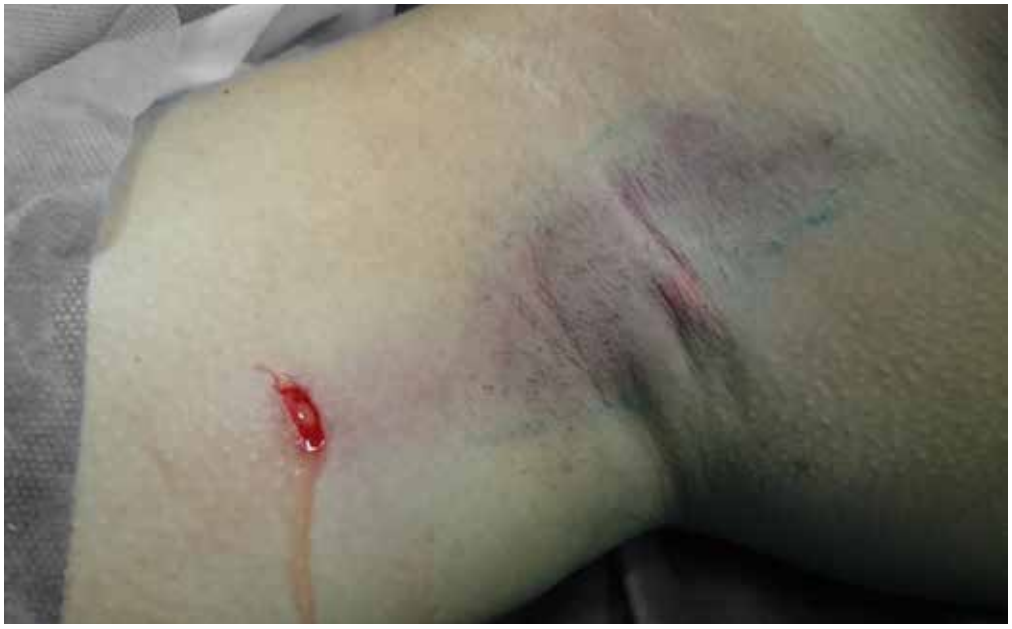

Figure 6: Note the pale purple color obtained after curettage

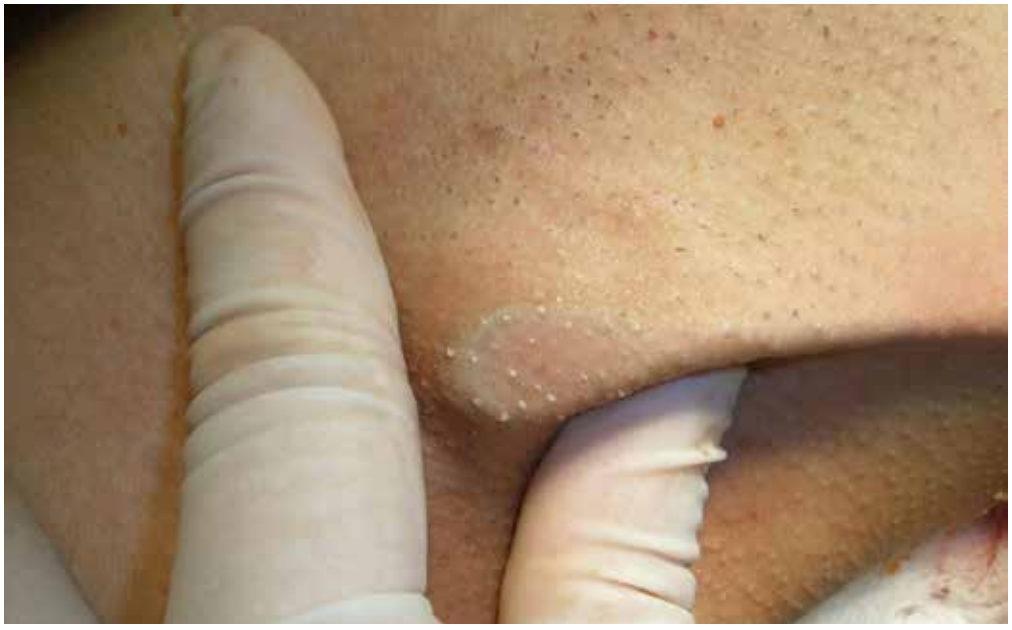

Figure 7: Visualization of the curette by transparency

Consequently, it is relevant to consider these sweat glands' location in the choice and application of the surgical technique. The surgeries developed for the treatment of axillary bromhidrosis are based on the apocrine glands' site, so eliminating the subcutaneous tissue is effective.[33]

It is important to emphasize that selecting the surgical method must also be based on individual characteristics, such as the sweat pattern, bromhidrosis severity, reduced degree of the axillary odor and sweating that the patient wants, and their preference regarding the scar and axillary hair loss.[32]

Regarding surgical methods, superficial liposuction has greater difficulty in eradicating the apocrine glands. It is indicated primarily for patients concerned with the scar and who can tolerate some residual odor and sweating.[32]

Curettage also proves to be effective because the technique causes mechanical trauma leading to degeneration and necrosis of the apocrine glands during the back and forth movement of the curette, consequently eliminating possible remaining glands.[31]

However, there is no consensus on which surgery should be employed. Although the most radical surgeries are very effective, some minimally invasive surgeries (such as aspiration and/

or curettage) can be therapeutic options as good as the radical ones but with better aesthetic results and fewer complications.[9]

It is essential to highlight that, despite its high efficacy, the complete resection of the axillary skin with the adjacent subcutaneous tissue excision is considered very aggressive. This method was practically abandoned due to the increased possibility of complications, such as infections, bleeding, necrosis, poor healing or scar contracture, and movement limitation.

CONCLUSION

Different surgical techniques are described for treating axillary bromhidrosis, with no standardization or consensus on which is the most effective. More radical methods are considered more effective, but there are reports of more frequent complications. Techniques that remove glandular tissue without skin resection have a low complication rate and relevant therapeutic success. ●

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AUTHORS ' CONTRIBUTION:

Flávio Barbosa Luz | ORCID 0000-0001-5454-8950
Approval of the final version of the manuscript; study design and planning; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical revision of the manuscript.

Lara Assunção Kriger | ORCID 0000-0003-0537-5402
Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; critical revision of the manuscript.

Review

Authors:
Luisa Preisler[1]
Luciana Gasques de Souza[2]
Marisa Gonzaga da Cunha[2]

[1] Private Clinic, São Paulo (SP), Brazil
[2] ABC Medical School, Santo André (SP), Brazil

Microinfusion of drugs into the skin - MMP®: An overview, review of indications, and safety profile

Microinfusão de medicamentos na pele (MMP®): uma visão geral, revisão de indicações e perfil de segurança

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ABSTRACT

Microinfusion of drugs into the skin (MMP®) is a technique described by Arbache in 2013. It uses a tattoo machine to infuse drugs to treat skin diseases. This study aims to review the literature and list the indications already published on this technique, the medications used in the procedure, and this technique's safety profile. Despite being widespread among dermatologists, microinfusion of drugs into the skin (MMP®) requires careful analysis, as many indications lack scientific literature. Even though it is a promising technique, it needs further studies to consolidate its indications and assess its safety profile.

Keywords: *Infusions, Intralesional; Research and New Techniques; Tattooing*

Correspondence:
Luisa Preisler
R. Guarará, 463 - Ap 141
01425-001 São Paulo (SP)
E-mail: luisapreisler@gmail.com

RESUMO

A microinfusão de medicamentos na pele (MMP®) é uma técnica descrita por Arbache em 2013, que utiliza uma máquina de tatuagem para infundir medicações na pele com intuito de tratar doenças. Este trabalho visa a revisar a literatura e elencar as indicações já publicadas bem como as drogas utilizadas no procedimento e seu perfil de segurança. Apesar de ser amplamente difundida entre os dermatologistas atualmente, a microinfusão de medicamentos na pele (MMP®) requer análise criteriosa, pois muitas indicações carecem de literatura científica. Mesmo sendo uma técnica promissora, maiores estudos são necessários para consolidar as indicações e avaliar o perfil de segurança.

Palavras-chave: Pesquisa e Novas Técnicas; Tatuagem; Vias de Administração de Medicamentos

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INTRODUCTION

The introduction of active ingredients in the dermis is still an obstacle. Topical medications have variable penetration according to the thickness of the corneal layer. Although intralesional infiltration is an efficient method (as it breaks the skin barrier and delivers the substances directly to the desired location), it has some downsides, such as technology-dependent application (difficulty in microdosing and in standardizing the quantity and depth of application of the active ingredient), challenging treatment of large or very superficial areas, and pain.[1]

Some authors have proposed methods aimed at solving these adversities. Shelley in the 90s suggested the treatment of

warts with the application of bleomycin followed by multiple needle punctures at the site with good therapeutic response.[2] España and later Naeini suggested the use of bleomycin followed by needle punctures on keloids and hypertrophic scars,[3,4] also with good result. Sadeghinia in 2012 was successful in the treatment of keloids with the application of 5-fluorouracil pre and post-punctures with needle.[5]

The first case describing the use of the MMP® technique used bleomycin microinfusion in keloid lesions.[1] After that, several other reports emerged, such as using the technique to treat androgenetic alopecia,[6] leukoderma punctata (guttata),[7] and psoriasis,[8] among others (Chart 1).

This study aims to review the literature on the already published indications, drugs used, and safety profile of this new treatment modality.

MMP®: AN OVERVIEW

The microinfusion of drugs into the skin (MMP®) is a technique described by Arbache and Godoy in 2013, which uses tattoo equipment to infuse medications into the skin to treat several diseases. Its performance requires the use of tattoo equipment, tips, and needles. There are hundreds of models, one of them with ANVISA certification for medical use. Simple energy sources power them, and many of them have adjustable operating speeds. The needles are available in sealed and sterilized packaging. They are made up of a variable number of solid microneedles of fine diameter, arranged parallel to each other or in a circular shape. The needles' length is adjustable from 0.1 mm to 2 mm, depending on the epidermis's thickness and the condition to be treated. When the equipment is turned on, the needles rotate in a "back and forth" motion allowing the medication's aspiration. The capillarity tangles the drug, and a container above the application tip accumulates it. The distal end of the needles' design allows the medical practitioner to precisely treat small and rounded areas or large linear areas. When the needles, soaked by the medication, penetrate the skin, the drug is "pushed" into the intercellular medium, tangled by the shearing force. The space between the needles allows healthy skin areas to exist between treated skin sites, favoring re-epithelialization, similar to what occurs in delicate fractionation.[1]

The percutaneously injected drug has a potent local effect and obtains a therapeutic response, avoiding first-pass hepatic metabolism and reaching the systemic circulation at low undetectable concentration.[8]

BOX 1: Indications reported in the literature on the use of the MMP® technique

Keloids
Psoriasis
Androgenetic alopecia
Guttate leukoderma
Warts
Vitiligo
Superficial scars
Red stretch marks
Achromic scar repigmentation

REVIEW OF THE INDICATIONS

Arbache and Godoy published in 2013 a study for the treatment of keloids comparing MMP® with saline and bleomycin. The first case divided the lesion into three segments: they infused bleomycin on the left, performed no therapy on the center, and introduced saline on the right. The study performed two infusions in 30 days. The second case divided the lesion into two segments: they infused bleomycin on the right, and introduced saline 0.9% on the left, with only one infusion. In both cases, it was possible to observe, visually and on palpation, the improvement in the lesions' thickness. In the area treated with bleomycin, the reduction was more significant. The treated areas' biopsies showed microscopical superiority in reducing the keloid thickness in the areas treated with bleomycin compared to those treated with saline.[1]

Contin in 2016 described two cases of androgenetic alopecia treatment with the MMP® technique. One case infused minoxidil 0.5% (sterile water for injection), and the other performed only micropuncture. The procedures used the Cheyenne® tattoo equipment (Germany Anvisa: 80281110016), with a cartridge with 17 microneedles in a row. The authors adjusted the depth manually at 1.5 mm and completed the procedure with the observation of bloody dew in the entire treated area. The patient who received MMP® combined with minoxidil underwent four monthly sessions, and the patient who received only MMP® underwent three sessions. There was a partial and cosmetically satisfactory response in both cases, without statistical significance.[6]

Okita et al. described in 2018 four psoriasis treatment cases with MMP® using methotrexate or cyclosporine (two with each medication). The study assessed patients with moderate to severe psoriasis and lesions resistant to other therapies. The results demonstrated good tolerability with no adverse events, and quick and effective response in both treated and distant lesions (those that did not receive the application).[8]

Arbache et al. in 2018 reported the preliminary analysis of eight patients who completed the randomized clinical trial for the treatment of guttate leukoderma with MMP® and 5-fluorouracil (5-FU). The intervention used the Cheyenne® tattoo equipment. The study treated the lesions on one leg with the MMP® technique combined with placebo (saline) and the other leg with the technique associated with 5-FU. The authors observed repigmentation in the lesions of both legs. However, in the leg treated with 5-FU, the repigmentation was statistically more significant (75.3% of repigmentation in the 5-FU group versus 33.8% in the placebo group, $p<0.001$). Two patients underwent a biopsy 40 days after the procedure, which demon-

strated numerous melanocytes in the area treated with 5-FU.[7]

Wambier in 2018 also described a series of cases treated with tattoo equipment and disposable needle cartridges, ranging from the use of double-row needles (magnum-27) for large surfaces to a single needle for more accurate treatment. The energy unit was set to 140 Hz, and the needles were kept moist by repeated insertion into the liquid used for each case. This article reported the use of MMP® combined with different medications for the treatment of several pathologies: five cases used 5-FU to treat guttate leukoderma (one session, with evaluation two months later); two cases treated warts with bleomycin (one session, with evaluation two months later); two cases treated vitiligo using triamcinolone acetate (one session, with evaluation two months later); five cases used dutasteride and minoxidil to treat androgenetic alopecia (three monthly sessions, with evaluation after three months); three cases treated superficial scars with 5-FU (one session, evaluation two months later); two cases used hyaluronic acid to treat red stretch marks triggered by a breast prosthesis (three monthly sessions, after three months). All of them presented good response.[9]

Arbache et al. described in 2019 a case of achromic scar repigmentation resulting from laser tattoo removal using MMP® combined with 5-FU. The study held five sessions, with monthly intervals, achieving complete scar repigmentation and sustained response in the case reassessment after three years.[10]

SAFETY PROFILE

One of the main issues regarding the MMP® technique safety is the quantity of the medication that is delivered when using this procedure. Despite differences reported in the literature, a recent study (2019) by Arbache et al. estimated that the mean value is 1,175μg/cm^2. This demonstrates the superiority of the technique by allowing the injection of such a small amount of medication in a 1 cm^2 surface, in relation to the use of syringes. Regarding the pharmacokinetics of drugs injected into the skin, whether by syringes, tattoo devices, rollers, or fractional CO2 laser, their systemic absorption is undeniable, although there may be differences in the path they take (blood or lymphatic), which depends on the technique, chemical nature, and molecular weight of the drug. A fundamental criterion to be considered when choosing a medication to be used in drug delivery is whether it and its respective vehicle have support for systemic and intradermal application.[11]

DISCUSSION

A new drug delivery technique is becoming popular in dermatological practice today: MMP®. In this technique, the needles of the tattoo equipment transfer drugs, instead of ink, into the skin. Thus, microneedling and infusion co-occur. The needle depth is gradually adjusted until a mild bloody dew is obtained, which is an indication that the dermis has been reached.[7] This promising technique is suitable for treating various dermatological conditions, overcoming the mechanical corneal barrier that impairs the topical application of the drug (superficial spreading) and the unwanted effects of the drug bolus obtained with intralesional infiltration.[9] The literature describes the treatment of pathologies such as leukoderma punctata (guttata), xanthelasma, viral warts, vitiligo, androgenetic alopecia, superficial scars, stretch marks, and psoriasis with results that motivate future studies.[8,9]

Despite widespread among dermatologists today, microinfusion of drugs into the skin (MMP®) requires careful analysis since some indications routinely performed in practice lack literature with scientific evidence. There are case reports on the treatment of keloids, viral warts, vitiligo, androgenetic alopecia, psoriasis, stretch marks, superficial scars, and achromic scars, as well as the preliminary analysis of a randomized clinical study[7] for the treatment of guttate leukoderma with eight patients.

When it comes to the technique safety, there is only one study[11] published by Arbache et al. in 2019, which discusses the volume of medication delivered every cm^2 by MMP®. However, but there are still no studies that demonstrate and quantify the drug's safety and systemic pharmacokinetics.

CONCLUSION

Microinfusion of drugs into the skin (MMP®) is a promising technique, but further studies are needed to consolidate its indications. Few studies have been published so far, and there is no standardization of the drugs to be used, their total dose, and the depth of application. There is still a discussion of what works: whether it is merely the trauma caused by the punctures, the medication's infusion, or both.

In addition to these questions, considerations about possible contraindications, complications related to the technique and medications, and systemic absorption and elimination of drugs used during the procedure are very relevant. ●

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AUTHORS ' CONTRIBUTION:

Luisa Preisler | ORCID 0000-0002-1600-9953

Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review; critical revision of the manuscript.

Luciana Gasques de Souza | ORCID 0000-0001-5160-7572

Approval of the final version of the manuscript; critical literature review; critical revision of the manuscript.

Marisa Gonzaga da Cunha | ORCID 0000-0002-4186-0643

Contribuição no artigo: Concepção e planejamento do estudo.

Original Article

Authors:
Érico Pampado Di Santis[1,2]
Samira Yarak[1]
Marcos Roberto Martins[3]
Sergio Henrique Hirata[1]

[1] Universidade Federal de São Paulo, São Paulo (SP), Brazil.
[2] Universidade de Mogi das Cruzes, Mogi das Cruzes (SP), Brazil.
[3] Universidade de Taubaté, Taubaté (SP), Brazil.

Correspondence:
Samira Yarak
R. Pedro de Toledo, 598
Vila Clementino
04039-001 São Paulo (SP)
E-mail: syarakdermato@gmail.com

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Deaths related to liposuction in Brazil

Mortes relacionadas à lipoaspiração no Brasil

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ABSTRACT

Introduction: Liposuction is one of the most performed cosmetic surgeries in the world. Its mortality varies from 2,6 (6) to 19 (7) deaths/100 thousand. Data were obtained through questionnaires from medical societies (4-10) and retrospective data from forensic medicine institutes. However, both methods present flaws: the first due to professional bias and information duplicity, and the second due to the lack of data on the cause of death.
Objectives: To identify the number and causes of liposuction deaths through documentary records of news published in the press and study of death certificates.
Methods: This is a documentary, descriptive-quantitative study. Knowing the deceased patients' names and the cities where the death occurred, we obtained death certificates from the civil registry offices.
Results: We surveyed 102 deaths and 86 death certificates. Pulmonary thromboembolism was the most cited cause of death in 17.44%, 45% on the same day of surgery. 53.6% of surgeries were performed in hospitals, and 61.76% of them, alone.
Most physicians responsible for the surgeries were plastic surgeons (74%). Still, none were registered as a specialist in Dermatology at the Federal Medical Council. In 12.98% cases, doctors who participated in the surgery filled out the death certificate.
Limitations: The ethical impossibility of accessing medical records and the inadequate filling of death certificates.
Conclusion: *The compulsory notification must be established by law to create a database to help develop guidelines for the prevention of these deaths.*
Keywords: *Liposuction; dead.*

RESUMO

Introdução: *A lipoaspiração está entre as cirurgias estéticas mais realizadas no Mundo. Sua mortalidade varia; 2,6 (6) a 19 (7) mortes/100 mil. Dados são obtidos por questionários a membros de sociedades médicas (4-10) e retrospectivo, obtidos em IML, (3, 11) ambos falhos. O primeiro pelo viés profissional e duplicidade, o segundo pela falta da causa mortis.*
Objetivos. *Identificar o número e causas das mortes relacionadas à lipoaspiração por registros documentais das notícias veiculadas na imprensa e estudo das certidões de óbito.*
Métodos. *Estudo documental, descritivo-quantitativo. Com a ciência, dos nomes e cidade do óbito, obtivemos certidões nos cartórios civis.*
Resultados. *102 mortes e 86 certidões de óbito. Tromboembolia pulmonar foi a causa mortis mais citada em 17,44%, 45% no mesmo dia da cirurgia; 53,6% realizadas em hospitais e 61,76% isoladas. Especialidade dos médicos responsáveis: cirurgião plástico (74%), None registrado na qualificação de especialista em dermatologia no CFM. 12,98% dos atestados preenchido por médicos que participaram da cirurgia.*
Limitações. A impossibilidade ética no acesso aos prontuários médicos e o preenchimento inadequado das certidões de óbitos.
Conclusão. *A notificação compulsória deve ser instaurada por lei para formação de um banco de dados que auxiliará na construção de diretrizes para prevenção desses óbitos.*
Palavras-chave: *Lipoaspiração; morte*

INTRODUCTION

Liposuction is the medical-surgical procedure for treating the accumulation of superficial adipose tissue that damages the body silhouette. Aspiration is done through cannulas connected to the vacuum pump (sucker) or syringe, which generate negative pressure.[1,2]

From 2011 to 2020, liposuction ranked among the first positions of the most performed cosmetic surgeries globally, with more than one million surgeries performed each year.

The number and causes of death, of young and healthy patients in general, are not well established.[2,8,10]

We believe that surveying the number of deaths through the news published in the press is a more effective method than sending questionnaires to members of medical societies or retrospectively studying legal medical records. The latter have deficiencies, such as the bias of responses and the lack of data on death certificates for reliable analysis. The data obtained may contribute indirectly to the establishment of prophylactic measures. Thus, this work aims to verify the incidence of causes of death from liposuction and to identify other variables that may be related to them.

METHODS

This is a documentary, descriptive-quantitative study, approved by the Ethics and Research Committee of UNIFESP-EPM (CEP 542.458) from 1987, the date of the first death from a liposuction surgery in Brazil, until September 2015.

We used news from the media to raise the number of deaths related to liposuction in Brazil in this period, from the first news of death after liposuction to when 100 reported cases were exceeded. Our databases were news written in the largest printed newspapers and analysis of the leading news portals on the World Wide Web.

The press generally reports the victim's name and surname, sex, age, marital status, local of the surgery institute, and surgery and death dates. With this information, together with the civil registry offices, we obtained death certificates. These documents allowed us to confirm the variables acquired by the press and to recognize other data such as color, causa mortis (reflected in the death certificate filled out by a medical professional), and the name of the professional involved. Data were also collected regarding sex, age, color, marital status, surgery and death dates, local of the surgery institute, and the cause declared by the sources (death certificate and press). Subsequent consultations on the websites of medical councils and societies allowed us to know the specialty of the doctor who performed the surgery.

RESULTS

We surveyed 102 cases of death related to liposuction between January 17, 1987, and September 15, 2015. Also, we obtained 86 death certificates (84.31%) from civil registry offices.

Women represented 98.04% of these 102 patients. The age varied between 18 and 62 years. The age group between 31 and 40 years represented 40% of the cases (Table 1).

Death on day zero (day of surgery) occurred in 45% of cases. When considering death between the day of surgery and the end of the first week (D7), this value increased to 82.82%; from the second week to the 28th day, 13.13%, and after the first month, 4.04% (N=99). It was possible to identify 97 institutional sites that performed the surgeries. Hospitals performed 53.6% of surgeries, and clinics outside hospitals conducted 46.4%. The association of liposuction with other procedures occurred in 38.24% of cases, while 61.76% of cases reported liposuction performed in isolation.

Regarding the specialties of the doctors involved, we were able to detect them in 86 cases. Of these, 66 doctors had a registered specialty, 61 in plastic surgery, two in general surgery, two in orthopedics, one in diagnostic imaging; 20 professionals had not registered any medical specialty; and 13.64% of doctors were involved in more than one surgery that resulted in the patient's death.

Of the causes of death, thromboembolism ranked first with 17.44%, followed by perforation (13.95%), infection (9.3%), hemorrhage (5.81%), fat embolism (4.65%), and acute lung ede-

Table 1: Data obtained by information from the media and death certificates

		N
Sex	**Women: 98%**	102
Age	**Between 31 and 40 years: 40%**	102
Death on D0 (surgery day))	45%	99
Death between D0 and D7	82,82%	99
Death after D30	4,04%	99
Surgeries in hospitals	53,6%	97
Isolated liposuction	61,76%	102
Specialty with the highest number of deaths	Plastic surgery	86
Number of cases in which the surgeon signed the death certificate	12,98%	86
Doctors who were involved in more than one death	13,64%	86

ma and anesthetic complications, with 2.32% each (N=86). In 44.18% of the cases, it was not possible to determine the cause of death.

DISCUSSION

Death resulting from liposuction is a misfortune in public health.[3] The lack of knowledge of its causes prevents us from having reliable data to elaborate protocols that can prevent it.

The sample found in the studies previously conducted is related to the difficulty in obtaining data regarding deaths. In the literature, we found two methods to obtain this information: questionnaires sent to members of medical societies, usually plastic surgery societies,[4-10] and the retrospective study of data obtained from a legal medical institute.[3, 11]

The method that used sending questionnaires was criticized[7] for the possibility of biased responses. It is reasonable to assume that the doctor did not answer or omit data, as he can use the legal benefit of not producing evidence against him. The low response rate observed in most of these studies confirmed this hypothesis.[4-6, 9,10] This type of result is expected since the doctor involved has the right not to present evidence that could harm him. Retrospective studies[3,11] of data obtained in legal medical institutes are also deficient, as the surgical procedure involved is often not mentioned, hindering the ability to identify deaths related to liposuction.

Because they are impactful news, deaths due to liposuction are widely reported in the press and generate enormous concern in gyms and medical councils. Based on this fact, the present study was initiated, which searched for news published in the printed and digital media and subsequently analyzed public documents.

With this methodology, we found 102 deaths related to liposuction, the largest sample among the scientific literature studied[4-10] (Box 1). The analysis of death certificates prevents the same case from being included two or more times, as can occur in studies using questionnaires that can send it to two doctors who participated in the same surgery.

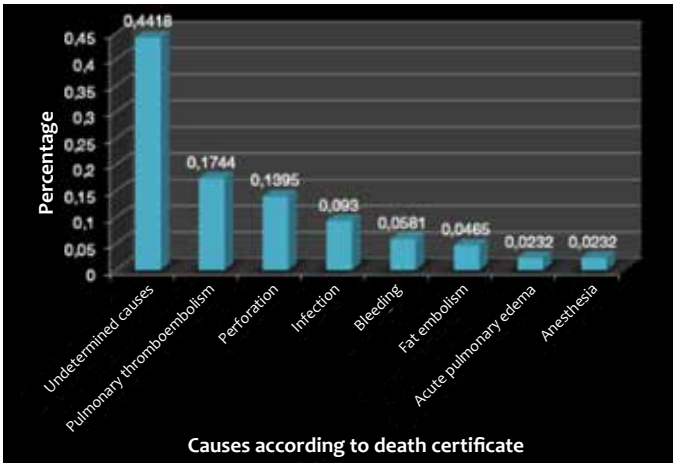

FIGURE 1: Relative number of causes according to death certificates

As this surgery is performed more frequently on women, the majority of deaths found were among women (98.04%) and among young people (97.05%), similar to data from the International Society of Aesthetic Plastic Surgery (84.9% of the patients submitted to liposuction in 2017 were women). These patients were healthy and underwent elective surgery expecting to remain in good health.

Regarding the reason for deaths, there are differences when consulting the literature. In the present study, it was impossible to establish the cause of death in 44.18% of the cases (undetermined). Thromboembolisms occurred in 17.44% and infection in 9.3% of cases.

The unknown cause also ranked first place in the Grazer and Jong's study,[7] with 28.5% of cases, and ranked fifth in the Lehnhardt et al. study,[9] with 4.35%.

Regarding the known causes, when compared with the Grazer and Jong's study,[7] (method used: questionnaires sent to doctors), the order of the first two causes coincides: thromboembolic phenomena are the first, with 23.1%, and perforation is the second, with 14.6%. The leading causes of death in Lehnhardt et al. study[9] are infection as the first cause, with 65%, perforation as second, with 13%, followed by thromboembolic phenomena in the third position, with 8%.

But we must take care when interpreting the data. Cupello et al.[10] stated that their data should be interpreted with caution, as the study included many missing responses. Unknown death cause ranked last place in Lehnhardt et al. study.[9] However, even with the support of several medical societies and sending three thousand questionnaires, only 23 cases of death were recorded.

Hughes[8] reported an alarming increase in the mortality rate when liposuction was performed concurrently with abdominoplasty compared to when it was performed alone, with one death in 3,281 surgeries versus one death in 47,415 surgeries, respectively. Combining these surgeries or large volume liposuction can play an essential role in the causes of death. We did not find the same result. The number of deaths found in liposuction performed in isolation, declared in media interviews by members of the surgical team, was 61.76%.

Our study showed that the critical period in liposuction surgeries is the first week after surgery, especially the first day (45% of patients died on the day of surgery and 82,82% on the first week). We believe that this data demonstrates the importance of care in the 24-hour postoperative period and the first week, with more frequent reevaluations.

For the 102 cases investigated, there was no evidence of deaths occurring with the use of tumescent local anesthesia, as described by Klein.[16] There was also no mention in the death certificates of lidocaine poisoning as a cause of death or process that led to it. Klein's technique is safer because the patient under local anesthesia still has a pain reflex and feels pain if the cannula touches the muscular fascia. It avoids the possibility of muscle perforation, which can occur when the cannula is not placed in the appropriate place. Also, the rate of blood depletion using this technique is significantly lower.

Box 1: Studies related to deaths in liposuction surgery

Authors	Year	Methods	Source	Deaths
Grazer e Goldwyn[4]	1977	Retrospective observational study	Questionnaires to members of specialty society	17
Pitman and Teimourian[5]	1985	Retrospective observational study	Questionnaires to members of specialty society	0
Teimourian and Rogers[6]	1989	Retrospective observational study	Questionnaires to members of specialty society	15
Rao et al.[3]	1999	Survey of medical records	Legal medical reports	05
Grazer and de Jong[7]	2000	Retrospective observational study	Questionnaires to members of specialty society	93
Platt et al.[15]	2002	Case report	Legal medical reports	03
Coldiron et al.[12]	2005	Retrospective observational study	Compulsory notification	05
Lehnhardt et al.[9]	2008	Retrospective observational study	Questionnaires to members of specialty society	23
Avelar et al.[11]	2010	Survey of medical records	Macroscopic reports	07
Starling et al.[13]	2012	Retrospective observational study	Compulsory notification	10
Cupello et a.[110]	2015	Retrospective observational study	Questionnaires to members of specialty society	40
Present study	2018	Documentary descriptive quantitative study	Media	102

Authors	Causes (1st)	Associated surgery	Time of death	Local	Specialty
(4)	P.T.				
(5)	None				
(6)	P.T.				
(3)	Anesthesia intoxication		D0		Plastic surgeon
	E.P. (trombo ou gordura)	Maioria associada		Consultório	
(7)	Unknown	Most associated	D0	Doctor's office	
(15)	F.E.				
	Desconhecida	Maioria associada		Consultório	
(12)	P.E. (thrombus or fat)	Most associated		Doctor's office	

Quadro 1: Estudos relacionados a óbitos em cirurgias de lipoaspiração					
Authors	**Causes (1st)**	**Associated surgery**	**Time of death**	**Local**	**Specialty**
(9)	Infection	Most associated		Doctor's office	
(11)					
(13)	T.P.			Doctor's office	
(10)	Unknown	Most associated		Doctor's office	
Present study	Unknown	Not associated	D0	Hospital	Plastic surgeon

P.T.: Pulmonary thromboembolism, F.E.: Fat embolism, P.E.: Pulmonary embolism, D0: Day of surgery.

Compulsory notification of cases would favor the creation of a database. This notification must document the detailed study of the surgery (technique performed, anesthesia used, amount aspirated, etc.), the preoperative health status, and the postoperative complications that led the patient to death. Also, it must be accessible so that committees can establish guidelines for death prevention in cosmetic surgery.

It is crucial that public health authorities develop strategies to identify deaths related to aesthetic procedures and that these cases undergo necropsy (including toxicological tests).[14] The data obtained will assist in the establishment of preventive measures. In the United States, Florida's and Alabama's governments determined the obligation to report complications occurring in extra-hospital surgical procedures.[12,13] Our study could only find data such as the type of anesthesia used in these surgeries by consulting patients' medical records and confidential documents.

Future studies with the records of these victims may clarify the gaps left in the present study. A standard access to medical records by medical researchers, with all ethical and legal rigor, will undoubtedly benefit public health.

The search for ways to best fill out death certificates can mean an improvement in the system, functioning, and knowledge of the real causes of deaths. It would allow us to be more efficient in preventing deaths.

We believe that the compulsory notification of complications by cosmetic procedures can act prophylactically against damage to individuals' health, families' suffering, and expenses in the health system.

CONCLUSION

The search for deaths related to liposuction reported in the media is a tool that adds to the other methods available in the literature. Among the 102 cases studied, thromboembolism was the most cited cause of death, and most deaths occurred in the first seven postoperative days. There was no relationship between fatalities and the performance of more than one procedure in the same surgery or the place where the surgeries were performed. ●

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AUTHORS ' CONTRIBUTION:

Érico Pampado Di Santis | ORCID 0000-0001-5782-9205
Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical revision of the manuscript.

Samira Yarak | ORCID 0000-0002-5657-6645
Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation.

Marcos Roberto Martins | ORCID 0000-0001-7985-0910
Approval of the final version of the manuscript; preparation and writing of the manuscript; data collection, analysis, and interpretation.

Sergio Henrique Hirata | ORCID 000-0003-4026-9664
Approval of the final version of the manuscript; preparation and writing of the manuscript; data collection, analysis, and interpretation.

Original Article

Authors:
Natacha Quezada Gaón [1]
Maria Isabel Herane Herane[1]
Mathias Yagnam Diaz[1]
Marlene Waissbluth Morales[1]

[1] Dermatology Service, School of Medicine, Pontifícia Universidade Católica do Chile, Santiago, Chile.

Correspondence:
Natacha Quezada Gaón
Av. Apoquindo, 3990 - 901
07.510-575 Santiago, Chile
E-mail: natachaq@yahoo.es

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Approved on: 26/11/2020

Study conducted at the Department of Dermatology, Pontificia Universidad Católlica de Chile, Dermatoplasty Study Group.

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Botulinum toxin for the treatment of erythema and flushing of rosacea with two different techniques: intradermal injections and facial electroporation

Tratamento do eritema da rosácea com toxina botulínica comparando-se a técnica de injeção com agulha e eletroporação

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ABSTRACT

Introduction: Facial erythema is a frequent and often distressing complaint in patients with rosacea. Botulinum toxin has been proposed as a treatment of facial erythema with relatively good results.

Objective: This study aims to assess botulinum toxin's safety and efficacy in a split-face trial in two different administration modalities: intradermal injections on one side of the face and facial electroporation on the other side.

Materials and methods: The trial enrolled 20 subjects aged between 25 and 75 years with erythematotelangiectatic rosacea. Subjects received five units of Botulinum toxin through intradermal injections on the right side of the face. The same amount was introduced through electroporation technique on the left side. We conducted the evaluation using a standardized erythema grading system (System Vectra) and digital photographs at baseline, 2, 6, and 12 weeks.

Results: The effectiveness in reducing the erythema of botulinum toxin with both the injection and electroporation was evident from the second week and persisted until week 12. Both techniques were effective.

Conclusions: Intradermal injection of botulinum toxin and electroporation seems both effective and safe for treating erythema related to rosacea. The mechanism of action is still controversial.

Keywords: Erythema; Mesotherapy; Botulinum Toxins, Type A

RESUMO

Introdução: *o eritema facial é queixa frequente e muitas vezes angustiante em pacientes com rosácea. A toxina botulínica tem sido proposta como tratamento do eritema facial com resultados relativamente bons.*

Objetivo: *o objetivo primário deste estudo foi avaliar a segurança e eficácia da toxina botulínica (TB) administrada num ensaio split-face, com duas modalidades diferentes de administração: injeções intradérmicas em um lado da face e eletroporação no lado contralateral.*

Materiais e métodos: *20 indivíduos entre 25 e 75 anos, fototipos I a IV e rosácea eritematosa foram incluídos no estudo. Os pacientes receberam 5U de TB através de injeções intradérmicas no lado direito da face e 5U com eletroporação no lado esquerdo. A avaliação foi feita por meio de um sistema padronizado de classificação de eritema em fotografias digitais tridimensionais e questionários padronizados no pré-tratamento e após duas, seis e 12 semanas.*

Resultados: *a efetividade da TB em reduzir o eritema tanto com o método com agulhas quanto com eletroporação fez-se evidente desde a segunda até a 12ª semana. As duas técnicas foram efetivas.*

Conclusões: *a injeção intradérmica de TB e a eletroporação mostraram-se eficazes e seguras para o tratamento de eritema da rosácea. O mecanismo de ação ainda é controverso.*

Palavras-chave: *Eritema; Mesoterapia; Toxinas Botulínicas Tipo A*

INTRODUCTION

Rosacea is a chronic inflammatory condition of the face with several clinical symptoms, such as transient and persistent erythema, telangiectasias, inflammatory papules, pustules, plaques, nodules, and pimples, and may have ocular involvement.[1]

Four subtypes were defined based on clinical characteristics: subtype I or erythematotelangiectatic rosacea (ETR), which includes individuals prone to flushing associated with persistent erythema with frequently telangiectasias; subtype II or papulopustular rosacea (PPR), characterized by a central facial eruption of multiple erythematous papules or small pustules, isolated or in groups, and the occasional presence of plaques and nodules; subtype III or phymatous rosacea, described as thickening of the skin with irregular contours (phymas) and preference for the ears (otophyma), eyelids (blepharophyma), chin (gnatophyma), forehead (metophyma), and nose (rhinophyma). The latter form is the most common and is present mainly in men. Finally, there is subtype IV, or ocular rosacea, characterized by multiple and non-specific signs, such as itching, dry eye sensation, blepharitis, sty, and chalazion. It can occur without cutaneous manifestation or associated with other subtypes.[1-3]

The exact pathogenesis of rosacea is still unknown. The literature reports some factors relevant to its occurrence, such as innate immune system dysfunction, ultraviolet radiation exposure inducing increased angiogenesis, reactive oxygen species (ROS) production, vascular changes with increased expression of vascular endothelial growth factor (VEGF), epidermal barrier dysfunction, and neurogenic inflammation with release of neuromediators at the inflammation site resulting in vasodilation.

The inflammatory cell recruitment, the plasma proteins extravasation, the microbial action through the activation of toll-like 2 receptors and mast cells, and the persistent cytokines and chemokines release intensify the inflammation and increase innate immune responses. In short, it is a chronic and persistent inflammatory state.[5]

Several treatments have been proposed for rosacea, including oral and topical therapies in association with lasers, intense pulsed light (IPL), photodynamic therapy, etc.[6] Erythema treatment is challenging. Different drugs have been used, such as oral beta-blockers, botanical products, and topical products such as ivermectin, azelaic acid, brimonidine, oxymetazoline, tranexamic acid, in addition to the use of laser, IPL, and even endoscopic thoracic surgery with sympathectomy, in general with partial results.[7]

Botulinum toxin (BT) has become another alternative treatment for refractory erythema and rosacea flushing.[9] Dayan et al. observed that patients undergoing BT rejuvenation treatment improved skin quality as well as wrinkles and decreased duration of erythema and flushing.[10] Since then, several reports of BT treatments in rosacea subtypes I or II have been published using intradermal injections in the affected regions.[11] As this procedure requires an injectable technique, we present the results of a group of treated patients in a split-face study. The group received BT by intradermal injections on one side of the face and the same number of BT units by the facial electroporation technique on the contralateral side.

This study aims to observe BT type A's efficacy in the treatment of erythema of erythematotelangiectatic rosacea.

MATERIALS AND METHODS

The study recruited men and women with facial erythema associated with mild to moderate erythematous rosacea and some cases with few papules and pustules recruited the authors' private clinic.

The inclusion criteria were patients aged 25 to 75 years old, with Fitzpatrick skin phototype I to IV, non-smokers in the last two years, with erythematotelangiectatic or papulopustular rosacea (up to two-four inflammatory lesions), bilateral involvement in the cheeks, and availability to meet all follow-up requirements.

We excluded individuals with any other dermatological disease on the face, human immunodeficiency virus, and hepatitis; with immunological suppression, myopathies, or neurodegenerative diseases; pregnancy, lactation, oral treatment with vasoconstrictors, vasodilators, or isotretinoin in the last 12 months; allergy to cow protein, known hypersensitivity to BT or any of its ingredients, or even if they had received BT applications on the face up to 12 months before. Individuals with electrical devices, such as cardiac pacemakers, and patients who worked more than four hours a day outdoors were also excluded.

The study was conducted according to the Helsinki declaration's ethical principles, and all subjects signed an informed consent form and authorization to be photographed. The dilution was 10 BT units per ml, obtained with 10 ml of saline in a 100U bottle of onabotulinumtoxin (Botox® Allergan, Santiago, Chile). The face's right side was treated with intradermal injections of 0.5 ml (5U) BT at every 2 cm^2. The left side was treated with 0.5 ml (5U) of BT delivered uniformly to the predetermined area by facial electroporation, using the Ecleris® electroporator (Buenos Aires, Argentina) (Figure 1).

Facial electroporation is a cosmetic technique based on exposing the skin to a light electric field, which reduces the cell wall's resistance to make it more porous. The objective is to allow the transfer of topically applied solutions into the skin cells. It is painless and has no adverse events.

Each patient received a micellar cleansing lotion, moisturizing cream, and SPF 50 + sunscreen of the same brand to avoid contact reactions between patients.

We monitored patients before treatment and at weeks two, six, and 12. We assessed the clinical response and adverse events in each control and took digital photographs on the Vectra® system (Canfield, Wentworth Point, Australia) with vascular programming.

The Vectra is a machine made up of eight cameras that take photos simultaneously, building 3D images. With its use, the degree of erythema can be detected and compared, among other functions.

We assessed the erythema using a red colorimetric scale,

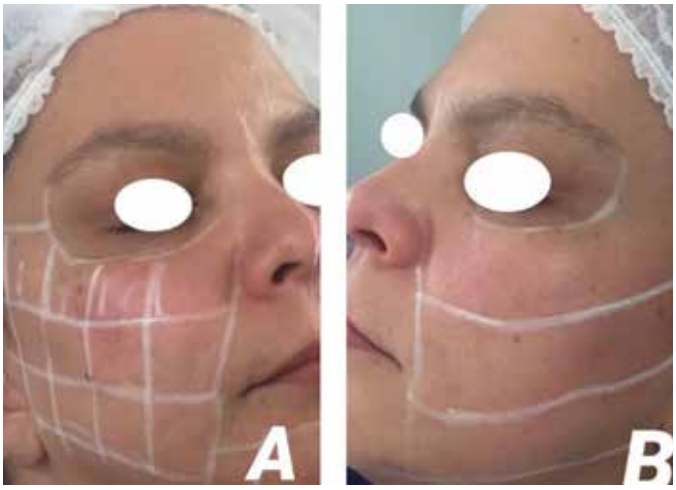

Figure 1: A - Right cheek: application with needles; markings every 2cm ²
B - Left cheek: electroporation; markings to pass the electroporator

considering each tone a degree of intensity. Light pink means absence of erythema, intermediate shades correspond to moderate erythema, and intense red correspond to severe erythema (Figure 2).

Clinical responses and adverse events, such as headache, erythema or pain at the injection site, muscle weakness, dysphagia, dry mouth, fatigue, vision changes, or dysphonia, were assessed using a questionnaire. On the final visit, we conducted a quality of life questionnaire to assess satisfaction and reveal which side of the face showed the best results.

RESULTS

We selected 20 patients, but two did not complete the study. Thus, we assessed 18 patients (17 women and one man) with a mean age of 41 years (range: 24 years - 68 years). Of these, 27.78% were skin phototype II (n=5); 66.67% were skin phototype III (n=12); and 5.56% were skin phototype IV (n=1). At the beginning of the study, 94.44% of patients presented erythematotelangiectatic rosacea (n=17), and 5.56% had papulopustular rosacea (n=1).

The assessment of the difference in erythema at baseline and two weeks after the electroporation therapy showed the following results: no changes (12.5%); erythema improvement by one degree (56,25%); erythema improvement by two degrees (12.5%); and erythema improvement by three degrees (18.75%). Mean: improvement of 1.375 (standard deviation: 0.96). In short, 87.5% improvement by one to three degrees.

The assessment of the difference in erythema at baseline and two weeks after the needle or mesotherapy therapy showed the following results: no changes (6.25%); erythema improvement by one degree (43.75%); erythema improvement by two degrees (43.75%); and erythema improvement by three degrees (6.25%). Mean: improvement of 1.5 (standard deviation: 0.73). In short, 93.75% improvement by one to three degrees.

The assessment of the difference in erythema at baseline and six weeks after the electroporation therapy showed the following results: erythema worsening by one degree (6.67%); no changes (13.33%); erythema improvement by one degree (26.67%); erythema improvement by two degrees (40%); and erythema improvement by three degrees (13.33%). Mean: improvement of 1.4 (standard deviation: 1.12). In short, 80% improvement by one to three degrees.

The assessment of the difference in erythema at baseline and 12 weeks after the needle therapy showed the following results: erythema worsening by one degree (7.14%); no changes (7.14%); erythema improvement by one degree (35,71%); erythema improvement by two degrees (35.71%); and erythema improvement by three degrees (14.29%). Mean: improvement of 1.43 (standard deviation: 1.09). In short, 85.71% improvement by one to three degrees (Chart 1).

We observed BT's effectiveness in reducing erythema, which has been evident since the second week, using both the needle and the electroporation technique. This effect persisted

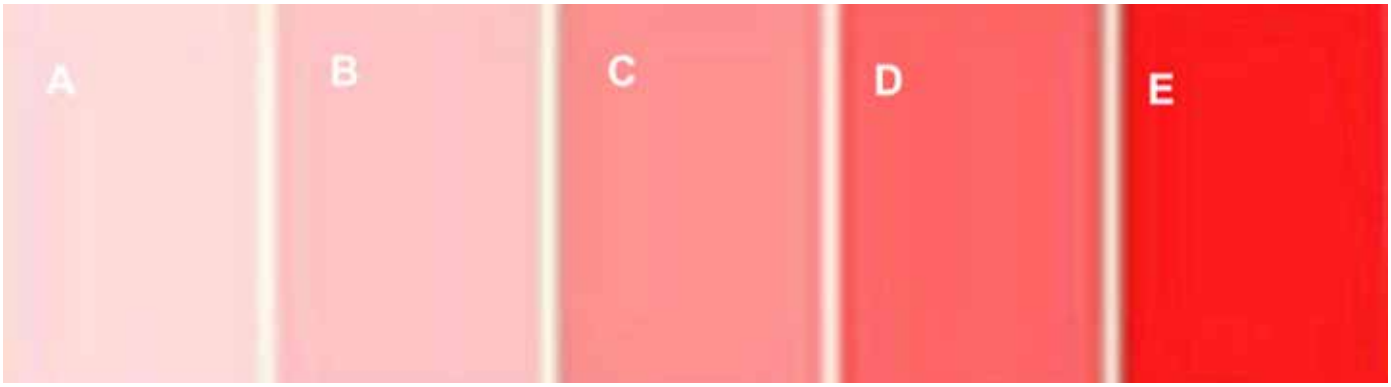

Figure 2: Erythema evaluation scale
A - No erythema, **B -** Mild erythema, **C -** Moderate erythema, **D -** Intense erythema, **E -** Severe erythema

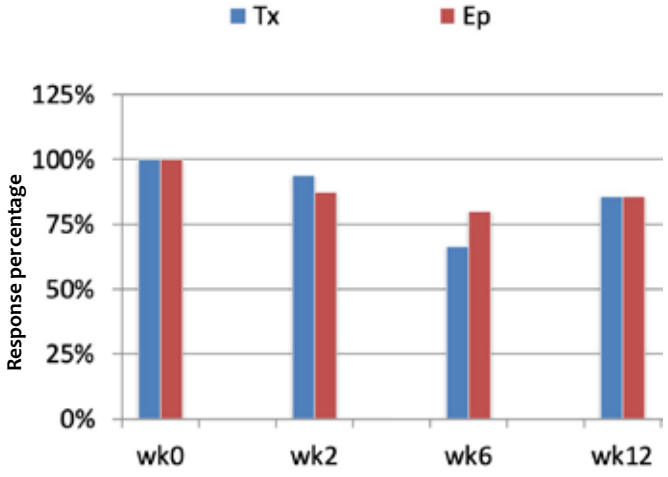

Chart 1: Summary of results.
Both techniques work from week 2 to week 12, showing a peak in week six

until week 12. It is interesting to point out that both therapies were effective, showing a peak at week six (Figures 3, 4, and 5).

Patients described the following adverse events: three cases of ecchymosis, three cases of temporary erythema after application, one case of pain, and one case of tingling at the application site.

DISCUSSION

BT is a potent neurotoxin. It inhibits the release of acetylcholine (Ach) in the presynaptic vesicle 11. Also, it modulates several other neuropeptides, such as substance P (SP), calcitonin gene-related peptide (CGRP), and vasoactive intestinal peptide (VIP).[12] Note that Ach and VIP are the primary mediators of vasodilation and flushing; its inhibition could be the mechanism of action for BT in rosacea.[12]

Recently, mast cells (Mcs) have emerged in importance in rosacea's pathogenesis,[13] since they are cathelicidin LL-37 activators, which induces skin inflammation, chemotaxis, degranulation, and release of pro-inflammatory cytokines. It is a fact that Mcs-deficient mice do not develop characteristics similar to rosacea after LL-37 injection. On the other hand, the Mcs' stabilization with sodium cromoglycate reduced the skin's inflammation in humans and mice. It emphasizes its importance in the cathelicidin inflammation and potential target in rosacea treatment.

It has also been shown that human's and mouse's Mcs express proteins SNARE (soluble N-ethylmaleimide sensitive fusion protein receptor), Snap-25, and VAMP (vesicle-associated membrane protein). SNAREs are the main components of coupling and fusion of vesicles with the presynaptic membrane. The blockade BTs A and B vesicles contain neuropeptides through SNAP and VAMP cleavage, respectively. Choi et al. demonstrated direct inhibition of Mcs degranulation in a rosacea model in mice, showing that onabotulinum A and B toxins increased SNAP-25 cleavage and decreased VAMP2 staining in Mcs. In mice, the injection of toxin Onabotulinum A significantly reduces cutaneous erythema induced by LL-37, Mcs degranulation, and mRNA expression of rosacea biomarkers (TRPV, MMP9, KLK5, and others).[14]

These findings show multiple BT targets and may offer therapeutic advantages over the treatments currently available. Our pilot study shows that, since the second week, there was an improvement in erythema in more than 80% of cases. The exciting fact is that electroporation and needle application had a very similar effect, maintained by more than 85% by week 12. We highlight the advantage of electroporation to avoid trauma.

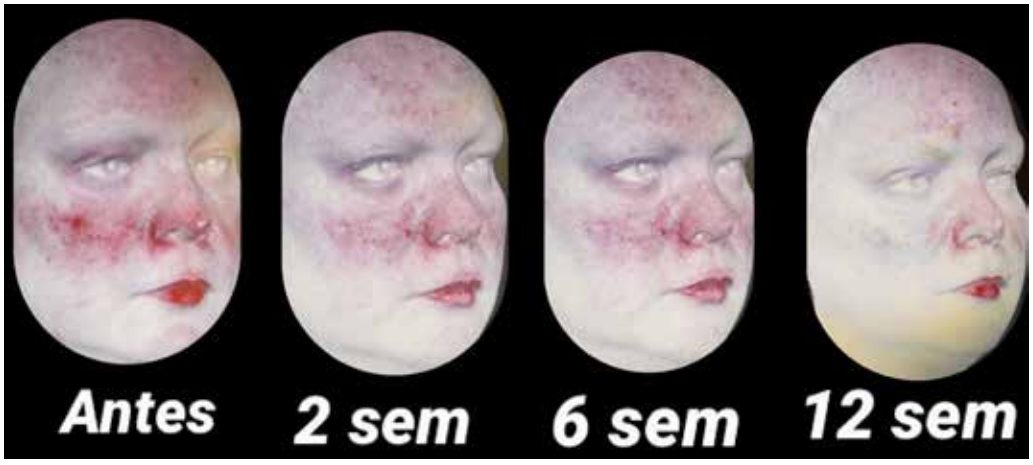

Figure 3: Evolution of application with needle or mesotherapy.
Progressive improvement of erythema is observed over the weeks

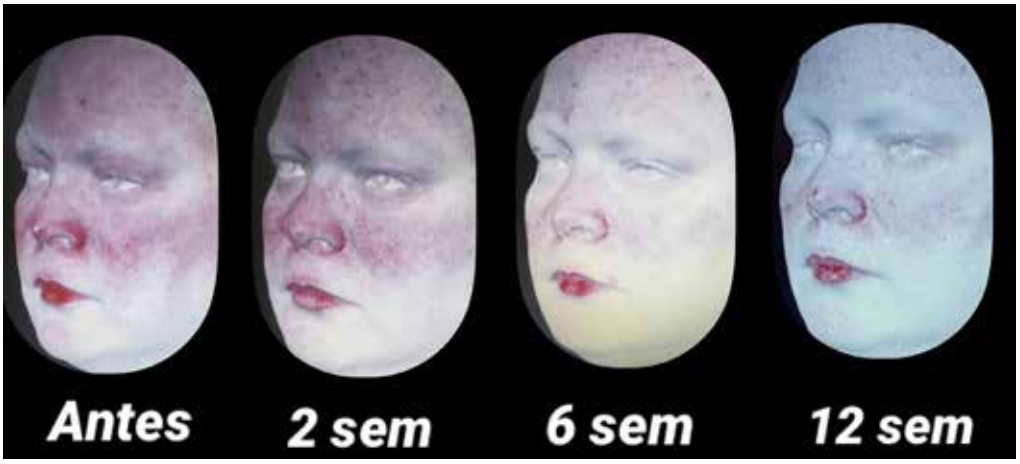

Figure 4: Evolution of the application with electroporation.
Improvement of erythema is observed over the weeks

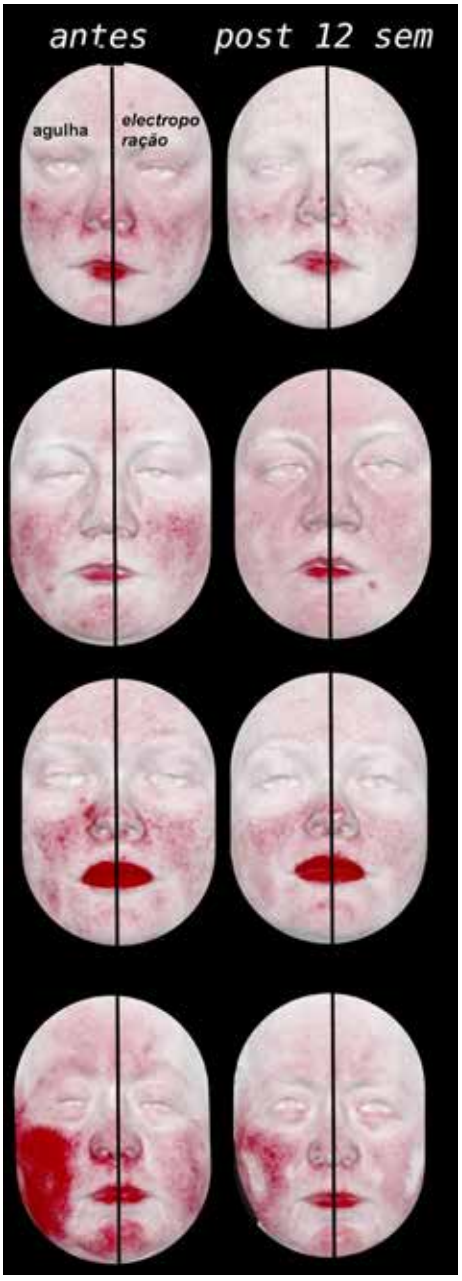

Figure 5:
Front view, comparing pre and post 12 weeks. Mild, moderate, intense, and severe cases in which it's possible to observe, in the frontal view, the positive response of both techniques

Assessing the quality of life questionnaire, more than 90% of patients had a positive impact on quality of life. As for adverse events, we did not observe facial dynamics changes; only minimal adverse events to the application are described.

CONCLUSIONS

BT is effective in reducing the erythema of patients with rosacea. It can be applied with a needle or electroporation, and its effect remains until week 12. Therefore, it is essential to consider it as a therapeutic tool in erythema and flushing of rosacea. It is a treatment of simple application and low adverse events.

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AUTHORS ' CONTRIBUTION:

Natacha Quezada Gaón | ORCID 0000-0003-2322-3402

Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Maria Isabel Herane Herane | ORCID **0000-0003-3362-1623**

Statistical analysis; approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Mathias Yagnam Diaz | ORCID 0000-0003-3562-537X

Statistical analysis; study design and planning; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases.

Marlene Waissbluth Morales | ORCID 0000-0002-8719-9117

Statistical analysis; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation.

Original Article

Authors:
Manoella Freitas Santos[1]
Ana Claudia Dal Magro[1]
Thaís Furtat Marques[1]
Fernando Eibs Cafrune[1]

[1] Santa Casa de Misericórdia de Porto Alegre, Porto Alegre (RS), Brazil.

Correspondence:
Ana Claudia Dal Magro
R. Professor Annes Dias, 295
Centro Histórico
90020-090 Porto Alegre (RS)
E-mail: dalmagro.anaclaudia@gmail.com

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Predictive factors for the highest number of stages in Mohs surgery: a study of 256 cases

Fatores preditores de maior número de estágios na cirurgia de Mohs: estudo de 256 casos

DOI: http://www.dx.doi.org/10.5935/scd1984-8773.20201243705

ABSTRACT

Introduction: Mohs micrographic surgery (MMS) can achieve high cure rates in skin cancer treatment and remove as little healthy tissue as possible.

Objective: This study aims to characterize patients undergoing Mohs micrographic surgery and to assess predictive factors for a higher number of surgical phases.

Methods: Observational, cross-sectional, retrospective, and descriptive study conducted in a reference service for micrographic surgery from 2013 to 2019. The medical records of 230 patients (256 lesions) were reviewed.

Results: Injuries with recurrence had significantly more stages than injuries without recurrence (1.69 stages versus 1.31 stages). Tumors greater than 2 cm had a greater number of phases than those smaller than 1 cm and between 1.1 and 2.2 cm (2.0 versus 1.08 and 1.22, respectively). When comparing the locations of the lesions with the number of phases, there was no significant difference. There was a considerable difference regarding the preoperative histological subtypes: aggressive basal cell carcinomas (BCC) required a higher number of phases than non-aggressive BCCs.

Conclusions: Our study demonstrates, corroborating data from the literature, that the risk factors described are directly related to a greater number of stages of Mohs micrographic surgery.

Keywords: Mohs Surgery; Skin Neoplasms; Carcinoma, Basal Cell; Carcinoma, Squamous Cell

RESUMO

Introdução: *a cirurgia micrográfica de Mohs (CMM) é capaz de alcançar altas taxas de cura no tratamento do câncer de pele e remover o mínimo possível de tecido saudável.* ***Objetivos:*** *caracterizar os pacientes submetidos à cirurgia micrográfica de Mohs e estudar fatores preditores de maior número de fases cirúrgicas.*

Métodos: *estudo observacional, transversal, retrospectivo e descritivo realizado em serviço de referência para cirurgia micrográfica no período de 2013 a 2019. Foram revisados os prontuários de 230 pacientes (256 lesões). Resultados: lesões com recidiva tiveram significativamente mais número de fases que lesões sem recidiva (1,69 vs 1,31 fase). Tumores acima de 2cm tiveram maior número de fases que os de tamanho menor de 1cm e que aqueles entre 1,1 e 2,2cm (2,0 vs 1,08 e 1,22, respectivamente). Quando comparadas as localizações das lesões com o número de fases, não houve diferença significativa. Em relação aos subtipos histológicos pré-operatórios, houve diferença significativa: carcinomas basocelulares (CBC) agressivos precisaram de maior número de fases que os CBCs não agressivos.*

Conclusões: *nosso estudo demonstra, corroborando dados da literatura, que os fatores de risco descritos estão diretamente relacionados a um maior número de estágios da cirurgia micrográfica de Mohs.*

Palavras-chave: *Cirurgia de Mohs; Neoplasias cutâneas; Carcinoma basocelular; Carcinoma de células escamosas*

INTRODUCTION

Frederic Mohs developed the Mohs technique in the 1930s, initially applying zinc chloride to the tumor lesions. It fixed the tissue in vivo and allowed its subsequent analysis under a microscope to preserve the tumor morphology and histological structure.[1] With the evolution of the technique, there was a change to the analysis of fresh tissue by freezing, consisting of the excision of tissue layers compromised by the neoplasm. The tissue is examined using special stains of horizontal cuts to evaluate the tumors' peripheral and deep margins microscopically.[1,2,3,4,5,6] The process of tumor removal and microscopic analysis after freezing the piece is called the surgical phase. Several stages may be necessary to remove the tumor entirely, increasing the surgery's time and cost.[2,3]

In Brazil, Mohs micrographic surgery (MMS) is still underutilized due to the need for additional specialized training and the long learning curve of the method, restricting its availability to larger centers. Although many therapeutic options are currently available, conventional surgical excision (SE) is still the most common treatment for non-melanoma skin cancer (NMSC). The main difference between the two treatments is the method of examining the histological margin. The standard SE exams the surgical margins mainly in random vertical sections, the so-called "bread loaf" technique.[7] Moreover, the MMS flats and cuts the sample horizontally. It offers the possibility to examine 100% of the resection margins compared to the small percentage of margin control in the SE, generally 0.01% to 1.0% of the total surgical margin.[2,3,7] MMS is the method that has the highest cure rates for the treatment of NMSC and allows the preservation of maximum peritumoral healthy tissue.[7,8]

Mohs micrographic surgery is a great therapeutic option for treating malignant skin neoplasms such as squamous cell carcinoma (SCC) and basal cell carcinoma (BCC).[6] It can achieve high cure rates in the treatment of skin cancer, preserving maximum healthy tissue, and, as a consequence, provide less functional and cosmetic damage.[2,3] The main indications in the literature are recurrent neoplasms, aggressive subtypes of skin cancer, and neoplasms in anatomical sites with high recurrence rates.[2,9] Mortality related to non-melanoma skin carcinomas is low due to the small percentage of metastatic disease. However, morbidity can be high due to local tissue destruction, mainly because most tumors occur in areas such as the head and neck.[7]

Currently, there is a trend to treat an increasing number of tumors, mainly primary SCCs and BCCs, with MMS. Indications include those primary tumors that, due to their large size or location in specific anatomical sites, present an increased risk of recurrence. It is also recommended to treat tumors in places that generate significant aesthetic damage, where it is necessary to save more healthy tissue.[2,9] Likewise, neoplasms not previously treated, located in critical locations, such as the eyelid or lip, benefit from the tissue-sparing aspects of the Mohs technique.[9] Since most BCCs are quite limited, most primary BCCs should be removed with MMS in the first two stages. However, there is a significant subset of primary tumors that require more steps to achieve a tumor-free plane. We studied the histological subtype of these tumors, and their depth, to determine whether we could use these resources to predict which primary BCC or SCC would be more challenging to remove with free margins in conventional surgery.[8,9]

OBJECTIVES

The study's main objective was to analyze preoperative characteristics of tumors treated with Mohs micrographic surgery associated with two or more surgical stages. This retrospective analysis of patient records identifies histological subtypes, size, and recurrences of skin tumors treated with MMS, and it studies their correlation with the largest number of stages during surgery. The second objective was to identify predictive factors for high-risk BCCs, eligible and treated with MMS, which have widespread subclinical tumor dissemination.

METHODS

This is an observational, cross-sectional, retrospective, and descriptive study. We retrospectively retrieved the medical records of 230 patients (256 lesions) treated with Mohs micrographic surgery at a referral hospital in dermatology in Porto Alegre between 2013 and 2019. The sample consisted of all patients treated during this period by the team. Data were obtained by analyzing medical records and filling in a standardized table containing sex, age, histopathological diagnoses, tumor location and size, history of previous treatments, number of surgical phases, and reconstruction type. After collection, we assessed the data to group information characterizing these patients' clinical, epidemiological, and histopathological profiles.

Statistical data were described in frequency, percentage, average, and standard deviation. The average number of phases was analyzed using t-test or ANOVA with Tukey multiple comparison test. The analyses were performed using the SPSS version 25 software, and $p<0.05$ were considered significant.

RESULTS

We assessed the medical records of 230 patients. A total of 256 lesions were treated with MMS. Table 1 describes the baseline characteristics of patients. The few cases with incomplete data had the missing aspect excluded from the analysis. Individuals had a mean age of 62 years, with a standard deviation of 14.48 years. Of 256 patients, 172 were women, and 84 were men.

Regarding recurrence, the study categorized 93 injuries as recurrence and 116 as primary injuries. When comparing the number of surgical phases, recurrent lesions had a significantly higher number of stages than primary lesions (1.69 ± 0.77 versus 1.31 ± 0.58 phases, respectively) (Table 2). Concerning the tumor's size, 12 lesions measured 0.1 cm to 1 cm, 18 lesions measured between 1.1 cm and 2 cm, and 13 lesions measured more than 2 cm. The medical record didn't describe the size of 188 lesions. Of these, 116 were excised in the first phase of surgery and 55 in the second phase. Tumors over 2 cm had a significantly greater number of phases than those with a size less than 1 cm and between 1.1 and 2.20 cm (2 ± 1 versus 1.08 ± 0.29

Table 1: Baseline characteristics of the patients

			%	
Sex	Men		84	32.82
	Women		172	67.18
Age	62		Standard Deviation = 14.48	
Pre-operative histological subtype	Aggressive BCC		101	39.45
	Non-aggressive BCC		104	40.62
	SCC		30	11.72
	Others		11	4.29
Tumor site	Not informed		10	3.9
	Upper third	72	28.12	
	Middle third		16	6.25
	Lower third		21	8.2
	Nose		119	46.48
	Ear		13	5.08
	Other		6	2.34

and 1.22±0.43 phases, respectively), according to Table 3.

Lesion sites were divided into upper third (72 lesions), middle third (16 lesions), and lower third (21 lesions) of the face, nose (119 lesions), ears (13 lesions), and others (6 lesions), which included all other neoplasms not located on the face. When comparing the sites with the number of phases, there was no significant difference (p = 0.128) (Table 4).

Histopathological subtypes were grouped into aggressive BCC (sclerodermiform, micronodular, infiltrated, and basal squamous subtypes), non-aggressive BCC (nodular and superficial subtypes), SCC (invasive and in situ), and dermatofibrosarcoma. They were also classified according to anatomopathology, categorizing no tumor cells found after the initial biopsy as without residual tumor.

The preoperative diagnoses analysis compared to the number of phases showed a significant difference: the aggressive BCC had more phases than the non-aggressive BCC (p=0.027) (Table 5). Among the injuries analyzed, 99 were diagnosed with aggressive BCC, 107 were non-aggressive BCC, and 28 were SCCs. The assessment of the histological subtypes of debulking compared to the number of phases demonstrated a significant difference: the aggressive BCC (n=97) had more stages than those without residual tumor (n=25; p=0.002) (Table 6). Furthermore, the evaluation of the postoperative histological subtypes compared to the number of phases presented a significant difference: aggressive BCC (n=96) had more stages than those without tumor (n=43; p=0.002) (Table 7).

Table 2. Relationship between recurrent tumors and the need for more surgical phases

			Phase numbers				Mean	Standard deviation	*p*
			1	**2**	**4**	**4**			
Relapse	**Yes**	**n**	45	33	14	1	1.69	0.77	**<0.001**
		%	48,4	35.5	15.1	1.1			
	No	**n**	86	25	4	1			
		%	74.1	21.6	3.4	0.9			

Table 3: Tumors size regarding the number of surgical phases

			Phase numbers					Mean	Standard deviation	*p*
			1	2	3	4	5			
Tumor size	0,1-1,0 cm	n	11	1	0	0	0	1.08	0.29	**0.001**
		%	91.7	8.3	0.0	0.0	0.0			
	1,1-2,0	n	14	4	0	0	0	1.22	0.43	
		%	77.8	22.2	0.0	0.0	0.0			
	>2cm	n	5	4	3	1	0	2.00	1.00	
		%	38.5	30.8	23.1	7.7	0.0			
	Unknown	n	116	55	15	1	1			
		%	61.7	29.3	8.0	0.5	0.5			

DISCUSSION

Aggressive subtypes, grouped in this study as infiltrative, sclerodermiform, basal-squamous, and micronodular, were found more frequently when more than one Mohs stage was needed, with statistical significance. The most aggressive subtypes of BCC require more MMS stages to obtain tumor-free margins, which is consistent with the concept that these subtypes generally require more aggressive treatment from the start. Weinstein et al.[10] also corroborated these findings, concluding that tumors with aggressive subtypes commonly present a subclinical extension that is challenging to evaluate properly. It hampers the analysis of margins in the conventional technique.[11]

We believe that the anatomopathological exams "without tumor" when debulking MMS are predominantly non-aggressive tumors, as we didn't find them in the postoperative sample. Also, we believe that in these cases, they could be small, well-defined tumors in which the initial biopsy may have been sufficient to obtain tumor-free margins.

Incisional punch biopsies are commonly used to confirm the clinical diagnosis of NMSC and determine the histopathological subtype before surgical excision. Preoperative biopsies can also coincide with the scar site or previously treated area without establishing an accurate diagnosis. The sample variations in preoperative biopsies could lead to a different interpretation of the histological subtype.[15] There is significant variability in the literature regarding the percentage of concordance between the histological diagnosis of incisional biopsies and the histological diagnosis found with complete excision of the tumor.[15] Previous studies have shown a moderate agreement ranging from 51.1% to 82% between the NMSC subtype in incisional biopsies and subsequent surgical excision. (15.16)

As for the histological type of the studied tumors, BCCs represented 67.2% of the sample and SCC, 7.89%. Data from the literature[7,10,14] indicate BCC as the more common type of skin cancer. Also, aggressive BCCs, relapsed and in high-risk areas, constitute one of the main indications for MMS, thus justifying their high prevalence in this series.

Mohs micrographic surgery avoids unnecessary excision of uninvolved tissue, allowing better preservation of function

Table 4: Tumor location regarding the number of surgical phases

			Phase numbers					Mean	Standard Deviation	*p*
			1	2	3	4	5			
Tumor site	**1. Upper third**	n	47	20	4	1	0	1.4306	0.66769	**0,128**
		%	30.5	28.6	20.0	50.0	0.0			
	2. Middle third	n	10	5	0	1	0	1.4667	0.83381	
		%	6.5	7.1	0.0	05.0	0.0			
	3. Lower third	n	18	2	1	0	0	1.1500	0.48936	
		%	11.7	2.9	5.0	0.0	0.0			
	4. Nose	n	66	37	15	0	1	1.5950	0.77005	
		%	42.9	52.9	75.0	0.0	100.0			
	5. Ears	n	9	4	0	0	0	1.3077	0.48038	
		%	5.8	5.7	0.0	0.0	0.0			
	6. Others	n	4	2	0	0	0	1.4000	0.54772	
		%	2.6	2.9	0.0	0.0	0.0			

Table 5: Preoperative diagnosis regarding the number of surgical stages

			Phase numbers					Mean	Standard Deviation	*p*
			1	2	3	4	5			
Diagnosis	**Aggressive BCC**	n	53	31	12	2	1	1.6566	0,84710	**0.027**
		%	34.2	44.9	60.0	100.0	100.0			
	Non-aggressive BCC	n	75	25	7	0	0	1.3645	0,83381	
		%	48.4	36.2	35.0	0.0	0.0			
	SCC	n	18	9	1	0	0	1.3929	0,48936	
		%	11.6	13.0	5.0	0.0	0.0			
	No tumor	n	3	2	0	0	0	1.4000	0,77005	
		%	42.9	52.9	75.0	0.0	100.0			
	Others	n	6	2	0	0	0			
		%	3.9	2.9	0.0	0.0	0.0			

and cosmetics. Compared with other treatment modalities, it has the highest cure rates in five years, ranging from 94% to 99% for primary BCCs and from 90% to 96% for recurrent BCCs.[11] Previous studies (with different excision margins and indication criteria) found that between 28% and 45% of BCCs treated with MMS were excised entirely in the first stage, suggesting that the use of MMS eligibility criteria could be worthy.[11]

According to a study by Van Loo et al.[7], the accumulated probability of recurrence in 10 years for both recurrent or primary BCCs ranges from 3.9-4.4% after MMS to 12.2-13.5% after conventional surgery. Of all recurrences, 44.0% were recorded in the first five years after treatment, 40.0% between five and ten years after treatment, and 16.0% after ten years of follow-up. It demonstrates that even in long-term follow-up, neoplasms excised by the Mohs technique have fewer recurrences.

Due to the absence of tumor size description in the medical record of most cases in this study, only 43 lesions were analyzed by tumor size. It is a common bias in retrospective, observational studies. Despite this, we found that tumor sizes >2 cm had a significantly higher number of phases than lesions <1.0 cm and 1.1-2.0 cm (2.0±1 versus 1.08±0.29 and 1.22±0.43 phases, respectively), which is compatible with the finding in the literature.[2,3]

As demonstrated in this study, skin neoplasms larger than 2 cm present a higher risk of recurrence if not adequately addressed. Therefore, MMS could be indicated in these cases, especially in tumors with aggressive histological subtypes or high-risk locations.

The aggressive BCC subtypes found in this study needed more stages for tumor clearance with statistical significance

Table 6: Relation of the histological type of debulking regarding the number of surgical phases

			Phase numbers					Mean	Standard Deviation	*p*
			1	2	3	4	5			
Debulking	**Aggressive BCC**	n	48	33	14	2	0	1.6907	0.79531	**0.002**
		%	31.0	47.8	70.0	100.0	0.0			
	Non-aggressive BCC	n	38	21	2	0	0	1.4098	0.55908	
		%	24.5	30.4	10.0	0.0	0.0			
	SCC	n	13	4	1	0	0	1.3333	0.59409	
		%	8.4	5.8	5.0	0.0	0.0			
	DFSP and others	n	1	1	0	0	0	1.5	0.70711	
		%	42.9	52.9	75.0	0.0	100.0			
	No tumor	n	23	1	1	0	0	1.12	0.4397	
		%	3.9	2.9	0.0	0.0	0.0			
	Unknown	n	32	9	2	0	1			
		%	20.6	13.0	10.0	0.0	100.0			

Table 7: Postoperative histological subtype regarding the number of surgical phases

			Phase numbers					Mean	Standard Deviation	*p*
			1	2	3	4	5			
Postoperative histological subtype	**Aggressive BCC**	n	49	33	12	2	0	1.656	0.779	**0.002**
		%	31.6	47.8	60.0	100.0	0.0			
	Non-aggressive BCC	n	41	25	4	0	0	1.471	0.607	
		%	26.5	36.2	20.0	0.0	0.0			
	SCC	n	12	5	1	0	0	1.3889	0.60768	
		%	7.7	7.2	5.0	0.0	0.0			
	DFSP and others	n	1	0	0	0	0	1.0000		
		%	0.6	0.0	0.0	0.0	0.0			
	No tumor	n	38	3	2	0	0	1.1628	0.48453	
		%	24.5	4.3	10.0	0.0	0.0			
	Unknown	n	14	3	1	0	1			
		%	9.0	4.3	5.0	0.0	100.0			

(p=0.002). It also agreed with the findings of other studies.[2,9,11]

When comparing the anatomical sites with the number of phases, our study showed no significant difference, differing from other studies. Alam et al. demonstrated in their case series that lesions in the nose and ear required more surgical stages than tumors in other extra-facial locations. Flohil et al.[11] described that BCCs located in the H zone of the face were 51% more likely to require several MMS stages than BCCs in other locations. We believe that we found no statistical difference for the anatomical site due to the predominance of nasal lesions and our sample size.

According to data from the international literature, men are predominant. In our sample, we obtained a predominance of women in 66.79% of the cases. We emphasize that our study assessed patients who underwent MMS in a particular scope. Also, the sample was non-random and with a limited number of patients (n=230), not representing all the population. The average age found was 61.54 years (24 to 94 years).

The study categorized 93 injuries as recurrent (40.4%) and 116 as primary (50.43%). When comparing the number of surgical phases, lesions with recurrence had significantly more numbers than lesions without recurrence (1.69 versus 1.31, respectively). Such data also agree with previous studies,[2,7,8,11] including MMS indication as another standard for recurrent tumors.

When analyzing the preoperative, debulking, and postoperative diagnosis compared to the number of stages, there was a significant difference. More surgical phases were necessary for aggressive BCC treatment in all analyses than for non-aggressive BCCs or samples without tumors (p<0.05).

CONCLUSION

Aggressive BCC subtypes often required more than one Mohs stage to obtain free margins. Our study demonstrated, confirming the literature data, that tumor size, recurrence, and histological subtype are related to a higher number of stages in Mohs surgery. It concluded that the risk factors described are directly associated with a more significant number of Mohs micrographic surgery stages, that is, higher subclinical growth of tumors. These data are relevant in the patient's initial assessment and can help decide the appropriate conduct for each case. ●

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AUTHORS ' CONTRIBUTION:

Manoella Freitas Santos | ORCID 0000-0002-5024-5976

Statistical analysis; approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Ana Claudia Dal Magro | ORCID 0000-0001-5472-4539

Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review; critical revision of the manuscript.

Thaís Furtat Marques | ORCID 0000-0001-6676-5872

Study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review; critical revision of the manuscript.

Fernando Eibs Cafrune | ORCID 0000-0002-6645-0122

Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Cognitive Impairment screening in elderly patients during a Skin Cancer Prevention Campaign

Rastreamento de déficit cognitivo em idosos participantes da Campanha de Prevenção ao Câncer de Pele

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ABSTRACT

Introduction and objective: The Campanha Nacional de Prevenção ao Câncer de Pele (National Skin Cancer Prevention Campaign), promoted by SBD, is an annual event to inform about the early diagnosis and prevention of skin cancer. Considering the participants' profile, composed mostly of older adults, and the campaign educational goals, it's opportune to identify the proportion of people with cognitive impairment to improve communication.

Methods: We perform a cognitive screening of 2018 Campaign participants using a "10-point cognitive screener" score. The participants included were ≥ 60 years. We excluded those who were unable to communicate or denied consenting.

Results: The study interviewed 66 participants. The median age was 68 years (p25-p75:63-73), and 42 (64%) were women. Twenty-four participants (36%) had some elementary school, and 13 (20%) had a neurological or psychiatric disease. The crude and adjusted by schooling 10-CS scores had a median of 8 (6-9). Twenty-five of the interviewed patients (38%) had adjusted score below eight, indicating cognitive impairment, and six (9%) had a probable impairment. The cognitive deficit was associated with a history of neurological disease and low schooling.

Conclusions: Despite covering all ages, the campaign prioritizes the risk population, including older adults. Therefore, campaign volunteers should adapt the communication to participants' profile.

Keywords: Dermatology; Skin Neoplasms; Disease Prevention; Mild Cognitive Impairment; Epidemiology; Early Detection of Cancer

RESUMO

Introdução e objetivo: *a Campanha Nacional de Prevenção ao Câncer de Pele, promovida pela SBD, é um evento anual de conscientização da população sobre diagnóstico precoce e prevenção dessa doença. Considerando o perfil dos participantes, em grande parte idosos, e seu caráter educativo, é válido identificar a proporção de pessoas com possível prejuízo cognitivo, de modo a aprimorar as informações transmitidas.*

Métodos: *neste estudo, realizamos triagem cognitiva em participantes da Campanha de 2018 usando escore 10-point cognitive screener, incluindo indivíduos ≥ 60 anos. Foram excluídos pacientes com dificuldades comunicativas e não anuentes.*

Resultados: *foram entrevistados 66 participantes com idade mediana de 68 anos (p25-p75:63-73), sendo 42 (64%) do sexo feminino. Desses, 24 (36%) possuíam ensino fundamental incompleto e 13 (20%) apresentavam doença neurológica ou psiquiátrica. O escore cognitivo 10-CS bruto e corrigido pela escolaridade apresentou mediana de 8 (6-9). Apresentavam escores ajustados menores que oito 25 entrevistados (38%), indicando déficit cognitivo possível, e seis (9%) apresentaram déficit cognitivo provável. Tal prejuízo cognitivo associou-se a antecedentes neurológicos e baixa escolaridade.*

Conclusões: *apesar de abranger todas as idades, a Campanha prioriza populações de risco, incluindo idosos. Assim, as informações e a didática dessas campanhas devem adequar-se ao perfil dos ouvintes.*

Palavras-chave: *Dermatologia; Neoplasias Cutâneas; Prevenção de Doenças; Epidemiologia; Detecção Precoce de Câncer; Comprometimento Cognitivo Leve*

Original Article

Authors:

Bianca Latance da Cruz[1]
Arthur Cesar dos Santos Minato[1]
Maria Vitória Yuka Messias Nakata[1]
Vítor Cercal de Oliveira[1]
Juliano Vilaverde Schmitt[1]

[1] Department of Dermatology, Diagnostic Imaging and Radiotherapy, Botucatu (SP), Brazil.

Correspondence:
Juliano Vilaverde Schmitt
Av. Prof. Montenegro, s/n
Distrito de Botucatu
18618-687 Botucatu (SP)
E-mail: julivs@gmail.com

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INTRODUCTION

The Brazilian Society of Dermatology has been promoting the National Skin Cancer Prevention Campaign for approximately 20 years. It is an annual event to raise the population's awareness for early diagnosis and skin cancer prevention. In addition to disseminating information in mass media, the campaign also offers a dermatological examination focused on identifying lesions suspected of skin cancer and a visual presentation to guide the general population regarding prevention and early diagnosis.[1]

Most tumors identified in prevention campaigns occur in elderly patients, with an average of 68.5 years for basal cell carcinoma (BCC) diagnosis.[2] The average age of participants ranges from 40 to 50 years, according to a study by the Brazilian Society of Dermatology (2006),[3] suggesting that a significant proportion of participants in prevention campaigns is elderly.

Considering the participants' profile and the campaign's educational character, it is valid to identify the proportion of people with possible cognitive impairment to improve the campaign's information, focusing on acquiring the desired knowledge for primary and secondary prevention of skin cancer.

METHODS

The present study conducted a cognitive screening assessment in 66 elderly participants of the National Skin Cancer Prevention Campaign in 2018. It used the 10-CS (10-point cognitive screener) score and included individuals aged 60 years or more. We excluded patients with communication difficulties or who did not consent to participate in the study. Research participants signed an informed consent form (ICF) at the time of the interview. The institution's ethics committee approved the study (Opinion: 3,748,844).

RESULTS

We interviewed 66 participants, with a median age of 68 years (p25-p75: 63-73), 42 (64%) of whom were women, and 24 (36%) had only incomplete elementary education.

Another adult accompanied 37 (56%) of the interviewed elderly. The companions were younger than those accompanied (63 [50-68] x 68 [63-73] years; $p<0.01$ - Mann-Whitney). However, a significant part of them was also elderly. Also, 13 (20%) respondents presented some neurological or psychiatric illness.

The cognitive 10-CS score, crude and corrected for education, had a median of 8 (6-9). Table 1 illustrates the variables studied regarding the association with the cognitive score so that low education and the presence of neurological or psychiatric diseases were associated with lower values.

Twenty-five respondents (38%) had adjusted educational scores below eight, indicating possible cognitive impairment, and six (9%) had probable cognitive impairment.

DISCUSSION

It is believed that dementia is a poorly recognized clinical situation. Up to 67% of carriers are not correctly identified, and up to 91% of patients with mild dementia are not recognized.[4] The 10-CS test performs a standardized assessment. It is quick to apply (up to five minutes) for cognitive screening in the elderly, showing a better performance than the Mini-Mental state exam and the 6-item screening to identify cognitive impairment.[5] In the study above, 58.3% of patients with a 10-CS score below eight had cognitive impairment, while 96.5% of patients with a score below six had this impairment.[5]

More than a third of respondents over 60 years had low scores in our study, and 10% had a high chance of dementia. As expected, the analysis associated cognitive impairment with the neurological history and low education, but it adjusted the scores for the latter characteristic.

Table 1: Characteristics of respondents according to the 10-CS score

Variable	Score < 8 n=30 (%)	Score ≥ 8 n=36 (%)	Relative risk	*p*
Woman	22 (73)	20 (56)	1.32 (0.92 a 1.90)	0.13
Man	8 (27)	16 (44)	-	-
Age (years)*	68.40 (9.59)	66.86 (9.42)	-	0.51
Incomplete elementary school or less	16 (53)	8 (22)	2.4 (1.20 a 4.82)	0.01
Neurological or psychiatric illness	10 (33)	3 (8)	4 (1.21 a 13.22)	0.01
Came accompanied	17 (57)	20 (56)	1.02 (0.66 a 1.57)	0.99

* *Mean (standard-deviation)*

Interestingly, adults did not accompany the participants with scores indicating deficit risk more often. Moreover, the adults who accompanied these participants were mostly elderly too, just a few years younger.

The present study has limitations related to the performance in a single center, and not having a control group. On the other hand, the study did not aim to verify risks associated with other groups but describe a cognitive characteristic of the studied population and possible implications in setting up educational strategies.

CONCLUSION

The National Skin Cancer Prevention Campaign aims at all age groups. However, there is a particular focus on at-risk populations, which include elderly individuals. Therefore, it is relevant that the information and the didactic structure of these campaigns are appropriate to the listeners' profile, focusing on the most pertinent and objective aspects of prevention and early diagnosis of skin cancer. ●

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AUTHORS ' CONTRIBUTION:

Bianca Latance da Cruz | ORCID 0000-0003-0412-3844
Approval of the final version of the manuscript; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review; critical revision of the manuscript.

Arthur Cesar dos Santos Minato | ORCID 0000-0003-2484-8631
Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review; critical revision of the manuscript.

Maria Vitória Yuka Messias Nakata | ORCID 0000-0003-4068-9714
Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review; critical revision of the manuscript.

Vítor Cercal de Oliveira | ORCID 0000-0001-6823-491x
Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review; critical revision of the manuscript.

Juliano Vilaverde Schmitt | ORCID 0000-0002-7975-2429
Statistical analysis; approval of the final version of the manuscript; study design and planning; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Original Article

Authors:
Dalva Regina Neto Pimentel[1]
Rafael Tomaz Gomes[1]
Cleonice Hirata[1]

[1] Stomatology Outpatient Clinic, Department of Dermatology, Escola Paulista de Medicina, Universidade Federal de São Paulo (UNIFESP), Brazil

Correspondence:
Rafael Tomaz
Departamento de Dermatologia – Setor de Estomatologia
Escola Paulista de Medicina (Universidade Federal de São Paulo)
R. Borges Lagoa, 612
Vila Clementino
04038-000 São Paulo (SP)
E-mail: gomes_rt@yahoo.com

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Study conducted at the no Stomatology Outpatient Clinic, Department of Dermatology of the Escola Paulista de Medicina (UNIFESP).

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Sclerotherapy as a treatment modality for oral venous lake: protocol of use

Escleroterapia como modalidade de tratamento do lago venoso oral: protocolo de uso

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ABSTRACT

Introduction: The venous lake is a venous ectasia that usually occurs on the lips and oral mucosa of the elderly. Although sclerotherapy is one of the most suitable treatments for this condition, dermatologists don't use this technique very often. Also, the concentration of the sclerosing agent, dose, and method of application are not standardized.

Objectives: This study aims to report the use of ethanolamine oleate 5% (EO5%) as a sclerosing agent to treat the oral venous lake and suggest a sclerotherapy protocol.

Methods: We used a standardized protocol to treat an oral venous lake in ten consecutive patients, based on the experience of a University Dermatology Clinic, specialized in Stomatology. EO5% was applied in deep and central intralesional injections, with a predetermined volume proportional to the lesion's dimensions. Results: Six patients had total lesion regression with one session. Another three patients achieved satisfactory regression with two monthly sessions, and one patient required three monthly sessions. All participants reported edema or burning for one to three days.

Conclusion: The oral venous lake treatment with EO5% is a safe and effective technique that can be used in the dermatologist's clinical practice.

Keywords: Venous Lake, Ethanolamine Oleate.

RESUMO

Introdução: *o lago venoso é uma ectasia venosa que ocorre geralmente nos lábios e na mucosa oral de idosos. Embora a escleroterapia seja um dos tratamentos mais indicados para esta condição, esta técnica é pouco utilizada entre os dermatologistas. Além disso, a concentração do agente esclerosante, a dose e o modo de aplicação não estão padronizados.*

Objetivos: *relatar o uso do oleato de etanolamina a 5% (OE5%) como agente esclerosante para o tratamento do lago venoso oral e sugerir um protocolo de escleroterapia.*

Métodos: *foi utilizado em dez pacientes consecutivos um protocolo padronizado para tratamento de lago venoso oral, baseado na experiência de um Ambulatório Universitário de Dermatologia, especializado em Estomatologia. Aplicou-se o OE5%, em injeções intralesionais profundas e centrais, com volume predeterminado, proporcional às dimensões da lesão.*

Resultados: *seis pacientes tiveram regressão total da lesão com uma sessão. Outros três pacientes alcançaram regressão satisfatória com duas sessões mensais e uma paciente necessitou de três sessões mensais. Todos os participantes relataram edema ou queimação por um a três dias.*

Conclusão: *o tratamento do lago venoso oral com OE5% é uma técnica segura e eficaz que pode ser usada na prática clínica do dermatologista.*

Palavras-chave: *Escleroterapia, Lago Venoso, Oleato de Etanolamina.*

INTRODUCTION

The venous lake is a venous ectasia that appears mainly on the lower lip, but it can also occur on the oral mucosa, being more frequent in the elderly[1]. It is generally asymptomatic, of variable size, and may present with aesthetic impairment or bleeding after local trauma.[1,2]

Sclerotherapy is a conservative technique consisting of intralesional injection of sclerosing agents that lead to inflammation of the vessels followed by occlusion and vascular sclerosis, resulting in lesion regression.[2,3]

Although sclerotherapy is affordable, effective, and has a low risk of complications, the concentration of the sclerosing agent, dose, and method of application are not entirely standardized in the treatment of the venous lake.[4,5]

This article aims to report the use of 5% ethanolamine oleate (OE5%) as a sclerosing agent for the treatment of the oral venous lake, both on the lip and oral mucosa, and to suggest a sclerotherapy protocol based on the experience of our clinical center.

METHODOLOGY

Box 1 describes the treatment protocol for oral venous lake using OE5% with a sclerosing agent (Ethamolin®, Farmoquímica - Brazil). We use the technique in 10 consecutive patients attending the Stomatology Outpatient Clinic of the Department of Dermatology at UNIFESP during 2019 (Box 1).

The procedure is contraindicated in pregnancy, uncontrolled diabetics, and infection at the application site.[2-3]

RESULTS

Most patients were women (7/10) and over 50 years old (9/10). The venous lake was observed in the lower lip in 6/10 patients, in the upper lip in 1/10 patients, and in the oral mucosa in 3/10 patients. The size varied between 3 mm to 10 mm in diameter. The patients reported asymptomatic lesions with an onset time greater than five years. Some individuals described accidental local trauma with mild bleeding.

Most patients (6/10) needed only one application of OE5% (Figure 1), while other patients required two or three monthly sessions. We observed complete regression of the lesions in the vast majority of cases (9/10), and in one case, the patient was satisfied with only a partial regression.

Most patients reported discomfort after applying the sclerosing agent, such as pain, edema, redness, and burning (Figure 2). These symptoms lasted from one to three days. In one case, ulceration and local necrosis occurred due to the application being more superficial, resolving in seven to ten days without leaving scars (Figure 3).

DISCUSSION

The diagnosis of the oral venous lake is based on the clinical characteristics and history of the lesion. Vitro pressure, polarized light dermoscopy, aspiration, and imaging exams can also constitute accessory resources for diagnosis and treatment planning in some cases. [3,6,8]

Histologically, dilated, thin-walled venules located close to the epithelial tissue can be observed. The differential diagnosis includes melanocytic nevus, melanotic macule, malignant melanoma, pyogenic granuloma, and Kaposi's sarcoma.[2,4,6]

Box 1. Protocol for the treatment of oral venous lake

1. The patient is informed about the procedure, the likely resulting discomfort, and possible local changes after treatment.
2. Local asepsis is performed with 2% aqueous chlorhexidine solution for lesions on the lip. Lesions located in the oral cavity use mouthwash with 0.12% chlorhexidine for 60 seconds.
3. The dose of OE5% is calculated according to the size of the lesion: lesion up to 5 mm in its longest length receives up to 0.1 ml of intralesional OE5%; for each additional 1 mm in the size of the lesion, the proportional quantity in ml is added to the initial dose.
4. With an insulin syringe, the sclerosing agent is applied to the center and the deepest portion of the vascular lesion, avoiding superficial infiltration. Aspiration is not necessary, as bleeding is visible from the puncture inside the vessel. Local anesthesia is unnecessary.
5. Application should be slow and gradual to avoid rupture of blood vessels and local discomfort.
6. For lesions larger than 1 cm, more than one injection is performed to distribute the drug homogeneously.
7. Patients should be evaluated after one week.
8. The procedure can be repeated at 4-week intervals until achieving a satisfactory result.

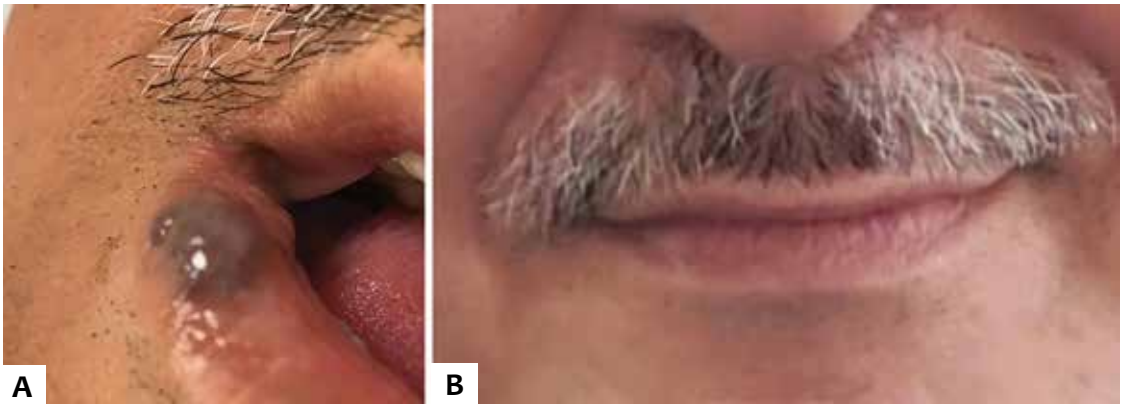

Figure 1: Clinical images: A) before treatment and B) after 4 weeks of treatment with a single dose of 0.2% intralesional OE5%

Table 1: Demographic and clinical characteristics of oral venous lake lesions

Case	Age	Gender	Site	Size	N of applications
1	> 50	F	LL	4mm	2
2	>50	F	OM	3 mm	1
3	>50	M	LL	6mm	2
4	>50	F	OM	5mm	1
5	>50	F	LL	4mm	1
6	<50	F	LL	8mm	1
7	>50	M	LL	6mm	2
8	>50	F	UP	5mm	1
9	>50	M	LL	10mm	1
10	>50	F	OM	10mm	3

LL = lower lip; UP = upper lip; OM = oral mucosa

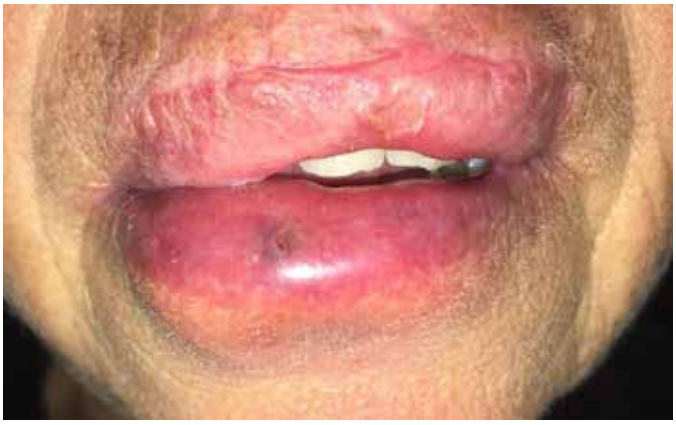

Figure 2: Edema after 5 minutes of infiltration of 0.1 ml of OE5%. The patient reported feeling a slight burning sensation

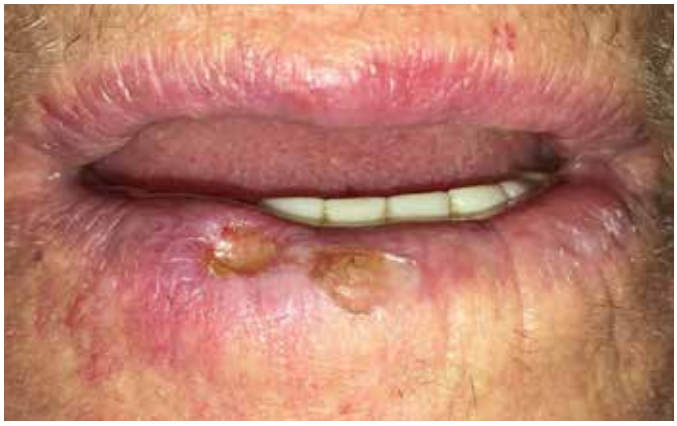

Figure 3: Ulceration and necrosis after 2 weeks of superficial intralesional infiltration of OE5% 0.1 ml in 2 lesions on the lower lip

The treatment modalities for venous lake include electrocoagulation, surgical excision, laser therapy, infrared coagulation, cryotherapy, and sclerotherapy.[5-8] OE5% is one of the most widely used sclerosing agents in treating vascular lesions. The literature describes it as a safe and effective method for injuries located in different body regions.[7-10]

Our outpatient clinic has used sclerotherapy to treat the oral venous lake for more than ten years with good results. We presented ten patients treated consecutively and who reached a complete resolution in 90% of cases. We suggest this protocol can guide the definition of the drug's necessary amount regarding the lesion's size. The application is performed in the outpatient clinic, and it does not require the use of the operating room. The technique is quick and does not require block anesthesia. The most uncomfortable adverse event was the temporary swelling after application, which usually occurs in all cases. It is easily

explained considering the inflammatory process caused by the sclerosing agent.

The most observed complication was the ulceration's appearance due to a very superficial application, which also occurred in some cases throughout our experience. The resolution occurred in 15 days without leaving a scar. The injection technique must be deep in the vascular lesion center to avoid this complication. Using a greater quantity of the sclerosing agent than what is recommended or its overflow may cause ulceration.

The recommended OE5% limit dose for sclerotherapy is up to 2 ml per application. Other complications reported in the literature include hemoglobinuria and hemolytic renal failure cases, but their occurrence was limited to the use of doses greater than 9.6 ml of OE5%.[8,10]

This protocol's description aims to share the authors' experience and the best practices accumulated in the last ten years in a specialized Stomatology service. The protocol can help professionals maximize the chances of success and minimize the appearance of adverse events in the oral venous lake treatment.

CONCLUSION

The oral venous lake treatment with OE5% is a safe and effective technique that can be used in the dermatologist's clinical practice. ●

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AUTHORS ' CONTRIBUTION:

Dalva Regina Neto Pimentel | ORCID 0000-0001-7783-4810
Study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review; critical revision of the manuscript.

Rafael Tomaz Gomes | ORCID 0000-0001-8775-2173
Preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review; critical revision of the manuscript.

Cleonice Hirata | ORCID 0000-0002-6336-961X
Study design and planning; data collection, analysis, and interpretation; critical revision of the manuscript.

Original Article

Authors:
Karvan Bekmaz[1]
Somayeh Hashemzadeh[2]
Hadiseh Okhli[2]
Fatemeh Mohaddes Ardebili[3]
Samira Khanmohammadi[2]
Leila Mamashli[2]

[1] Orumieh Branch, Islamic Azad University, Orumieh, Iran
[2] Ali Abad Katoul Branch, Islamic Azad University, Ali Abad Katoul, Iran
[3] Iran University of Medical Sciences, Tehran, Iran

Correspondence:
Leila Mamashli
Urmia – 342
8879376182 Irã
E-mail: nosratollahmas@gmail.com

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Study conducted at the Nursing Department, Gonbad Kavoos Branch, Islamic Azad University, Gonbad Kavoos, Iran

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The effect of multimedia training on social function of burned patients in Shahid Motahhari Hospital, Tehran: A clinical trial study

O efeito do treinamento multimídia na função social de pacientes queimados no Hospital Shahid Motahhari, Teerã: um estudo clínico

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ABSTRACT

Introduction: Burn is a tissue injury and affects social functioning and relationships. Complications of burns lead to disruption of social relationships and, consequently, social dysfunction.

Objective: This study aims to determine the effect of multimedia training on burned patients' social functioning in Shahid Motahhari hospital in Tehran.

Methods: This clinical trial study assessed 100 burned patients. The intervention group received multimedia self-care discharge training on a CD in addition to the standard education. The social function of the quality of life was examined in both groups before the intervention, 3 months and 6 months after the intervention.

Conclusions: Results showed that before the intervention, the mean score of social function of quality of life in intervention and control group was 1/55± 0/46, 1/92± 0/6, respectively, which was statistically significant (p <0.001). Mean and standard deviation of social function of quality of life in the intervention and control groups three and six months after intervention were2/47± 0/56, 4/05± 0/77, 2/15±0/39, 3/29 ± 0/95, also statistically significant (p<0.001).

Keywords: Self care; Multimedia; Patient discharge; Social adjustment; Burns

RESUMO

Introdução: *a queimadura é uma lesão tecidual que afeta o convívio social e os relacionamentos. Complicações de queimaduras levam à ruptura das relações sociais e, consequentemente, à disfunção social.*

Objetivo: *este estudo objetiva determinar o efeito do treinamento multimídia no comportamento social de pacientes queimados no hospital Shahid Motahhari em Teerã.*

Métodos: *este estudo clínico investigou 100 pacientes queimados. O grupo de intervenção recebeu, na alta hospitalar, um treinamento de autocuidados em multimídia num CD, além das informações de rotina. A função social da qualidade de vida foi examinada em ambos os grupos antes da intervenção, três meses e seis meses após a intervenção.*

Conclusões: *os resultados mostraram que, antes da intervenção, o escore médio da função social da qualidade de vida no grupo intervenção e controle foi de 1/55 ± 0/46 e 1/92 ± 0/6, respectivamente, o que foi estatisticamente significativo (p<0,001). A média e o desvio-padrão da função social da qualidade de vida nos grupos intervenção e controle três e seis meses após a intervenção foram 2/47±0/56, 4/05±0/77, 2/15±0/39 e 29/3±0/95, respectivamente, também estatisticamente significativo (p<0,001).*

Palavras-chave: *Autocuidados; Multimídia; Alta do Paciente; Ajuste Social; Queimaduras*

INTRODUCTION

Burn has been described as one of the most devastating disasters on the human body,[1] seriously damaging one's life and health. It is considered the fourth most common injury.[2] The World Health Organization (WHO) estimates that the incidence of severe burns is 1% of life expectancy, and more than 300,000 people die from burns worldwide each year.[3] According to the Forensic Medicine Organization statistics, 379 people died from burn injuries in Iran in the first quarter of this year. Of these, 213 were men, and 166 were women.[4] Thus, burn injuries are one of the most dangerous health incidents in Iran.

Over the past decade, advances in health care led patients with more severe burns to survive.[5] However, even when urgent management is successful, burn injuries can create many obstacles for patients. In addition to their physical problems, they suffer from social problems, and ultimately their quality of life is affected.[6] Also, these patients have severe seizure disorders, which can last longer.

High-end living is attractive in most places where a lot of space for cabins can be appealing. Marriage, relationships, and residence location occupy a prominent place in patients' lives and ultimately cause them to become overwhelmed by fear and anxiety.[7] These patients have trouble meeting new people and dating, worrying about developing relationships, and exhibiting various reactions, such as shyness, aggression, or extreme social avoidance. Therefore, it is necessary to design appropriate support programs to improve their quality of life.[8]

To help these patients, they need to learn how to live with their situation and to meet their own needs, being less dependent on others and showing that they can deal with these shortcomings. Thus, they need training, learning, and rehabilitation.[9] Patient education's philosophy is to apply the information and skills learned to control and cope better with the disease. The health care team, especially the nurses, are responsible for conducting patient education programs.[10] The role of nurses in the last few years as an essential member of the health care team has undergone a historical transformation, from promoting patient-centered health education to empowering patients to self-care and achieve health. Informing the patient and contributing to decision-making speeds recovery and reduces hospital stay and readmission.[11] This is a critical challenge in achieving donation.

Multimedia education is a traditional teaching tool for patients with disabilities.[12] The lecture-based training requires a great deal of time and expense. Moreover, a patient with a burn injury during hospitalization is less prone to learn and remember education due to mental and physical injuries, physical weakness, painful daily activities, intellectual discomfort, and lack of focus on decision-making. The empowerment and self-care are not.[9]

In recent decades, traditional approaches to learning with the advent of new technologies such as multimedia virtual education have undergone dramatic changes.[13] The purpose of the multimedia application is to make meaningful learning happen, and meaningful learning occurs when the learner can make sense of the material presented, building a coherent mental image from multiple sources of information.[14] It seems that learning is better if the patient can carry out a self-care program using a comprehensive audiovisual CD to suit any time and circumstances they wish.[9] Also, due to the gradual rehabilitation process in patients, education during discharge for these patients to return to the community must be sufficient and carefully planned.[15]

OBJECTIVES

Since humans are social beings and communicating with others is an essential factor in life and patients with burns suffer from this, the researchers investigated the impact of multimedia training on burn patients' social functioning at the Shahid Motahhari Hospital in Tehran.

MATERIALS AND METHODS

Setting

This research was a randomized controlled clinical trial conducted in the hospitalization wards of Shahid Motahari Burn Center, Tehran, Iran, from 2016 to 2017. The study population consisted of all burn patients admitted to Shahid Motahari Burn Center and participated in the study based on the inclusion criteria.

Inclusion and Exclusion Criteria

The criteria for participating in the study were individuals aged between 18 to 60 years; who were able to use audiovisual compact discs (CDs); with a percentage of burn 10-45%; burn degrees 1, 2, and 3; minimum reading and writing literacy; and understanding of Persian language. The study also included subjects who lacked sensory and motion problems and brain and mental disorders or mental retardation; living in Tehran and its suburbs; with burns due to accident, non-self-immolation, and non-electrical burn. The exclusion criteria were the withdrawal of continued study and severity of the disease, disability, and death.

Sampling Method

The study used convenience sampling and continuous variables. The patients were randomly assigned into intervention and control groups. According to the studies conducted in this regard, we considered the effect of educational interventions with a 95% of confidence interval (CI) and 80% of testing capacity on the number of samples needed for each group. Also, we considered ten scores of difference in the psychological dimension of both groups' quality of life. Thus, we estimated the population to be 55 people so that each group included 50 subjects, considering 10% of the probability of not participating. Finally, we considered 100 participants in the study using the formula $n=2(z1-\alpha/2+z1-\beta)2s2/(\mu1-\mu2)2$. In this formula, $z1\alpha/2=1.96$, $z1-\beta=0.84$, $s=9$ and $\mu1-\mu2=5$.

Measures

The current study used two questionnaires: the demographic information and disease status questionnaire and the Burning Specific Health Scale. The demographic information and disease status questionnaire included questions about gender, age, occupation, marital status, burning agent or source of heat (gasoline, gas, flame, hot liquids, oil, hot food, etc.), level of education, degree and percentage of burns, burning area, city, incident location, and economic status. The patient and a research associate selected this questionnaire on the first day to complete the study's sample inclusion. The other instrument was a questionnaire on quality of life in burn patients (Burning Specific Health Scale - BHS-B). We used the social dimensions of this questionnaire. The questionnaire included 40 questions about skin sensitivity to heat, body image, hand performance, care for burnt areas, communication, ability to perform simple activities, sexual function, and psychological dimension with the options high, moderate, low, and never, which had been scored from 1 to 5, respectively. Each questionnaire had at least one and at most five scores. Based on this questionnaire, each dimension of the quality of life was determined separately and in all domains. Of the 40 questions of the questionnaire, 18 were related to the physical dimension of quality of life, 11 were about the psychological dimension, and 11 questions assessed the social dimension of quality of life.

Ten faculty members of the school of medical sciences received the demographic information and disease status questionnaire to validate it. Their opinions were applied as the reliability. Kildal et al. in 2001 validate the BHS-B, using its dimensional analysis to measure it.[16] In Iran, Pishnamaazi et al. (2009) estimated its validity and reliability using Cronbach's Alpha of 94% in the burn patients at the Shahid Motahari and Hazrat Fatemeh hospitals.[17] At the Qotboddin Shirazi Hospital,[18] this tool's reliability was calculated with Cronbach's Alpha of 98%. Our study measured a Cronbach's Alpha of 94%.

Education and Treatment Program

Based on the implementation of this method, the researcher referred to the Burn Medical Educational Center of Shahid Motahari Hospital after receiving the study confirmation from the Iran University of Medical Sciences and the ethical code from the university's ethics committee (93-02-28-24922-106366 on 8/12/2014 and registered in a clinical trial with the code IRCT 2014112920145.). After introducing the principal investigator and the collaborators of the research and the study objectives to the hospital's officials and obtaining permission, he referred to the departments. While introducing him, his research colleagues, and the study objectives to the departmental authorities, the samples were randomly provided according to the inclusion criteria as the control or intervention group. After explaining the procedure and ensuring the anonymity of the samples, each participant signed the informed consent. The researcher also informed the participants that he would compensate for their transportation and absence from work costs at 3 and 6 months.

Before the intervention, the patient, with the help of a research associate and using medical records, completed the demographic information and burn characteristics questionnaire. Then the intervention and control groups received face-to-face routine training. However, in addition to routine training, the intervention patients received the self-care discharge education for burn patients in an educational CD containing text, slide, film, and recorded sound. Then the researcher gave this CD to the patients to perform at home. In the educational session, they used CDs and answered questions for 30-60 minutes at the time of discharge. Educational content was prepared based on the sources of self-care education in burn patients.

The patient completed the psychological, physical, and social dimensions of the quality of life in burn patients' questionnaire before the intervention, on the day of discharge, and 3 and 6 months after the intervention. The patients also received the researcher's telephone number, email address, and telegram number to contact if necessary. The researcher conducted a weekly phone contact with the patients in the intervention and control groups to follow up and ensure the samples' preservation. After 3 and 6 months of intervention, researchers contacted the patients in both the control and intervention groups by phone to complete the questionnaire. Patients completed the questionnaires in the manner of the self-report. At the end of the research, the educational CD was provided to the control group for observing ethics in the research.

Ethical consideration

The Ethics Committee of the Iran University of Medical Sciences and the research sites approved this study (Ethic code: 93-02-28-24922-106366). The Iranian Registry of Clinical Trials (IRCT) approved the clinical trial under N. IRCT2014112920145N1. The CONSORT checklist was used to report the study.

Statistical Analysis

After collecting raw data for the analysis, we used the descriptive and inferential statistics (Chi-square, and independent and paired t-tests for the distribution of normal variables), Fisher's exact test, nonparametric tests (Mann-Whitney, Wilcoxon, Friedman, and Dunn tests), with Bonferroni correction, and Spearman's correlation coefficient by SPSS software (version 21, Chicago, IL, USA). It should be noted that the process included all participants and excluded no one during the investigation.

RESULTS

Among the study participants, 56% of the subjects were men, and 56% were women. Only 34% of the intervention group was 39-48 years, and 44.9% of the control group was 29-38 years. According to the statistics, most of them (44% in the intervention group and 79.6% in the control group) were married. In the intervention group, 48% were employed, and in the control group, 62.5%. Also, 52.1% had complete superior education in the intervention group and 66.7% in the control group.

Moreover, 36% in the intervention group and 34% in the control group were burned by fire flame, and 60% in the intervention group and 64% in the control group had a degree of burns of 1, 2, and 3. Furthermore, 24% in the intervention group had a burn percentage of 15-20%, and 36% in the control group had a burn percentage of 21-26%. About 46% of participants had burns in the trunk, hand, and foot in the intervention group. In the control group, 47.9% had burns in the whole body. Most patients in the intervention and control group (58.1% and 79.2%, respectively) resided in Tehran. Furthermore, most patients in the intervention and control group (58.1% and 53.5%, respectively) were burned at home. In the intervention group, 56.5% were at an average economic level, and 37.8% were at a weak economic level.

The Mann-Whitney test showed that before the intervention, the mean of social function in intervention and control groups was 1.92±0.6 and 1.55±0.46, which was statistically significant ($p<0.001$). The mean difference of the social function score in both intervention and control groups before the intervention was statistically significant. The mean score of the social dimension in the intervention group was slightly higher than the control group. Mean and standard deviation of social function scores in intervention and control groups three months after intervention were 3.29±0.95 and 2.15±0.39, respectively. Six months after the intervention, the mean and standard deviation of intervention and control groups were 4.05±0.77and 2.47±0.56, which were statistically significant ($p<0.001$) (Table 1). Considering the chi-square value (=95.14) and the value of significance level ($p<0.001$) in Table 2, we rejected the assumption of the equality of the mean scores of social function during three periods since the level of significance was less than 0.05, statistically. This is the average score of social function varied at least in two of the three periods. Therefore, to determine which of the two periods had a significant difference, we used the Dunn follow-up test. Tables 2 and 3 present the results of the test. Each period's mean score had substantial differences with other periods because the corrected significance level value was less than 0.05. Figure 1 shows that the social dimension score before intervention in the intervention group was slightly higher than the control group. However, after 3 and 6 months of intervention, the intervention group's social function score demonstrated a significant difference compared to the control group ($p<0.001$).

DISCUSSION

The results of this study showed that discharge multimedia self-care education improves the social functioning of burn patients. This finding is consistent with the study by Li et al., which found that burn patients' social functioning five weeks after rehabilitation was better than the control group.[19] Tang et al. (2015) also showed that rehabilitation interventions and self-care measures increased patients' social function dimension three months after the intervention, consistent with the present study.[20] Radwan et al. (2011) found that running a 7-day rehabilitation program for two weeks improved social performance in the experimental group, also consistent with our study.[21]

Burn injuries affect the individual's ability to cope with life's stresses and interact socially.[8] These individuals feel ashamed and embarrassed about being in the community and communicating with others due to the apparent changes caused by burn injuries. The look and sometimes curiosity of others suggest that they feel compassion and sympathy. For this reason, the lack of communication and social skills requires intervention.[23] Hojati et al.'s study showed that psychosocial interventions significantly affected life satisfaction, occupational activity, mental health, physical health, quality of life, and social relationships. Therefore, these interventions increase patients' life satisfaction and social relationships.[24] The Fatimid study results showed that patients' quality of life in the social dimension was relatively undesirable, so it recommended the patients to learn communication skills.[25]

The consequence of education in the community is maintaining and promoting health. It brings many benefits, including reduced illness length, accelerated independence, and maintained self-confidence in self-care.[26] A study by Elalem et al. (2018) showed that nursing interventions to promote self-care were effective in burn patients. The self-care intervention led to an active participation of patients in their treatment and a significant improvement in quality of life and self-esteem, consistent with the present study. It also correlates with self-esteem and quality of life later.

The social skills of these individuals experienced a significant impact.[27] Hospital discharge is associated with stress and anxiety and an increased need for patients to receive information. Information training is essential for the well-being of patients because they experience discomfort after discharge.[28] Discharge does not mean the end of treatment for burn patients, but that the patient and their family must resume the responsibility of managing their lives without assistance from the hospital staff. Burn patients need to adapt to new situations that include self-care at home, lifestyle change, and return to society.

Limitation and Recommendation

One of the limitations of the present study was the patient's mental state, that is, if they could answer the questions effectively. Also, the researchers emphasized the importance of the subject in the results, asked the samples to comply with the CDC's care instructions thoroughly, and followed up with the patients by telephone.

CONCLUSIONS

Given the present study's findings, it is essential to provide virtual and multimedia education and institutionalize a self-care culture. It allows the patient to engage in self-care. Nurses and caregivers in burn centers must know that these patients will be socially isolated and need to return to the community. Nurses usually deal with patients' behaviors and attitudes more than other health professionals. So they can help these individuals get back into the community with proper education. However, education through lectures does not meet their educational needs because they are involved in their burn accident's mental illness, especially while they are still in the hospital. And it may

affect their ability to understand and learn in this situation. Thus, they need virtual training to use it in the right conditions and in a comfortable place. Self-care education should be continuous, accessible, monitored, and economically viable. So using educational CDs, which is a virtual teaching method, can be a good option. It is recommended that nurses use this method in clinical centers. ●

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AUTHORS ' CONTRIBUTION:

Karvan Bekmaz | ORCID 0000-0001-7780-7636
Approval of the final version of the manuscript; preparation and writing of the manuscript; critical literature review.

Somayeh Hashemzadeh | ORCID 0000-0002-6543-6214
Statistical analysis; active participation in research orientation; critical revision of the manuscript.

Hadiseh Okhli | ORCID 0000-0002-3638-9244
Study design and planning; data collection, analysis, and interpretation; critical literature review; critical revision of the manuscript.

Fatemeh Mohaddes Ardebili | ORCID 0000-0001-9175-0090
Approval of the final version of the manuscript; data collection, analysis, and interpretation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical revision of the manuscript.

Samira Khanmohammadi | ORCID 0000-0002-2374-9108
Approval of the final version of the manuscript; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical revision of the manuscript.

Leila Mamashli | ORCID 0000-0003-2647-6341
Statistical analysis; approval of the final version of the manuscript; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical revision of the manuscript.

Original Article

Authors:
Débora Aparecida O. Modena[1]
Renata Michelini Guidi[1]
Ciro Dantas Soares[1]
Everton Cazzo[1]
Elinton Adami Chaim[1]

[1] Universidade Estadual de Campinas, Campinas (SP), Brazil.

Correspondence:
Débora Aparecida Oliveira Modena
Av. Dr. Carlos Burgos, 2800
Jardim Itália
13901-080 Amparo (SP)
E-mail: de_modena@yahoo.com.br

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Electromagnetic shock wave therapy in dermatology: Microscopic analysis of its interaction with the possible reduction of adipose tissue in obese individuals

Ondas de choque eletromagnéticas na Dermatologia: análise microscópica de sua interação com a possível redução do tecido adiposo em indivíduos obesos

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ABSTRACT

Introduction: Obesity is a disease that affects public health worldwide due to its comorbidities and premature death risk. Therefore, extracorporeal shock wave therapy (ESWT) technology can help treat and prevent its comorbidities.

Objective: This study aims to assess whether ESWT can stimulate lipolysis and/or apoptosis of the fat cells of obese individuals.

Methods: This is a comparative interventional study based on immunohistochemical analyzes of a set of subcutaneous tissue samples from women with obesity submitted to ESWT treatment. The biological material was collected at the time of bariatric surgery.

Results: The survey included 14 obese women. Positivity was shown in the expression of Casp3 ($p<0.0001$), cCasp3 ($p<0.0024$), CD68+ macrophages ($p<0.0001$), HSL ($p<0.0001$), and adipophilin ($p<0.0013$) in the intervention sample compared to the control.

Conclusions: We conclude that ESWT stimulates apoptosis with consequent autophagic lipolysis in the adipose tissue of obese women. Thus, ESWT can be considered useful, safe, and promising adjuvant therapy for reducing adipose tissue and, consequently, for preventing and/or treating obesity.

Keywords: Dermatology; Obesity; High-Energy Shock Waves; Apoptosis

RESUMO

Introdução: *a obesidade é uma doença que afeta a saúde pública em nível mundial devido a suas comorbidades e ao risco de morte prematura. Diante disso, a tecnologia de terapia de ondas de choque extracorpóreas (ESWT) pode ser útil em seu tratamento e na prevenção de suas comorbidades.*

Objetivos: *o objetivo foi avaliar se a ESWT é capaz de estimular a lipólise e/ou apoptose da célula adiposa de indivíduos obesos.*

Métodos: *trata-se de um estudo comparativo de intervenção baseado em análises imuno-histoquímicas de um conjunto de amostras de tecido subcutâneo de mulheres com obesidade, submetidas ao tratamento ESWT. O material biológico foi coletado no momento da cirurgia bariátrica.*

Resultados: *14 mulheres obesas foram incluídas na pesquisa. Foi evidenciada positividade na expressão de Casp3 ($p<0,0001$), cCasp3 ($p<0,0024$), macrófagos CD68+ ($p<0,0001$), HSL ($p<0,0001$) e adipofilina ($p<0,0013$) na amostra intervenção quando comparada ao controle.*

Conclusões: *a ESWT estimula a apoptose com consequente lipólise do tipo autofágica no tecido adiposo de mulheres obesas. Assim, a ESWT pode ser considerada uma terapia adjuvante útil, segura e promissora para redução do tecido adiposo e, consequentemente, para prevenção e/ou tratamento de obesidade.*

Palavras-chave: *Obesidade; Dermatologia; Ondas de Choque de Alta Energia; Apoptose*

INTRODUCTION

Obesity is a worldwide public health problem. It reaches pandemic levels and generates great health professionals' concern due to its comorbidities and patients' risk of premature death.[1,2]

The excessive amount of fat and its influence on fat cells characterizes obesity. The increase in body mass above cut-off values previously established by the Body Mass Index (BMI) determines the condition, classified as Grade 1, with a BMI of 30 to 34.9; Grade 2, BMI up to 39.9; and Grade III, with BMI ≥40. Thus, BMI is proportional to body fat and is related to the risk of diseases associated with obesity.[3- 6]

Recent researches with experimental and clinical studies have seen great potential in electromedical resource development aiming to act in the adipose cell's physiology to stimulate its breakdown, lipolysis, and even its death, apoptosis. It helps the weight loss process contribute to a possible decrease in risk factors for the development of comorbidities associated with obesity simultaneously with current non-invasive treatments and minimal adverse events.[7,8]

Extracorporeal shock wave therapy (ESWT) is one of these resources. The technology was developed based on the extracorporeal lithotripsy equipment used until now to treat kidney and urethral stones. The technological evolution allowed adaptations to the resource, and it started to be used in the rehabilitation of musculoskeletal diseases and bone consolidations. Recent studies demonstrate its ability to stimulate the proliferation of fibroblasts and the development of neocolagenesis and neoelastogenesis, improving skin tone. Some clinical investigations have been exposing that the resource can also act in the fat cell's metabolic stimulation.[7-11]

Based on these studies on ESWT and the difficulty in reporting weight loss and tackling comorbidities associated with obesity, this study aims to assess whether ESWT can act to stimulate lipolysis and/or apoptosis of the adipose cell and thus contribute to reducing the risk factors in the development of comorbidities associated with obesity, validating its possible use in the conservative treatment of obesity.

MATERIALS AND METHODS

Ethical considerations

The institutional ethics committee of the State University of Campinas (Unicamp) approved this clinical study under opinion No. 2.281.487.

We selected women with a weight loss of 10% of the initial weight to participate in the preoperative preparation group for bariatric surgery at the Clinics Hospital of Unicamp, with obesity with an indication for bariatric surgery. The exclusion criteria were women with metabolic diseases, skin lesions, history of deep venous thrombosis, smokers, or with an electronic device implanted as a cardiac pacemaker.

ESWT procedures

The participants received the treatment protocol established by the Thork Shock Wave® device's manufacturer (IBRAMED- Industria Brasileira de Equipamentos Eletromédicos, Amparo, São Paulo) approved by Anvisa No. 10360310036. (Figure 1). The parameters were 4,000 shots with 180 mJ of energy and 15Hz of frequency, using 15 mm stainless steel tip, and 2,000 shots with 100mJ of energy and 15Hz of frequency, using 15 mm plastic tip. For the tip slip, Neutral Thork® Lotion, RMC was used. The study held seven ESWT sessions, with an average time of seven minutes each, twice a week. The seventh session was held minutes before the bariatric surgery procedure. The therapy was performed in an area of 150 cm^2 on the left side of the abdominal region following the midline. The right side of the participants' abdomen did not receive ESWT and was termed as control.

Sample collection

We collected the samples at the time of the bariatric surgery procedure. Participants were under general venous anesthesia and mechanical ventilation. At the time of the surgical incision, the doctors removed two fragments of adipose tissue with an average size of 5 cm in diameter, with one sample from the left side of the intervention and another from the right side, which was considered a control.

Histological procedure

After collection, we stored the material in a container with 10% formaldehyde for 48 hours. Samples were processed, embedded in paraffin, and then cut with a rotating microtome in sections of 3-5 μm thickness.

Immunohistochemical procedures

Immunohistochemical reactions were performed in sections of 3 μm thickness arranged on silanized slides. We used the antibodies polyclonal anti-Caspase3 (polyclonal; ref. 9662S; Cell Signaling Technology, Danvers, MA, USA), monoclonal anti-Cleaved Caspase 3 (clone (Asp175)(5A1); dilution 1:1000; ref. 9664S; Cell Signaling Technology), monoclonal anti-CD68 (clone KP1; dilution 1:1000; ref. ab955; Abcam, Cambridge, MA, USA), monoclonal anti-Hormone-sensitive lipase – HSL – (clone G-7, dilution 1:500, ref. sc-74489, Santa Cruz Biotechnology, Dallas, TX, USA) e Adipophilin (clone 2C5A3, dilution 1:500, ref. ab181463, Abcam). After preparing the slides, we analyzed them with a DMR microscope (Leica) and took photographs at 400X magnification. We used the ImageJ® software (NIH, Bethesda, USA) to quantify the analyzes.

All reactions were performed according to the manufacturers' protocol and standardized by the laboratory of pathological analysis at the Clinics Hospital of Unicamp. We conducted the immunostaining quantification considering the number of positive cells and the intensity, with final scores ranging from 0-300.

Statistical analysis

Data were subjected to normality tests and then analyzed by test t student since they had a regular distribution. Values of $P<0.05$ were considered statistically significant.

RESULTS

In total, 20 women participated in the research; however, only 14 finished the treatment and underwent surgical procedure. The remaining six participants were excluded for not following the internal preoperative program's protocol for bariatric surgery at the Clinics Hospital of Unicamp.

Participants had a mean age of 35.0 ± 8.6 years, initial weight of 110±5.2 kg, final weight of 95.2±6.3 kg, height of 1.63±0.05 cm^2, body mass index (BMI) of 41.4±2.2 kg/cm^2, and final BMI of 35.8±2.1 kg/cm^2, considered obesity grade II and III. None of the participants had associated pathologies such as diabetes and hypertension.

Immunohistochemical analysis

Morphologically, the control group's adipose tissue showed uniformity in the mature fat cells, with similar sizes. The treated group showed fat cells of different sizes, disorganized, often with a degeneration process. We also observed a chronic inflammatory process with fibrosis in the treated group, indicating repair and remodeling process in the deep dermis.

Fat and inflammatory cells adjacent to the adipose tissue revealed expression of Caspase 3 (Casp3) and Cleaved Caspase 3 (cCasp3) (Figure 1). The treated group presented higher scores of both markers than the control group ($p<0.0001$ for Casp3 and $p<0.0024$ for cCasp3).

As for CD68 expression, the control sample showed an absence of macrophages and HSL-positive inflammatory cells. However, the treated group presented a moderate amount of macrophages (CD68+) and inflammatory cells positive for HSL in the region adjacent to the adipose tissue. The scores had statistically significant differences ($p<0.0001$ for CD68+ macrophages, $p<0.0001$ for HSL).

Adipophilin demonstrated immunopositivity in sebaceous glands, macrophages, and inflammatory cells present in the dermis. After quantification, it was possible to observe a significant increase in the number of adipophilin-positive cells in the treated group compared to the control group ($p <0.0013$).

Adverse events

The most common adverse events reports were presented by 14.28% of the participants: presence of erythema, formation of petechiae, and mild edema in the treatment region. All of them were resolved after the end of treatment. None of the participants claimed painful discomfort during treatment.

DISCUSSION

The present study results demonstrate that treatment with ESWT was able to alter the fat cell's metabolism with consequent stimulation of autophagic lipolysis through the apoptotic pathway, increasing the number of apoptotic cells, as well as inducing chronic inflammation and expression of adipophilin and HSL in macrophages. Together, these results may indicate a possible benefit of ESWT in the conservative treatment of obesity and its comorbidities, stimulating the lipolysis process through the apoptotic pathway.

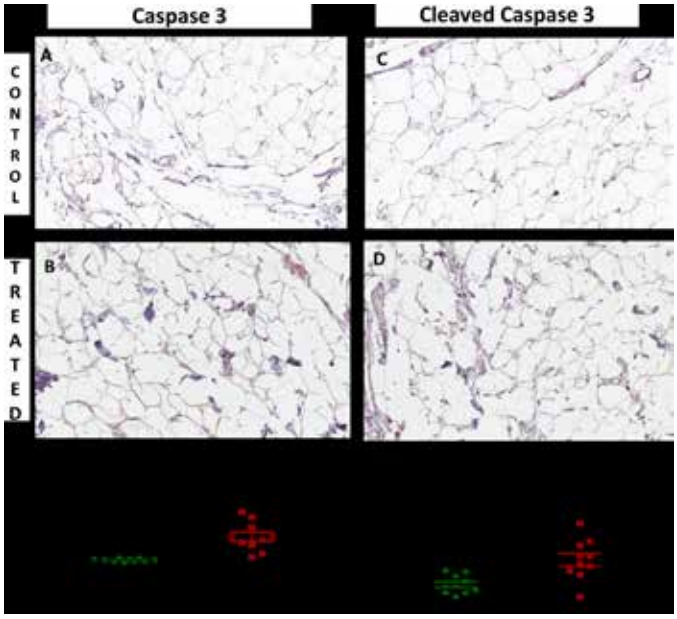

Figure 1: Immunoexpression of Caspase 3 (Casp3) and cleaved Caspase 3 (cCasp3) in adipose tissue and inflammatory cells. It was possible to observe a significant increase in the expression of Casp3 ($p<0.0001$) and cCasp3 ($p<0.0024$) in the adipose tissue of the treated group compared with the control group, indicating apoptosis process in the adipose tissue of the treated group.

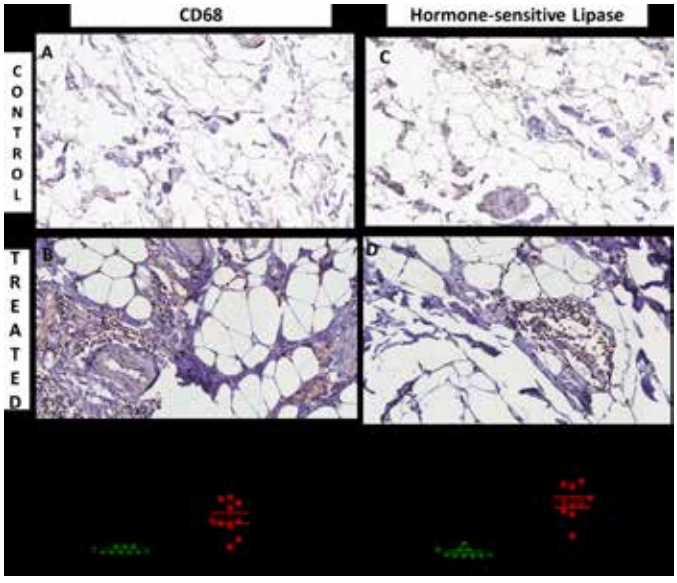

Figure 2: Immunoexpression of CD68 and Hormone-sensitive lipase (HSL). It was possible to observe that the treated group showed a significant increase in macrophage cells positive for CD68 (**A and B,** $p<0.0001$) and HSL (**C and D,** $p<0.0001$). These biological processes confirm a greater degeneration process of adipose tissue (lipolysis) in the treated group.

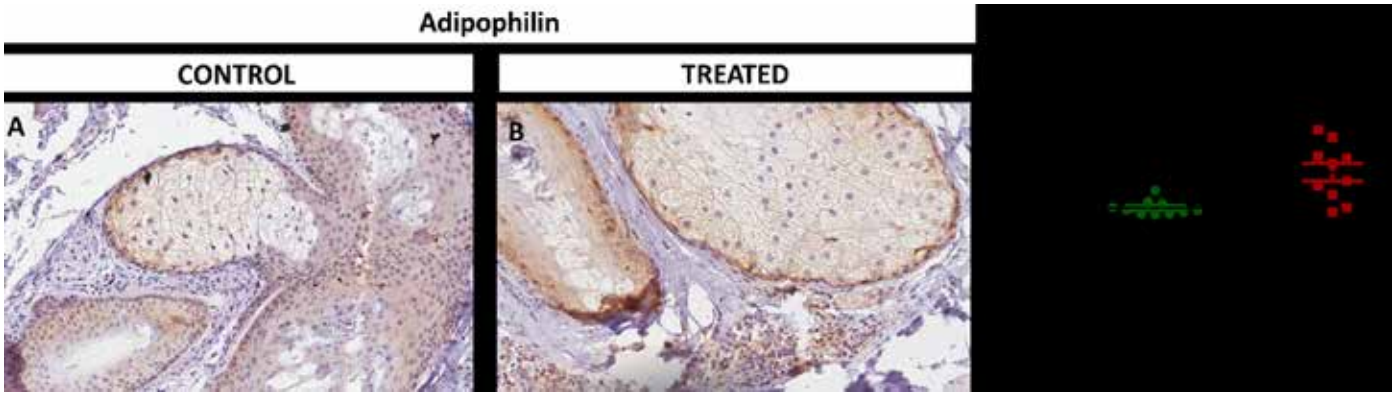

Figure 3: Analysis of adipophilin immunoexpression. It was possible to observe adipophilin positivity in inflammatory cells adjacent to adipose tissue and sebaceous glands. This process indicates that the treated group had higher lipolysis levels and reabsorption of adipose tissue than the control group (value p<0.0013).

The rapid increase in the global prevalence of obesity is a worrying fact and a serious public health problem. The molecular changes in the obese individual result in glucose and lipid metabolism deregulation and other metabolic diseases development, including insulin resistance, hyperglycemia, fatty liver, dyslipidemia, and chronic inflammation. In short, the main consequences of obesity are an increase in the prevalence and severity of Type II Diabetes and chronic heart disease, diseases that generate comorbidities and are involved in the process of premature death of these individuals.[12-16]

Lipolysis is a complex biological process mediated by several molecular pathways. Among them, the apoptotic pathway directly associates with decreased adipose tissue. Apoptosis can be considered crucial for maintaining homeostasis in various tissues, regulating programmed cell death, and avoiding energy imbalance. Several endogenous stimuli can lead to apoptosis, and each cell responds according to the energy and intensity of that stimulus, leading to the activation of proteases called "caspases". Depending on the stimulus intensity, the cell may even suffer necrosis. After apoptosis or necrosis, macrophages phagocyte and digest cell debris, reducing the number of cells. [16-19]

Aware of the endogenous and routine physiological events in our organism and the growing advance of obesity in an alarming way, big electromedical equipment companies started to invest in science and technology to develop equipment that could stimulate fat cell lipolysis and/or apoptosis. They used extracorporeal resources to help in weight loss and reduction of comorbidities associated with the disease. [19-21]

According to Loap and Lathe, 2018, cryotherapy was one of the first resources to be investigated for obesity treatment because adipocytes are more sensitive to cold. When in contact with low temperatures (-5°C), lipids undergo crystallization and consequent inflammatory reaction, generating cell death via apoptosis and even necrosis. It leads to a decrease in subcutaneous tissue for weeks to months without damaging the skin and metabolism. Thus, the first cryolipolysis equipment appeared, allowing adipose tissue cooling by extracting temperature and stimulating the adipocyte death process. [20-21]

Such as cryolipolysis, several other resources, such as focused ultrasound and radiofrequency, have scientific evidence proving their effects on the extracorporeal stimulus of fat cell lipolysis and/or apoptosis without damaging the metabolism. Therefore, ESWT technology has also been adapted for the same therapeutic purpose. [21-23]

ESWT produces high-intensity mechanical energy that leads to the activation of mechanotransduction signal and cellular mobilization. It responds to cavitation's indirect effect, a phenomenon known for forming gaseous microbubbles in a fluid medium. There are two types of cavitation: stable, where these microbubbles are formed and do not undergo implosion; and unstable, where microbubbles implosion occurs. Each cavitation type has an intensity of physiological action. The stable cavitation can stimulate the lipolysis process, while the unstable cavitation can cause cell death. The present study showed that its physiological stimulus could occur through the biological process of apoptotic lipolysis. [7, 24-26]

We demonstrated that ESWT-treated tissue showed a significant increase in Caspase-3 and Cleaved Caspase-3 positive fat cells. Both extrinsic (mediated by cellular receptors) and intrinsic pathways (mitochondrial) activate Caspase-3 in the apoptotic cell.[24] Thus, the expression of caspase-3 in adipose tissue indicates that ESWT can activate apoptotic pathways and, consequently, stimulate the lipolysis process. These results agree with previously published studies. [27-30]

The present study also showed that, in tissues treated with ESWT, there was an increase in CD68+ macrophages, mainly in adipose tissue adjacent areas. Macrophages play a central role in the lipolysis process. Their presence indicates inflammation during autophagic lipolysis, that is, during the mechanism of cell self-destruction via apoptosis, a well-recognized and scientifically established process. [31- 33]

This evidence shows that ESWT can stimulate fat cell death and consequent lipolysis. Such ability correlates with the energy dose used during the procedure. Our study used a dose

of 180 mJ with a stainless steel tip of 15 mm, generating a high concentration of mechanical energy in the treatment area and promoting unstable cavitation. Thus, the damage is more significant, leading to cell morphological changes, cell membrane rupture, and consequent fat cell apoptosis and lipolysis.[34,35]

It is important to note that other biological processes are also associated with autophagic lipolysis, such as necrosis and autophagy due to other mechanisms. Thus, it is essential to study different processes to clarify the exact action of EWST during apoptosis and lipolysis. [31-33]

Another interesting finding that confirms the presence of autophagic lipolysis is the presence of positive cells for HSL and adipophilin in adjacent adipose tissue areas. HSL is an enzyme present in adipocyte metabolism, which breaks down triacylglycerides (TAG) when activated. This positive marker in adipose tissue indicates when there is a lipolysis process. Thus, we can say that ESWT stimulates lipolysis of the fat cell in the apoptotic pathway. [36,37]

Adipophilin is one of the main proteins induced in the early stages of adipocyte differentiation. Also, this protein plays a vital role in the metabolism of fatty acids, cholesterol, and neutral lipids storage. Both markers, mainly expressed in inflammatory cells adjacent to the ESWT intervention group's fatty tissue, demonstrate a phagocytosis process of the lipid droplets confirming the process of autophagic lipolysis. [31]

Assuming that ESWT can perform unstable cavitation and before this phenomenon, we have stable cavitation in a liquid medium, we can infer that ESWT stimulates apoptosis through unstable cavitation in a concentrated area. Consequently, the mechanical wave is dissipated to a lesser extent around the area that received the treatment. These regions receive the stable cavitation stimulus that generates the lipolysis process.[7,10]

Our result corroborates with clinical studies, which showed that ESWT could reduce adipose tissue thickness and, consequently, decrease the body circumference of regions that have undergone treatment. The studies reported that an average of 6 to 12 therapy sessions with high energies (150 mJ to 200 mJ) was necessary to validate the results. However, the authors did not demonstrate which were the pathways of physiological stimulation of ESWT. Thus, this is the first study that confirms the real physiological effect of the therapy on the fat cell.

Obesity is a chronic low-level inflammatory condition. Such phenotype is a risk factor in the etiology of cardiovascular diseases, type 2 diabetes mellitus, cancers, and associated metabolic diseases. However, the inflammatory process observed in individuals with obesity differs from the classic inflammatory response in other circumstances, as it is a systemic inflammatory process.[4,6] The present study shows it because it did not present inflammatory infiltrates and positivity of the evaluated markers in the control sample's adipose tissue analysis, as they are not specific markers in obesity disease.

Altogether, data from the present study demonstrate that ESWT treatment favors fat cell death and breakdown. One hypothesis would be that the therapy could also lead to the prevention or reduction of systemic inflammation caused by obesity since it leads to a decreased number of fat cells. Consequently, we would have less risk in the development of comorbidities such as insulin resistance. Because of the clinical evidence about ESWT, researchers report that this is a safe therapy, as supported in the present study, once we reported minimal adverse events and that resolved right after the first treatment sessions.

Given the evidence present in this study, ESWT can be safely used to reduce adipose tissue in individuals with obesity. It can stimulate cell metabolism, generating apoptosis in the area of energy concentration and fat cells autophagic lipolysis. This finding in the immunohistochemical analysis proves the results of clinical studies of adipose tissue reduction. Thus, this therapy aims at assisting the conservative and even preventive obesity treatment.

CONCLUSION

It is possible to conclude from our results that ESWT causes adipose tissue apoptosis with consequent autophagic lipolysis in obese individuals. Thus, ESWST can be considered a useful, safe, and promising adjuvant therapy for reducing adipose tissue and, consequently, preventing and/or treating obesity. ●

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AUTHORS ' CONTRIBUTION:

Débora Aparecida Oliveira Modena | ORCID 0000-0002-2800-3620
Statistical analysis; approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Renata Michelini Guidi | ORCID 0000-0002-2800-3620
Critical literature review; critical revision of the manuscript.

Ciro Dantas Soares | ORCID 0000-0002-6861-6640
Statistical analysis; data collection, analysis, and interpretation; critical literature review.

Everton Cazzo | ORCID 0000-0002-5804-1580
Statistical analysis; approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Elinton Adami Chaim | ORCID 0000-0003-4627-0631
Statistical analysis; approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Topical use of a blend of bleaches associated with moisturizers in immediate post-peeling care for melasma treatment

Uso tópico de clareadores associados a hidratantes nos cuidados imediatos após peelings para tratamento de melasma: um estudo-piloto

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ABSTRACT

Introduction: Melasma is a recurrent and challenging dermatosis despite several clinical and interventional therapeutic approaches.

Objective: This study aims to assess the safety and efficacy of using a bleaching cream in the period immediately after serial surface peels.

Methods: Five women with melasma used a cream containing bleaches, moisturizers, and tranquilizers during the treatment period with serial surface peels. We assessed them in D0, D7, D30, D37, D60, D67, and D90 through photographs, record of the physician's and patient's opinion, description of adverse events, need to interrupt using the product, and the MELASQol questionnaire.

Results: We observed improved hydration, skin quality, and bleaching, with little discomfort and a significant reduction in MELASQol scores, with statistical evidence.

Conclusions: The use of a topic cream with bleaching and tranquilizing properties is an effective and safe alternative to avoid interruption of melasma treatment during the period of serial surface peels.

Keywords: Chemexfoliation; Hyperpigmentation; Pigmentation disorders

RESUMO

Introdução: *melasma é uma dermatose de difícil controle e de características recidivantes, com diversas abordagens terapêuticas clínicas e intervencionistas.*

Objetivo: *avaliar a segurança e a eficácia de um creme clareador no período imediatamente após peelings superficiais seriados.*

Métodos: *cinco mulheres portadoras de melasma utilizaram creme contendo clareadores, hidratantes e calmantes durante o período de tratamento com peelings superficiais seriados. Foram avaliadas em D0, D7, D30, D37, D60, D67 e D90 por meio de: fotografias, registro da opinião do médico e paciente, descrição de eventos adversos, necessidade de interrupção do uso do produto assim como preenchimento do MELASQol.*

Resultados: *houve melhora na hidratação, qualidade da pele e no clareamento, com pouco desconforto e redução significativa dos escores do MELASQol, com comprovação estatística.*

Conclusões: *a utilização de tópico com propriedades clareadoras e calmantes é uma alternativa efetiva e segura para evitar a interrupção do tratamento de melasma durante o período da realização de peelings superficiais seriados.*

Palavras-chave: *Abrasão química; Clareadores; Pigmentação; Hiperpigmentação*

Original Article

Authors:

Elisete Isabel Crocco[1,2]
Ana Paula Kayo[2]
Renata Alves[2]
Bomi Hong[2]

[1] Department of Medicine, Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo (SP), Brazil.
[2] Dermatologia Dra. Elisete Crocco Dermatology Clinic, São Paulo (SP), Brazil.

Correspondence:
Elisete Crocco
Av. Lavandisca, 777 - 10o andar
Moema
04515-011 São Paulo (SP)
E-mail: elisete@elisetecrocco.com.br

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Study conducted at the Elisete Crocco Dermatology Clinic, São Paulo (SP), Brazil.

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Libbs Pharmaceuticals sponsored this study; however, the researchers conducted all the methodology, execution, and analysis of the results obtained with no interference from the pharmaceutical industry.

INTRODUCTION

Melasma is a chronic dermatosis that is difficult to control and affects many of the adult population. The disorder has a significant impact on the quality of life, causing social and psychological stress. Despite much research involving its etiology, pathogenesis, and treatment options, this disease remains a therapeutic challenge for dermatologists. A definitive treatment modality is still a distant reality.[1]

Serial superficial chemical peels are useful methods in clinical practice due to their low cost and ease of application.[2] However, repeated sessions cause erythema and post-inflammatory hyperpigmentation, especially in patients with higher skin phototypes.[1] In this scenario, one of the difficulties of melasma therapy is maintaining the topical use of skin bleaching products during the period of repeated sessions of this procedure. Usually, the patient keeps only the use of moisturizers and calming agents.

The proposal to use a topical bleaching product with soothing properties emerged as an alternative to avoid interruption of melasma treatment, even during the period of peels.

In this study, we report the use of a bleaching, moisturizing, and soothing cream immediately after the application of serial chemical superficial peels in patients with melasma.

METHODS

This pilot, single-center, prospective, clinical study was structured according to the Declaration of Helsinki's ethical rules. All patients signed the informed consent form.

We selected five women with mixed melasma on the face, with no history of procedures for this dermatosis in the last six months.

All patients underwent a monthly series (D0, D30, D60) of three superficial peels with Jessner's solution applied to the whole face, followed by retinoic acid 5%, after skin cleansing with water and neutral soap and degreasing with Hoffmann's liquor. The patients were instructed to wash their face only after six hours, using a light soap with moisturizing properties (Figure 1).

The volunteers were instructed to use the product under study (Lumixyl® - Libbs Pharmaceutical, São Paulo, Brazil)

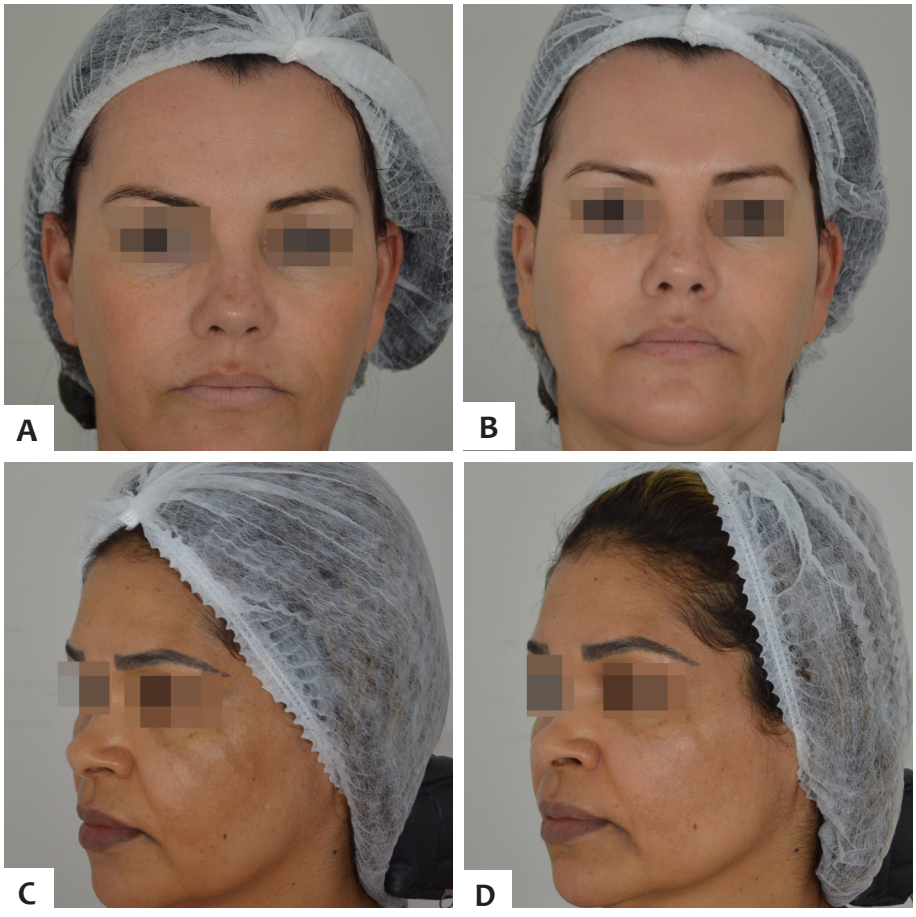

FIGURE 1:
A and **C** - Previous pictures
B and **D** - Pictures 90 days after superficial chemical peels and topical bleaching

twice daily, stopping its use on the day of applying the peeling and restarting it the following day. The study product is a blend of the bleaching products decapeptide-12, phenylethyl resorcinol, and Phyllanthus emblica combined with calming agents (allantoin, aloe vera, panthenol, licorice), and moisturizers (hyaluronic acid, glycerin, sodium PCA).

The patients were assessed on seven dates: D0, D7, D30, D37, D60, D67, and D90, using photographs, records of the physician's opinion on the skin characteristics, adverse events description, need for interrupting the use of the product or association with topical corticosteroids, as well as the volunteer's opinion regarding skin quality and MELASQol answering.

The MELASQoL (Melasma Quality of Life Scale) is an instrument used to assess the quality of life of people with melasma, covering three areas: social life, recreation/leisure, and emotional well-being, generally those most affected by dermatosis.[3] The use of the questionnaire in countries where English is not the official language requires a correct translation and cultural adaptation. In Brazil, it was translated into Portuguese in 2006 (MELASQoL-BP), following the standards of the World Health Organization (WHO).[4,5,6]

Regarding statistical studies, categorical data were summarized using the absolute (n) and relative (%) frequency of the number of patients concerning the total evaluated at each study visit.

For the assessment of MELASQoL, the data were summarized using the mean and standard deviation at each study visit. A mixed model of analysis of variance with repeated measures and Tukey's multiple comparisons were used to verify the variation of the score at evaluation time. Statistical significance was considered for p values <0.05.

RESULTS

The five patients had a mean age of 48.4 years ± 10.06 years and skin phototypes I to V. They performed all scheduled visits, responded spontaneously to questionnaires, and took the required photographs.

There were no reports of serious adverse events. One patient temporarily stopped using the product at D4 and resumed use after guidance from the medical team at D8. The interruption occurred due to edema and erythema after the peeling, an unusual condition for the volunteer, who decided to stop the application for three days.

The volunteers did not need to use topical corticosteroids or moisturizers, although the medical team advised it if there was a lot of discomfort after the peeling. No patient stopped using soap and sunscreen.

The total MELASQol score was assessed using a mixed model with repeated measures demonstrating a significant reduction in MELASQoL when comparing all visits (p=0.001) (Table 1). When evaluating graphs 1 and 2, a very similar pattern is observed between visits D0 and D30, and between D60 and D90.

The assessments conducted one week after applying the peeling followed by continuous use of the product under study showed that after the first application (D7), there was discomfort from the patients and perception of little hydration by the medical team. However, the two other post-procedure visits (D37 and D67) showed that the volunteers had a better hydration profile, skin quality, skin whitening, and little discomfort (Tables 2 and 3).

DISCUSSION

The product used in this study consists of substances with bleaching action: decapeptide 12, symwhite® (phenylethyl resorcinol), licorice, Phyllanthus emblica; in addition to substances with a calming effect: allantoin, aloe vera, panthenol, licorice; along with moisturizers substances: meadowfoam seed oil, sodium hyaluronate, glycerin, Sodium PCA (Table 4).

Currently, melasma dyschromia is considered a multifactorial dermatosis, a disease of photoaging.[7] The difficulty in improving the pigmentation in keratinocytes and the decrease in melanin production justifies the approach of multiple substances and treatment strategies.

This technique aimed to early introduce bleaching actives after the epidermal loss and renewal procedure that occurs in serial superficial peels combining Jessner's solution and retinoic acid, availing from the loss of the skin barrier and creating a "drug-delivery-like" situation. The presence of calming agents amid bleaching actives allowed the protocol's conduction without sensitization or serious adverse events in these reported cases.

The volunteers used a product that allowed bleaching and improved skin quality, assessed through MELASQol.

Table 1: Demonstration of the reduction in the total MELASQuol score in 5 volunteers with melasma over 90 days

Total score	D0 (n=5)	D7 (n=5)	D30 (n=5)	D37 (n=5)	D60 (n=5)	D67 (n=5)	D90 (n=5)
Mean ± SD	35.2 ± 10.2	28.8 ± 12.4	26.6 ± 14.2	21.6 ± 16.2	12.0 ± 2.5	15.8 ± 7.2	13.0 ± 5.1
Median	37	28	24	16	11	12	11
Minimum - maximum	19 - 45	10 – 41	11 – 49	10 – 49	10 - 16	10 - 25	10 - 22
(95% CI for the mean)	(22.6; 47.8)	(13.4; 44.2)	(9.0; 44,2)	(1.5; 41.7)	(8.8; 15.2)	(6.9; 24.7)	(6.7; 19.3)

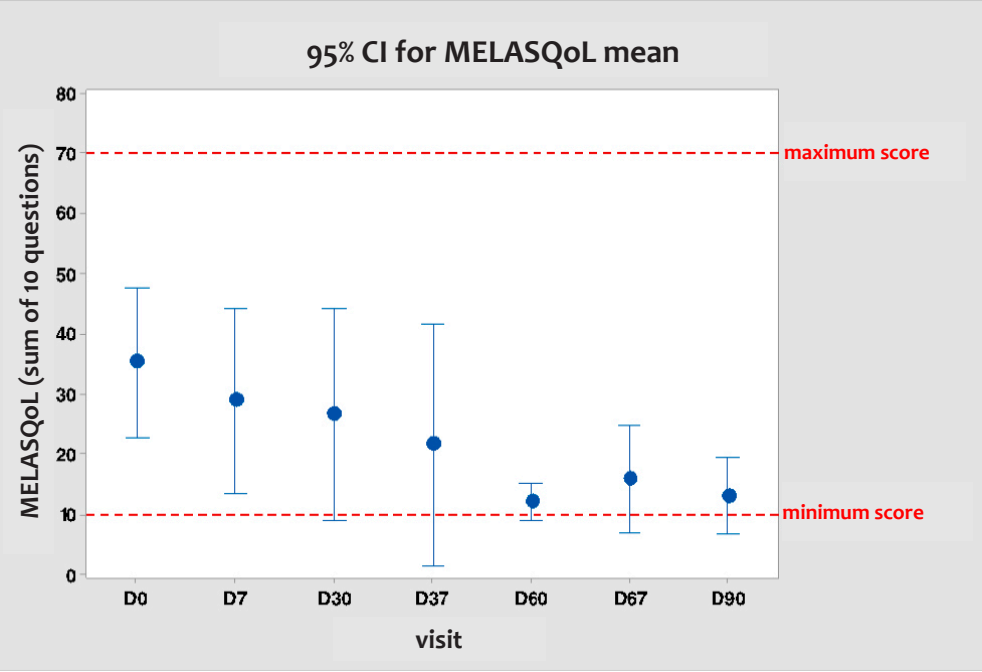

CHART 1: 95% CI for the MELASQoL mean (sum of 10 questions) per visit

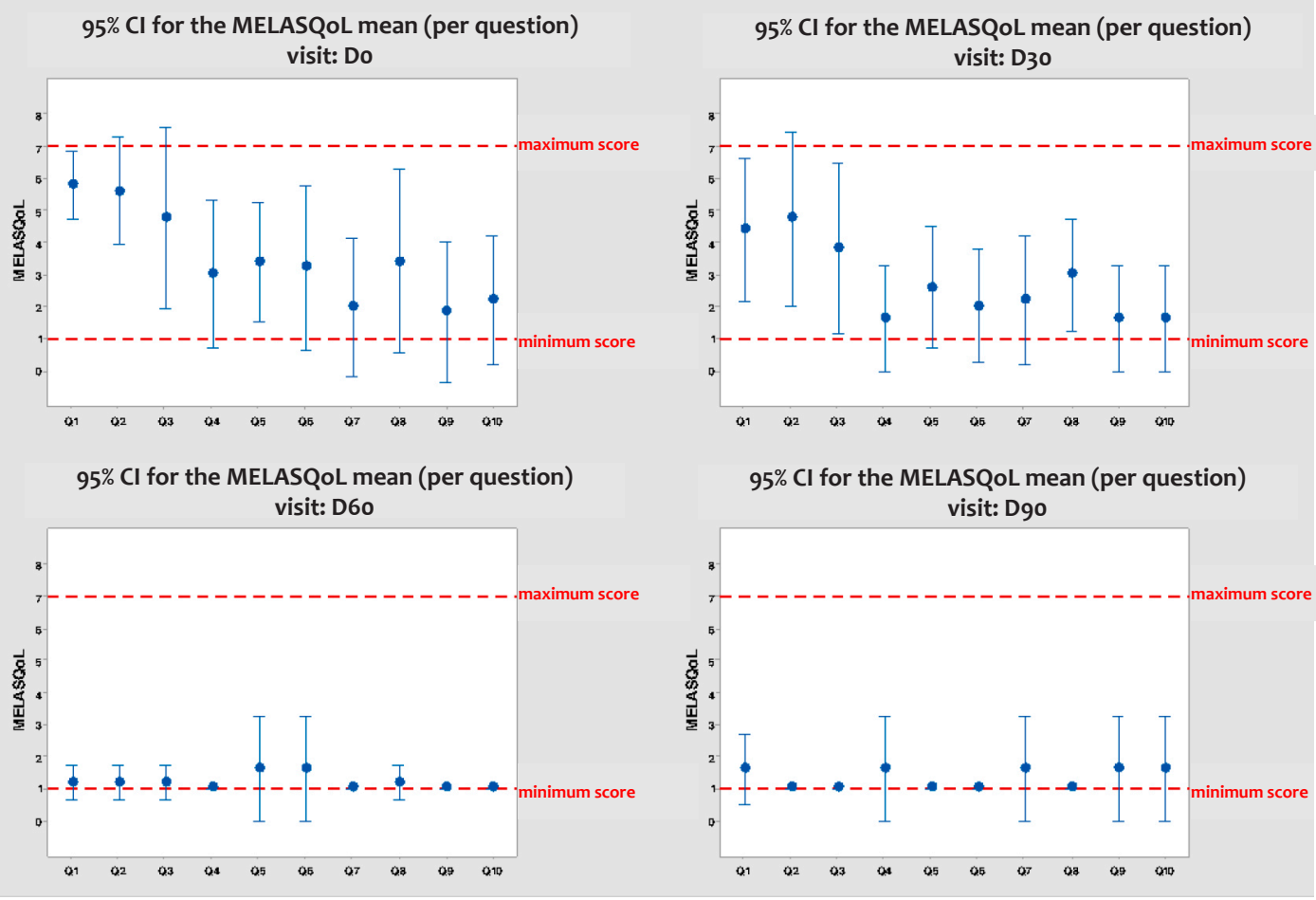

CHART 2: 95% CI for the MELASQoL mean (per question), for visits made with an interval of 30 days: comparison between D0, D30, D60, and D90

Table 2: Skin assessment by the patient

	D0 (n=5)	D7 (n=5)	D30 (n=5)	D37 (n=5)	D60 (n=5)	D67 (n=5)	D90 (n=5)
Sensitivity, n (%)							
More sensitive than usual	0 (0%)	3 (60%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Less sensitive than usual	0 (0%)	0 (0%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)
Not sensitive	5 (100%)	2 (40%)	5 (100%)	4 (80%)	5 (100%)	5 (100%)	5 (100%)
Itching, n (%)							
Not itchy	5 (100%)	2 (40%)	5 (100%)	4 (80%)	5 (100%)	0 (0%)	5 (100%)
Feels itchy but it doesn't bother	0 (0%)	3 (60%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)
Feels itchy and it bothers	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	5 (100%)	0 (0%)
Feels itchy and it bothers a lot	0 (0%)	(0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Scratchy sensation, n (%)							
Not scratchy	5 (100%)	2 (40%)	5 (100%)	4 (80%)	5 (100%)	5 (100%)	5 (100%)
Feels scratchy but it doesn't bother	0 (0%)	2 (40%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)
Feels scratchy and it bothers	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Feels scratchy and it bothers a lot	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 3: Skin assessment by the physician

	D0 (n=5)	D7 (n=5)	D30 (n=5)	D37 (n=5)	D60 (n=5)	D67 (n=5)	D90 (n=5)
Hydration, n (%)							
Very hydrated	0 (0%)	0 (0%)	1 (20%)	2 (40%)	0 (0%)	1 (20%)	3 (60%)
Hydrated	2 (40%)	1 (20%)	4 (80%)	2 (40%)	5 (100%)	4 (80%)	2 (40%)
Little hydrated	2 (40%)	2 (40%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)
Not hydrated	1 (20%)	2 (40%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Softness, n (%)							
Very soft	0 (0%)	1 (20%)	1 (20%)	2 (40%)	0 (0%)	1 (20%)	3 (60%)
Soft	2 (40%)	0 (0%)	4 (80%)	2 (40%)	5 (100%)	4 (80%)	2 (40%)
Little soft	3 (60%)	3 (60%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)
Not soft	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Scaling, n (%)							
Absent	5 (100%)	1 (20%)	5 (100%)	4 (80%)	5 (100%)	5 (100%)	5 (100%)
Mild	0 (0%)	1 (20%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)
Moderate	0 (0%)	2 (40%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Erythema, n (%)							
Absent	4 (80%)	1 (20%)	5 (100%)	5 (100%)	4 (80%)	4 (80%)	5 (100%)
Mild	1 (20%)	3 (60%)	0 (0%)	0 (0%)	1 (20%)	1 (20%)	0 (0%)
Moderate	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dryness, n (%)							
Absent	3 (60%)	1 (20%)	5 (100%)	4 (80%)	5 (100%)	3 (60%)	5 (100%)
Mild	2 (40%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (40%)	0 (0%)
Moderate	0 (0%)	3 (60%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Table 4: Components of the evaluated product and their actions

	SUBSTANCE	ACTION
BLEACHING PRODUCTS	Decapeptide 12	Oligopeptide with potent tyrosinase inhibiting action
	Symwhite® (phenylethyl resorcinol)	Bleaching and antioxidant active, tyrosinase inhibitor.
	Licorice	Active with soothing action and because it contains flavonoids with glycosides, it has a lightening effect.
	Phyllanthus emblica	Active with antioxidant and lightening action, tyrosinase inhibitor and tyrosinase receptor.
CALMING AGENTS	Allantoin	Active soothing and repairing of the skin barrier.
	Aloe vera	Plant-based active with calming properties.
	Panthenol	Active with soothing properties, improves skin elasticity and helps regenerate damaged skin.
	Licorice	Plant-based active with calming properties.
HIDRATANTES	*Meadowfoam Seed Oil*	Active rich in fatty acids with potent emollient action.
	Sodium hyaluronate	Hydrating action, acts on water retention in the epidermis.
	Glycerin	Plant-based active with potent moisturizing action.
	Ajidew (Sodium PCA)	Active with moisturizing action.

CONCLUSION

Melasma remains a difficult-to-control dermatosis, in which some interventions often worsen the condition with hyperpigmentation. We demonstrated the possibility of using a bleaching active to enhance the action of serial superficial peels with Jessner's solution and retinoic acid safely in patients with melasma. ●

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AUTHORS ' CONTRIBUTION:

Elisete Isabel Crocco | ORCID 0000-0002-8844-2887
Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Ana Paula Kayo | ORCID 0000-0001-6357-4835
Data collection, analysis, and interpretation.

Renata Alves | ORCID 0000-0001-6441-4091
Data collection, analysis, and interpretation.

Bomi Hong | ORCID 0000-0003-1656-601X
Data collection, analysis, and interpretation.

Diagnostic Imaging

Authors:
Emerson Henrique Padoveze[1]
Nilton Gioia Di Chiacchio[2]
Thais Cardoso Pinto[2]
Aarão Andrade Napoleão Lima[2]
Gabriel Lucchesi de Santana[3]

[1] São Leopoldo Mandic School of Medicine, Campinas (SP), Brazil.
[2] Hospital do Servidor Público Municipal de São Paulo, São Paulo (SP), Brazil.
[3] Hospital do Servidor Público Municipal de São Paulo, São Paulo (SP), Brazil.

Correspondence:
Thais Cardoso Pinto
R. Castro Alves, 60
01532-000 São Paulo (SP)
E-mail: tha.lucelia@gmail.com

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Study conducted at the Hospital do Servidor Público Municipal de São Paulo, São Paulo (SP), Brazil.

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Basal cell carcinoma originating in a tattoo: report of two cases

Carcinoma basocelular originado de uma tatuagem: relato de dois casos

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ABSTRACT

Basal cell carcinoma over the tattoo region has been poorly reported in the literature, with a total of 13 cases. All cases describe the clinical aspect of the lesion and its pathogenesis but do not characterize the dermoscopy. We report two cases of basal cell carcinoma on tattoos with clinical and dermoscopy features, treated with Mohs micrographic surgery. It was challenging to establish the tumor's clinical and dermoscopic margins due to the tattoo's exogenous pigment.

Keywords: Carcinoma, Basal cell; Dermoscopy; Tattooing; Mohs surgery

RESUMO

Carcinoma basocelular sobre a região da tatuagem foi pouco descrito na literatura, com um total de 13 casos. Todos descrevem o aspecto clínico da lesão e sua patogênese, porém não caracterizam a dermatoscopia. Descrevemos dois casos de carcinoma basocelular na tatuagem, com características clínicas e dermatoscópicas, tratados com a cirurgia micrográfica de Mohs. Houve dificuldade em estabelecer as margens clínicas e dermatoscópicas do tumor em decorrência do pigmento exógeno da tatuagem.

Palavras-chave: *Carcinoma basocelular; Dermoscopia; Tatuagem; Cirurgia de Mohs*

INTRODUCTION

The art of tattooing is an ancient practice that is becoming increasingly popular, both for cosmetic and therapeutic purposes. Although well-tolerated, it is not without risks.[1] Several benign and malignant complications can result from the tattooing process, according to the literature.[1,2,3,4,5,6] There are reports of neoplastic evolution in the form of cutaneous lymphoma, keratoacanthoma, squamous cell carcinoma (SCC), melanoma, and basal cell carcinoma (BCC).[1,2,3]

Basal cell carcinoma (BCC) has already been described in scars (burns and post-vaccination). However, the appearance on a tattoo is uncommon, and the pathogenesis is unclear. The literature has only reported 13 cases, most in photoexposed areas and containing black pigment.[3] There is a possibility that the pigment has a direct carcinogenic effect or that the lesion is associated with trauma and sun exposure.[1,3,5,6]

Dermoscopy is an additional high sensitivity and specificity tool for BCC diagnosis. The most commonly described findings are arboriform telangiectasias, bright white areas, and bluish-gray ovoid nests.[7] The reported cases do not describe the dermoscopic findings of the tumor on the tattoo. We report two cases with clinical and dermoscopic characteristics.

CASE 1

A 32-year-old woman, Caucasian, presenting a single infiltrated erythematous nodule measuring 1.4 x 2.0 cm in the right lower back region for nine years (Figure 1). The lesion was on a tattoo done 12 years ago. Dermoscopy revealed blue-gray globules, ulceration, maple leaf structures, and bright white areas (Figure 2). Histology showed dermis' infiltration by atypical basaloid cells, forming small blocks with peripheral palisade, characteristic of BCC.

CASE 2

A 50-year-old woman, brown, presenting an erythematous-infiltrated plaque on the upper back measuring 1.0 x 0.8 cm, for one year, on a tattoo performed six years ago (Figure 3). Dermoscopy revealed arboriform telangiectasias, blue-gray globules, and bright white areas (Figure 4). The anatomopathological examination showed infiltration of atypical basaloid cells, forming small blocks, invading the dermis with a palisade peripheral disposition, compatible with BCC diagnosis.

Figure 1: Nodular basal cell carcinoma presents as an erythematous plaque over the tattoo on the right lower back region of a 32-year-old woman. Note the areas where the tattoo ink does not allow a good view of the tumor margins

Figure 3: Nodular basal cell carcinoma presents as an erythematous plaque over the tattoo on the upper back of a 50-year-old woman. Note the areas where the tattoo pigment does not allow a good view of the tumor margins

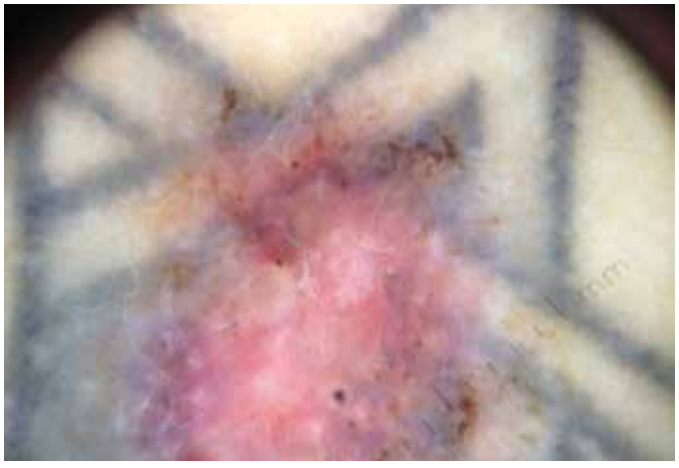

Figure 2: Dermoscopy shows gray-blue globules, maple leaf structures, and bright white areas. Note the ill-defined margins

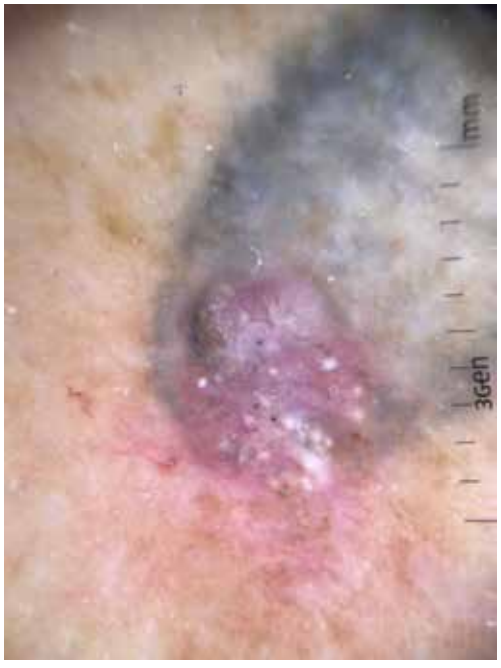

Figure 4: Dermoscopy shows arboriform telangiectasias, blue-gray globules, and bright white areas. Note the areas with ill-defined margins

Both patients underwent Mohs micrographic surgery and are undergoing clinical follow-up for four and three years, respectively, with no lesion recurrence.

DISCUSSION

The art of tattooing has been practiced for millennia for aesthetic and therapeutic purposes. The literature reported numerous medical complications related to tattoos, including lichenoid dermatitis, pseudolymphoma, tetanus, cancer, syphilis, molluscum contagiosum, warts, HIV, hepatitis, granulomas, mycoses, and hypersensitivity reactions. It has also described malignant lesions after tattooing, although rare, such as dermatofibrosarcoma protuberans, keratoacanthoma, leiomyosarcoma, melanoma, and squamous cell carcinoma (SCC).[1,2,3]

Bashir described the first BCC report on the tattoo region in 1976, reporting two cases.[4] Since then, the literature has depicted only 11 more patients. None of them described the dermoscopic characteristics.

The pathogenesis is still uncertain. The trauma hypothesis is considered a possible factor related to its carcinogenesis. It generates greater sensitivity to sun exposure due to the low vascularization and elasticity of the injured tissue. Such changes, consequently, could result in localized nutritional deficiency, chronic irritation, and prolonged release of toxins, leading to cell mutation.[1,5,6]

The dermoscopic features most commonly seen in BCC are the arboriform vessels (59%), bright white structures (49%), and large blue-gray ovoid nests (34%).[7] In our cases, we observed bright white areas, blue-gray globules, and arboriform vessels in only one of them.

It is essential to establish safe tumor margins, both clinically and with the aid of dermoscopy, for its complete removal. In our cases, it was difficult to accurately establish tumor margins due to pigment, both clinically and with Dermoscopy. It resulted in performing the Mohs surgery in a larger number of phases.

Although our cases are the first described with dermoscopic characteristics, we can conclude that dermoscopy did not contribute to a good delimitation of the tumor margins. ●

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AUTHORS ' CONTRIBUTION:

Emerson Henrique Padoveze | ORCID 0000-0003-1106-0992
Approval of the final version of the manuscript; preparation and writing of the manuscript; critical literature review; critical revision of the manuscript.

Nilton Gioia Di Chiacchio | ORCID 0000-0001-5944-7737
Approval of the final version of the manuscript; preparation and writing of the manuscript; critical literature review; critical revision of the manuscript.

Thais Cardoso Pinto | ORCID 0000-0001-9907-6141
Preparation and writing of the manuscript; critical literature review; critical revision of the manuscript.

Aarão Andrade Napoleão Lima | ORCID 0000-0003-0648-6884
Preparation and writing of the manuscript; critical literature review; critical revision of the manuscript.

Gabriel Lucchesi de Santana | ORCID 0000-0001-6406-2831
Preparation and writing of the manuscript; critical literature review.

Surgical options in vitiligo: skin graft and epidermal suspension diluted in hyaluronic acid gel

Opções cirúrgicas no vitiligo: enxerto de raspado cutâneo e suspensão epidérmica diluídos em ácido hialurônico gel

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ABSTRACT

Introduction: Vitiligo is an acquired skin dyschromia characterized by the physical and/or functional reduction of melanocytes. We present two surgical proposals for the treatment of vitiligo.

Case reports: 1) Implant of skin graft diluted in hyaluronic acid gel: We obtained the material through curettage, diluted it in hyaluronic acid gel, and applied it to receptor areas. 2) Epidermal suspension obtained through curettage and diluted in hyaluronic acid gel: After the curettage of the donor area, we treated the material with trypsin-EDTA, centrifuged it, and diluted it in hyaluronic acid gel. The receptor area received the graft.

Conclusion: These are safe, easy, and satisfactory surgical procedures for the presented cases.

Keywords: Vitiligo; Keratinocytes; Ambulatory surgical procedures

RESUMO

Introdução: *vitiligo é dermatose caracterizada por redução física e/ou funcional dos melanócitos. Apresentamos duas propostas cirúrgicas para tratamento do vitiligo.*

Relato de caso: *1) Implante de enxerto cutâneo diluído em gel de ácido hialurônico: material obtido a partir de curetagem da área doadora, diluído em ácido hialurônico gel e aplicado na área receptora. 2) Suspensão não cultivada obtida por curetagem e diluída em gel de ácido hialurônico: material obtido por curetagem da área doadora é tratado com tripsina, centrifugado, diluído em ácido hialurônico gel e aplicado na área receptora.*

Conclusão: *Trata-se de técnicas seguras, de fácil execução e com resultado satisfatório nos casos apresentados.*

Palavras-chave: *Vitiligo; Procedimentos cirúrgicos menores; Queratinócitos*

INTRODUCTION

Vitiligo is an acquired, idiopathic cutaneous dyschromia characterized by physical and functional reduction of melanocytes. The global prevalence is around 0.5% to 1%. Clinically, it presents achromic macules and patches of different sizes and forms.[1] Stable vitiligo cases resistant to clinical treatment are candidates for surgical treatment, including non-cultured epidermal suspension grafts treated enzymatically with trypsin 0.25%; thin dermo-epidermal skin grafts; suction blister epidermal grafts (SBEG); total punch grafting; epidermal grafting or in vitro isolation; and culture of melanocytes.[2,3]

How I do?

Authors:

Juliano Cesar de Barros[1]
Isabella Parente Almeida[1]
Jefferson Alfredo de Barros[1]
Andrés Maurício Lopez Munoz[1]
Carlos D'Apparecida Santos Machado Filho[1]

[1] Department of Dermatology, Faculdade de Medicina do ABC, São Paulo (SP), Brazil.

Correspondence:
Isabella Parente Almeida
Departamento de Dermatologia
Av. Príncipe de Gales, 821
09060-870 Santo André (SP)
E-mail: isabellaparente@hotmail.com

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Approved on: 06/12/2020

Study conducted at the Faculdade de Medicina do ABC, São Paulo (SP), Brazil.

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Additionally, Machado (2000)[3] demonstrated the feasibility of obtaining material for grafting through simple epidermal curettage of the donor area to be implanted in a recipient area, also curetted. The obtained graft is humidified with physiological saline to obtain a "paste"; it is applied to the recipient area and fixed with an adhesive semi-permeable membrane.

The present article describes two surgical techniques for treating vitiligo, considering variations of the curettage technique used for obtaining the graft from the donor area.

Implant of epidermal curettage graft diluted in hyaluronic acid gel

The technique's characteristic is the dilution of the obtained graft in a gel of hyaluronic acid. This biocompatible and hygroscopic substance provides greater viability and adhesion to the receptor area.[4] The curettage of the donor area to the papillary dermis obtains the material (Figure 1A). It is then diluted in 1-2 ml of hyaluronic acid gel at 0.5-2% (Figure 1B) (Figure 1B). The recipient area is also curetted reaching the papillary dermis and obtaining the same size as the donor area. Finally, the graft is applied over the recipient area (Figure 1C) and covered with a dressing of porous membrane of cellulose, maintained in site for seven days. Topical medications and phototherapy are reintroduced 14 days after the procedure. Satisfactory results are observed after 90 days (Figure 1D and 1E).

Non-cultured melanocyte-keratinocyte cells suspension obtained by curettage and diluted in hyaluronic acid gel

It corresponds to the association of the techniques curettage grafting and uncultured epidermal suspension methods. Mulekar (2003 and 2005)[5,6] and van Geel (2001)[2] initially described the use of hyaluronic acid in epidermal suspensions. After curettage of the donor area until the onset of the papillary

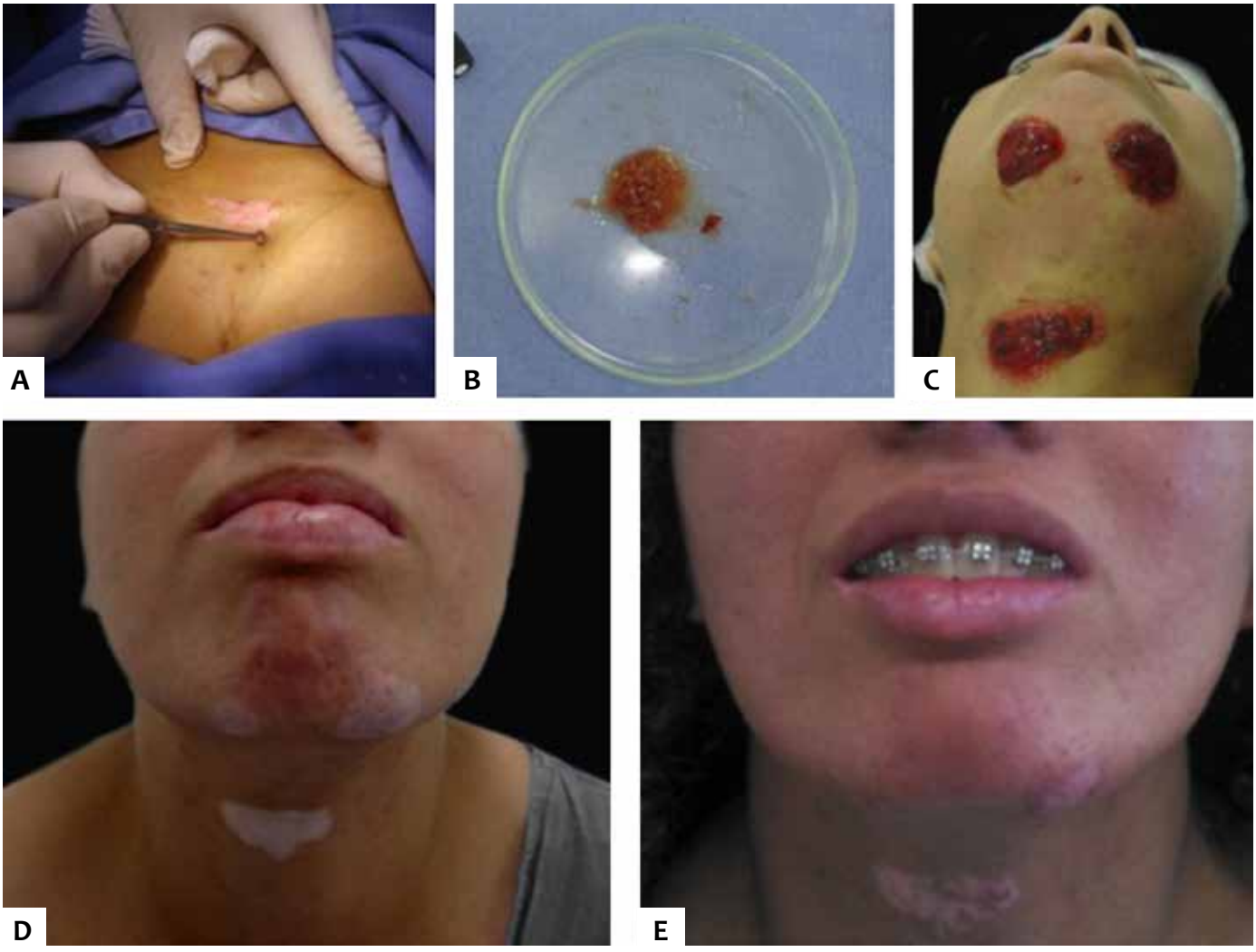

Figure 1: Implant of curreted skin graft diluted in hyaluronic acid gel. **A -** Curettage of the donor area. **B -** Graft diluted in hyaluronic acid gel. **C -** Post-grafting recipient area. **D -** Preoperative. E) Postoperative (90 days)

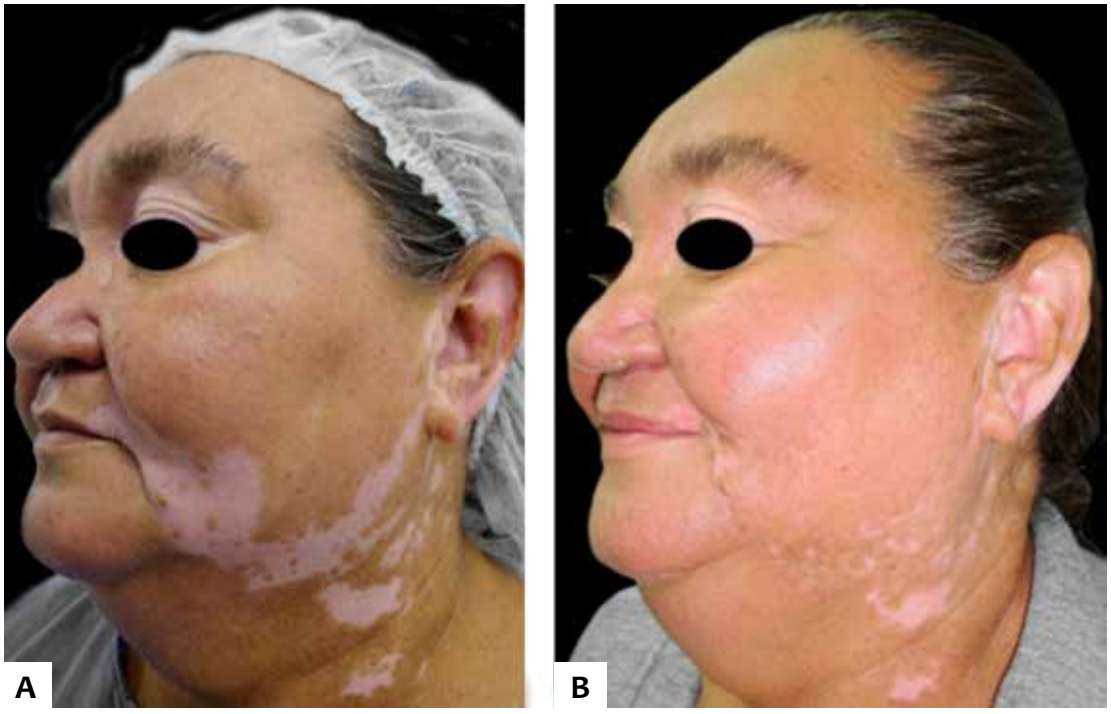

Figure 2: Uncultivated suspension obtained from curettage with subsequent dilution in hyaluronic acid gel.
A - Preoperative.
B - Postoperative (180 days)

dermis's punctate bleeding, the collected graft is exposed to a proteolytic solution (Trypsin EDTA 0.025% - LGC Biotechnology™ - Brazil) and incubated for 20 minutes at 98.6º Fahrenheit. After incubation, a pipette aspirates the trypsin. The sample is then washed with 0,9% saline solution and transferred to a centrifuge tube containing the DMEM culture medium (LGC Biotechnology™ - Brazil). After six minutes of centrifuging at 1500 rpm, the supernatant of epidermal cells is discarded, and the pellet is suspended in 1-2 m of hyaluronic acid gel 0.5-2% (Paulista Center for Pharmaceutical Development™ - Brazil). The suspension concentration, which can vary according to the clinical case of vitiligo, generates a donor to receptor area ratio ranging between 1:10 to 1:20. The recipient area is curetted or dermabrased to the papillary dermis. After applying the epidermal graft, it is occluded with a porous cellulose membrane, which should remain on the site for seven days. The topical medications and phototherapy should be reintroduced after 14 days. Satisfactory results are observed after 90 days and improve 180 days after the procedure (Figures 2A and 2B).

CONCLUSION

In conclusion, curetting the skin until the papillary dermis is an affordable procedure, easy to perform, which provides a satisfactory sample for grafting. When this technique is associated with hyaluronic acid, it allows greater viability and adherence of the graft to the recipient area. Nowadays, there are not indexed publications of those described techniques, and future studies are necessary for further elucidation and improvement of these treatment modalities.

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AUTHORS ' CONTRIBUTION:

Juliano Cesar de Barros | ORCID 0000-0003-1494-7118
Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Isabella Parente Almeida | ORCID 0000-0002-6283-4065
Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Jefferson Alfredo de Barros | ORCID 0000-0001-5073-0747
Study design and planning; data collection, analysis, and interpretation; active participation in research orientation.

Andrés Maurício Lopez Munoz | ORCID 0000-0003-2319-2351
Study design and planning; preparation and writing of the manuscript; critical literature review; critical revision of the manuscript.

Carlos D'Apparecida Santos Machado Filho | ORCID 0000-0003-4362-1563
Approval of the final version of the manuscript; study design and planning; active participation in research orientation; critical literature review; critical revision of the manuscript.

Case Report: Persistent Intermittent Delayed Swelling (PIDS) of Hyaluronic Acid filler triggered by COVID-19

Relato de caso: edema tardio intermitente e persistente (ETIP) de implante de ácido hialurônico desencadeado pela Covid-19

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ABSTRACT

Persistent Intermittent Delayed Swelling (PIDS) due to hyaluronic acid implantation is an immune-mediated inflammatory reaction resulting from immunogenic phenomena to the filler itself, and its ability to retain water, thus configuring local edema. Viral or bacterial infections can trigger the condition. As with many infectious diseases, COVID-19 may have several signs and symptoms on the skin that are not yet fully understood, but many associated skin manifestations have already been described. Through this case report, we report the novelty of an ETIP-type reaction triggered by SARS-CoV-2 infection.

Keywords: Hyaluronic acid; Coronavirus; Coronavirus infections; Foreign-body reaction

RESUMO

O edema tardio intermitente e persistente (ETIP) por implante de ácido hialurônico é uma reação inflamatória imunomediada decorrente de fenômenos imunogênicos ao próprio preenchedor bem como de sua capacidade em reter água, conFigurendo assim o edema local. Pode ser desencadeado após infecções virais ou bacterianas. Assim como em muitas doenças infectocontagiosas, a COVID-19 pode vir a apresentar na pele diversos sinais e sintomas que ainda não são completamente compreendidos, porém muitas manifestações cutâneas associadas já foram descritas. Vimos, por meio deste relato de caso, apresentar o ineditismo de uma reação do tipo ETIP, desencadeada pela infecção por Sars-CoV-2.

Palavras-chave: *Coronavírus; Hipersensibilidade; Reação a corpo estranho; Implantes absorvíveis*

INTRODUCTION

Persistent intermittent delayed swelling (PIDS) is characterized by transient, recurrent, and sporadic episodes that may occur after filling with hyaluronic acid (HA). These episodes are marked with the appearance of diffuse, non-depressible edema located along the product implantation area, usually 30 days after the implantation. Therefore it is named delayed, and it only occurs as long as there is HA in the tissue.[1] These reactions were initially attributed to infectious processes along with the implant (biofilm), but today it is believed that only the immunological phenomena can trigger them.[2-3] The literature identified factors such as systemic viral and/or bacterial infections, as well as local infections such as rhinosinusitis and odontogenic, in about 39% of cases, which can trigger the onset of the reaction.[4]

Sars-CoV-2 is a zoonotic virus emerging from the coronaviruses family that caused the pandemic named COVID-19, which started and was identified in November 2019 in Wuhan province, China.[5] The most common clinical signs are fever, sore throat, runny nose, cough, anosmia, dysgeusia, myalgia, leucopenia, and lymphopenia.[6] The incubation period is from two to 14

How I do?

Authors:
Ivana Nascimento Garcia de Santana[1,2]
Renato Roberto Liberato Rostey[2]

[1] Dra. Ivana Garcia Clinic, Cuiabá (MT), Brazil.
[2] Hospital Universitário Júlio Muller, Cuiabá (MT), Brazil

Correspondence:
Ivana Nascimento Garcia de Santana
Av. das Flores, 111
Jardim Cuiabá
78043-178 Cuiabá (MT)
E-mail: draivanagarcia@gmail.com

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days, with a potential for asymptomatic transmission. However, symptoms usually manifest until the fifth day of infection.[7]

CASE REPORT

A 34-year-old woman presented with a history of sudden prostration and the appearance of an elevated, painless, and well-defined area on the upper lip. The lesion appeared in the same site of the hyaluronic acid filling application to define the lip contour performed one year and four months ago. She reported having already presented edema in the same location a few times, usually associated with rhinitis and pharyngitis, but at the moment, she did not have any respiratory complaints. After six days, the patient presented a new episode of intense prostration, this time accompanied by myalgia, headache, and 38.5 °C fever. She waited three more days to collect nasal and pharyngeal swabs for RT-PCR exam for Sars-CoV-2, which detected the presence of viral RNA, confirming the diagnosis of COVID-19. The patient evolved with no return of fever, improved general condition, and spontaneous reduction of the edema in the upper lip 15 days after its onset.

Figure 1: Painless nodule on the upper lip

Figure 2: Appearance before COVID-19 infection

DISCUSSION

Since its identification, COVID-19 has affected people at different levels of complexity, proving to have mainly a respiratory character. The most severe cases are complicated with the severe acute respiratory syndrome (SARS).[8] However, it can also cause serious diseases in other organs in the nervous, cardiovascular, and renal system, in addition to affecting all other organs of the body and favoring the emergence of secondary infections.[9-18]

The literature has already described that the disease affects other organs, and descriptions of skin involvement have also emerged, with the first compilations and case reports already published. Skin rash, acro-ischemia, maculopapular rash, cyanosis, blisters, purpura, petechiae, gangrene, hives, varicella-like vesicles, pictures resembling perniosis, and COVID toes have been observed.[19-26] However, no picture resembling PIDS has yet been described in a patient with the disease. Thus, this is the first case report of this association.

PIDS episodes associated with infections are premature, of short duration, and can resolve spontaneously.[3] The use of intralesional and oral corticosteroids, and, eventually, hyaluronidase was the usual treatment, leading to the resolution of the condition in most cases, which also corroborates the hypothesis of its immune-mediated etiology.[27]

As it is a new disease, with many signs and symptoms still not entirely known, the presentation of a PIDS condition, as the first symptomatology of COVID-19 in a healthy patient who presented paucisymptomatic evolution, becomes of paramount importance. This is important especially for us, dermatologists, so that we can identify possible COVID-19 patients performing the early diagnosis and increase their chances of having more appropriate treatment, thus taking the necessary measures to prevent the disease's community spread.

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We thank all health professionals who have been fighting COVID-19 at this time. And all our families in these moments of absence. ●

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AUTHORS ' CONTRIBUTION:

Ivana Nascimento Garcia de Santana | ORCID 0000-0001-7029-4882

Approval of the final version of the manuscript; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical revision of the manuscript.

Renato Roberto Liberato Rostey | ORCID 0000-0001-8656-4111

Approval of the final version of the manuscript; preparation and writing of the manuscript; critical literature review; critical revision of the manuscript.

Case Reports

Authors:
Gustavo Vieira Gualberto[1]
Cassio Ferreira Guimarães[1]
Luisa Coutinho Teixeira[1]
Marina Rodrigues Costa Lages[1]
Guilherme Henrique Silveira Teixeira[1]

[1] Santa Casa de Misericórdia de Belo Horizonte, Belo Horizonte (MG), Brazil

Correspondence:
Luisa Coutinho Teixeira
R. Aníbal Benévolo, 92 - Apto 601
Santa Efigênia
30260-250 Belo Horizonte (MG)
E-mail: luisacoutinhodermato@gmail.com

Received on: 30/08/2020
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Study conducted at the Santa Casa de Misericórdia de Belo Horizonte, Belo Horizonte (MG), Brazil.

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Blue nevus of the nail apparatus: a case report

Nevo azul no aparato ungueal: relato de um caso

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ABSTRACT

Blue nail dyschromia has several differential diagnoses. Lesion growth, associated nail dystrophy, and nail extension require evaluation for surgical excision. We report the case of a 27-year-old woman presenting a bluish, semicircular stain, occupying about 50% of the lunula. The patient presented no changes in the overlying lamina, small alteration of the distal nail portion, localized onychoschizia-type layers, and no previous trauma or bleeding history. We performed partial avulsion of the plaque and shave biopsy, evidencing an intensely pigmented lesion. Histopathological examination was compatible with blue nevus. In this case, the nevus should be located in the sub-matricial position, thus not interfering with the nail plate color.

Keywords: Nevus, Blue; Nail diseases; Surgical procedures, Minor; Ambulatory surgical procedures; Nevus, pigmented; Skin neoplasms

RESUMO

A discromia azul das unhas possui vários diagnósticos diferenciais. Crescimento da lesão, distrofia ungueal associada e extensão periungueal requerem avaliação para excisão cirúrgica. Mulher, 27 anos, apresentava mancha azulada, semicircular, ocupando cerca de 50% da lúnula, sem alteração da lâmina suprajacente, com pequena alteração da porção distal da unha, com camadas do tipo "onicosquizia localizada", sem história prévia de trauma ou sangramento. Realizada avulsão parcial da placa e biópsia excisional por saucerização da lesão fortemente pigmentada. O exame histopatológico foi compatível com nevo azul. Sugere-se que, neste caso, o nevo se situasse em posição submatricial, não interferindo, portanto, na coloração da lâmina ungueal.

Palavras-chave: *Nevo azul; Nevo pigmentado; Nevos e melanomas; Unhas; Procedimentos cirúrgicos ambulatoriais*

INTRODUCTION

Blue nail dyschromia has a wide variety of differential diagnoses, including mainly malignant and benign vascular and melanocytic lesions. Although most of these lesions are benign and have a good prognosis, the presence of lesion growth, associated nail dystrophy, and periungual extension require evaluation for surgical excision.[1]

Blue nevus of the nail apparatus is a rare entity, with at least 11 cases described in the literature so far. It was first described in 1984 in a 4-year-old child with Klippel-Trenaunay syndrome who had a periungual nodule with satellite lesions on the back of the corresponding hallux and inguinal lymphadenopathy. An examination later showed a blue nevus composed of benign lymph node extension of the nevus component. Sub-matrix presentation (without striated melanonychia) is even rarer.

CASE REPORT

A 27-year-old woman sought medical consultation complaining of a dark spot in the lunula region of the right first digit for seven years, asymptomatic. Initially, the patient reported that she noticed the spot only when she moved the cuticle away. She observed progressive lesion growth, becoming more evident even without the cuticle removal. The patient also reported a small change of the distal portion of the nail, with localized onychoschizia. She denied a previous history of trauma or bleeding. The physical examination revealed a bluish semicircular macula, occupying approximately 50% of the lunula, without altering the overlying nail plate. Dermoscopy showed a homogeneous bluish background without longitudinal lines (Figure 1). There were no periungual changes, signs of trauma, or axillary lymphadenopathy. The patient reported no previous personal or family history of melanoma.

Due to the inaccurate report of lesion growth and its extension, the nail plate was surgically removed proximally to the nail bed halfway in the longitudinal direction. It evidenced an intensely pigmented, blackened, semicircular, well-delimited lesion with approximately 7 mm in its largest diameter (Figure 2). We opted for the pigmented lesion's shave excision biopsy to preserve the aesthetic aspect (Figure 3).

The microscopy observed hyperpigmented spindle and dendritic melanocytes' proliferation, forming bundles amid collagen fibers and sometimes permeating neural threads and some melanophages. These findings are consistent with blue nevus (Figures 4 and 5). The tissue studied showed no signs of malignancy.

Figure 2: Intensively pigmented lesion observed after mobilization of the proximal nail fold

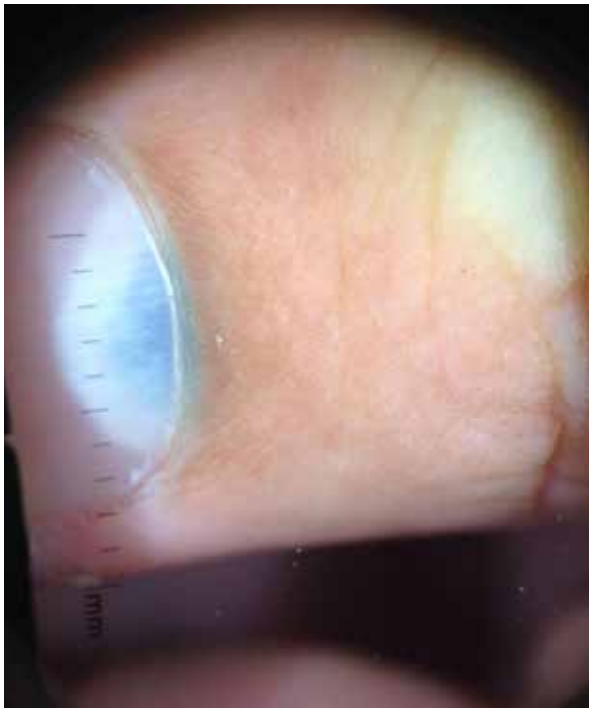

Figure 1: Dermoscopy of the subungual lesion - bluish semicircular spot on the lunula

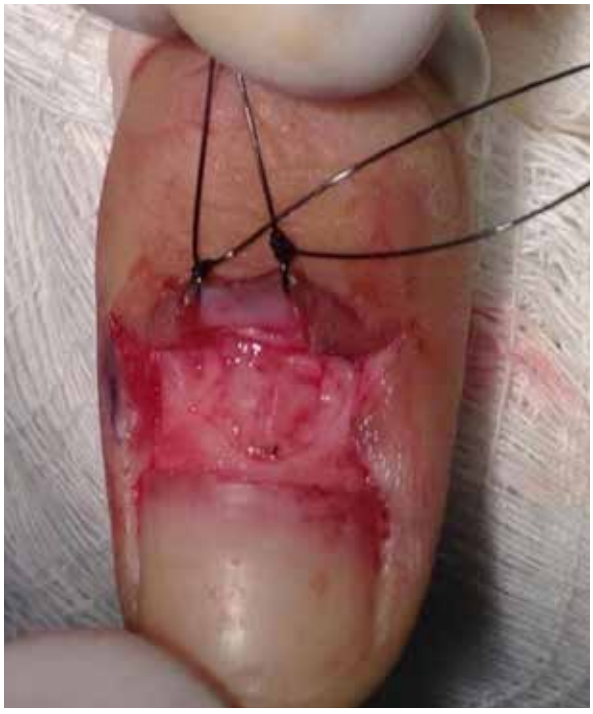

Figure 3: Shave excision biopsy of the lesion was performed

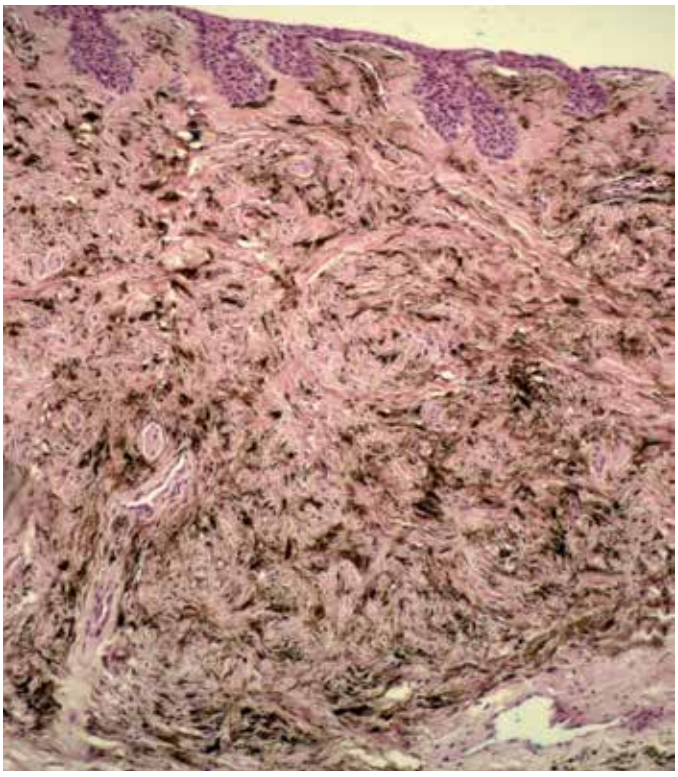

Figure 4: Histology showing proliferation of hyperpigmented fusiform and dendritic melanocytes, forming bundles in the middle of collagen fibers

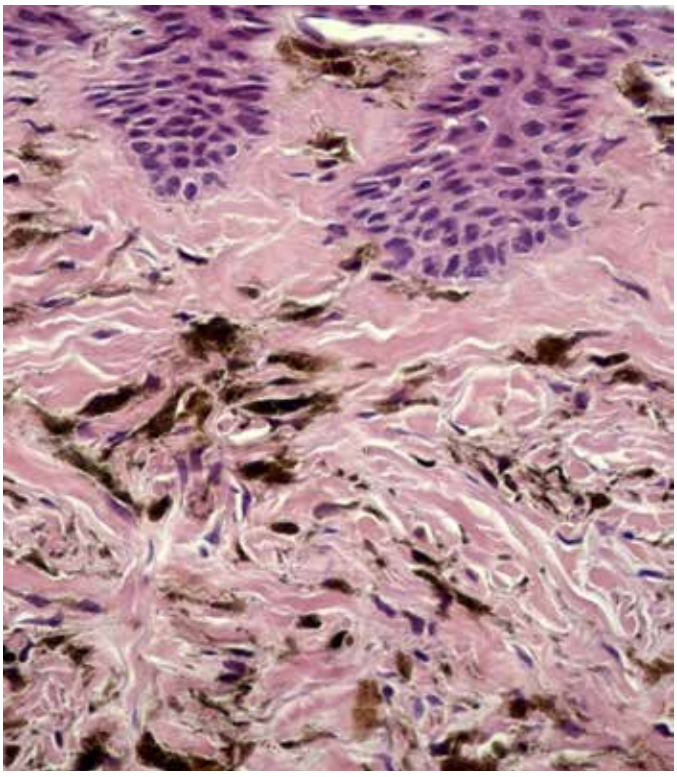

Figure 5: Histology in greater magnification

DISCUSSION

Blue nevus represents a benign proliferation of dermal melanocytes with active melanin production, unlike intradermal nevi and common compound nevi, which produces little or no melanin. The literature suggests that its pathogenesis arises from the interruption of neural crest cell migration in the dermis on the way to the epidermis during embryogenesis. The bluish color of the lesion occurs by preferential absorption of long wavelengths of light by melanin in the dermis, while the skin reflects short wavelengths of the blue spectrum, a phenomenon called the Tyndall Effect.[2]

Blue nevi can be acquired or congenital and affect preferentially young women. They usually occur on the skin and are rarely reported on extracutaneous sites such as orbital and conjunctival region, oral cavity, esophagus, lymph nodes, vagina, penis, and prostate.[3]

The blue nevi of the nail apparatus may originate from the matrix, the bed, or the deep periungual dermis. Because they are dermal structures, they usually present as longitudinal melanonychia-like lesions. Pigment-producing nevus cells can incorporate melanin into the nail matrix, leading to a nail-streak formation with brown stripes. The literature suggests that in the case here reported, the nevus would be in a sub-matrix position. Thus, it would not interfere with the lamina's color and present only as a subungual stain, without longitudinal melanonychia. The bluish color of the lesion is due to the Tyndall effect observed on the translucent nail plate.

The surgical approach of a pigmented lesion in the subungual apparatus is essential to rule out possible differential malignant diagnoses, especially melanoma and its metastatic form. Also, there are reports of malignant transformation of cellular blue nevus. However, the choice of operative conduct must be cautious, as it may lead to permanent dystrophy and functional limitation of the affected digit. In this scenario, one should consider the personal history, the clinical aspect of the lesion, and its dermoscopy. It is also recommended to evaluate any periungual lesions present.

The definition of non-conservative conduct is also based on observing aspects that suggest malignant behavior. Some of them are the presence of longitudinal melanonychia with a thickness higher than 5 mm, irregularities in color, increased thickness of the band distally to proximal, involvement of the first finger, dystrophy of the blade, and periungual pigmentation. Another evidence of malignancy to be highlighted is the report of recent lesion growth.[4]

Regarding the biopsy technique, removing the lesion only in its periphery should be avoided since the concentration of atypical cells in melanoma is predominant in the central portion of the neoplasia. With complete excision of the lesion, it is uncommon to resort to it. Thus, when clinical recurrence is observed, it is necessary to consider the possibility of malignant transformation, which is a rare event.[5]

CONCLUSION

In the presence of a pigmented lesion in the subungual apparatus, the propaedeutic is often based on a clinical-pathological correlation. However, there are factors to be considered to avoid unnecessary intervention resulting in aesthetic and functional impairment. ●

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AUTHORS ' CONTRIBUTION:

Gustavo Vieira Gualberto | ORCID 0000-0001-5349-2449
Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Cassio Ferreira Guimarães | ORCID 0000-0002-4328-8994
Preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review.

Luisa Coutinho Teixeira | ORCID 0000-0003-4281-1170
Preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review; critical revision of the manuscript.

Marina Rodrigues Costa Lages | ORCID 0000-0001-9956-7733
Preparation and writing of the manuscript.

Guilherme Henrique Silveira Teixeira | ORCID 0000-0003-0740-6153
Preparation and writing of the manuscript.

Case Reports

Authors:
Karina Bittencourt Medeiros[1]
Guilherme Athanasio Shwetz[1]
Graziela Junges Crescente Rastelli[1]

[1] Hospital Universitário Evangélico Mackenzie, Curitiba (PR), Brazil.

Correspondence:
Karina Bittencourt Medeiros
R. Luiz Leitner, 50
Bigorrilho
80710-290 Curitiba (PR)
E-mail: karinabm18@gmail.com

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Study conducted at the Hospital Universitário Evangélico Mackenzie, Curitiba (PR), Brazil.

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Basal Cell Carcinoma in the Face of Non-Syndromic Adolescents: From Rarity to a New Reality?

Carcinoma basocelular na face de adolescente não sindrômico: de raridade para uma nova realidade?

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ABSTRACT

The increase in the incidence of basal cell carcinoma (BCC) affects all age groups, including young patients under twenty years old. Because it is poorly remembered in this group of patients, late diagnosis and treatment of this neoplasia may be more common. Like other age groups, excessive exposure to ultraviolet radiation is the main associated risk factor; however, genetic factors may also be involved in non-syndromic cases. We report a case of BCC on the face of an adolescent treated with Mohs micrographic surgery.

Keywords: Adolescent; Carcinoma, Basal Cell; Epidemiology; Mohs Surgery; Solar Radiation

RESUMO

O aumento na incidência do carcinoma basocelular (CBC) atinge todas as faixas etárias, incluindo jovens abaixo dos 20 anos. Por ser pouco lembrado nesse grupo de pacientes, o atraso no diagnóstico e o tratamento tardio da neoplasia podem ser mais comuns. Assim como para outras faixas etárias, a exposição excessiva à radiação ultravioleta é o principal fator de risco associado, porém fatores genéticos também podem estar envolvidos nos casos não sindrômicos. Descreve-se um caso de CBC na face de um adolescente, tratado com cirurgia micrográfica de Mohs.

Palavras-chave: *Adolescente; Carcinoma Basocelular; Cirurgia de Mohs; Epidemiologia; Radiação Solar*

INTRODUCTION

Basal cell carcinoma (BCC) is the most common malignancy in humans, and its incidence is increasing in recent decades. In Brazil, non-melanoma skin cancer represents 30% of all registered malignant tumors, with an estimate of approximately 176 thousand new cases for 2020.[1] Despite the low mortality rates, the tumor may present local invasive behavior and relapse after treatment, causing significant morbidity. Exposure to ultraviolet radiation represents the leading environmental risk factor associated with its genesis. Other factors are also related, such as light skin phototypes, advanced age, family history of skin carcinomas, and immunosuppression, in addition to behavioral aspects, such as a professional activity that requires frequent exposure to the sun, rural activity, and sunburn in youth.[2,3,4]

This article reports a case of basal cell carcinoma in an adolescent, emphasizing the importance of its diagnosis at an early age.

CASE REPORT

A 16-year-old man reported a progressive facial lesion for two years. He had previously treated the lesion as nodular acne using topical medications. The patient had no personal history of continuous sun exposure and did not report previous intense acute exposure. He also did not have a family history of skin cancer.

The patient was skin phototype II, and the physical examination showed a 1.5 cm diameter pearly plaque in the left malar region, infiltrated, well delimited, and ulcerated (Figure 1). Dermoscopy revealed arboriform vessels on the lesion's entire surface, shiny white structures, and ulceration (Figure 2). We also observed grade II acne on the face. The patient did not present any other clinical alterations, such as palmoplantar pitting, breast hypertelorism, changes in the thoracic diameter, and frontal bone prominence. Skull tomography and panoramic radiography of the face, dental arch, ribs, and thorax showed no changes.

The skin biopsy proved it to be basal cell carcinoma, solid nodular subtype, with an infiltrative growth pattern invading the deep reticular dermis (Figure 3). The patient underwent surgical excision by Mohs micrographic surgery, with free margins in the first stage and closure by a sliding flap (Figure 4), with good evolution and good aesthetic result after six months of evolution (Figure 5).

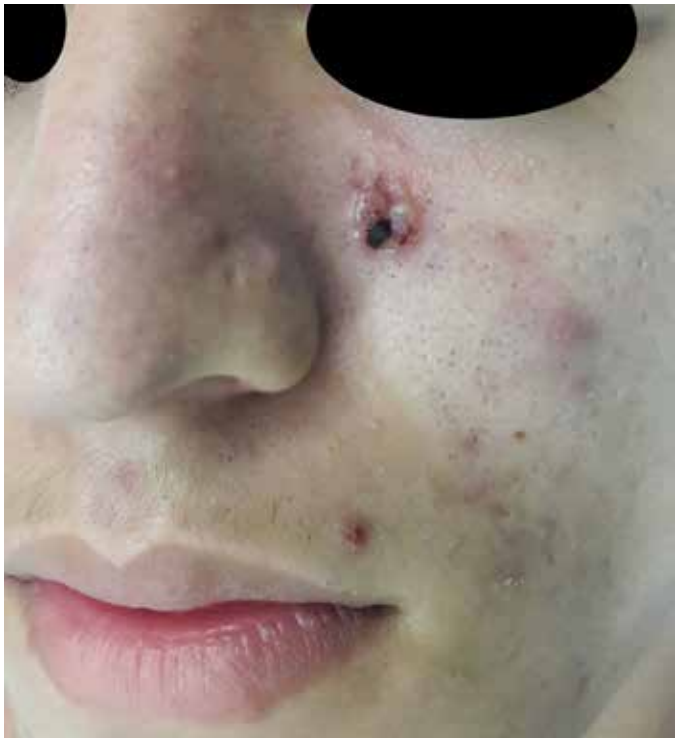

Figure 1: Clinical aspect of the lesion: 1.5 cm plaque in the largest diameter, pearly shine, infiltrated edges, and central ulceration with hematic crust in the left malar region. Open comedones and erythematous papules are observed in the facial center (acne vulgaris)

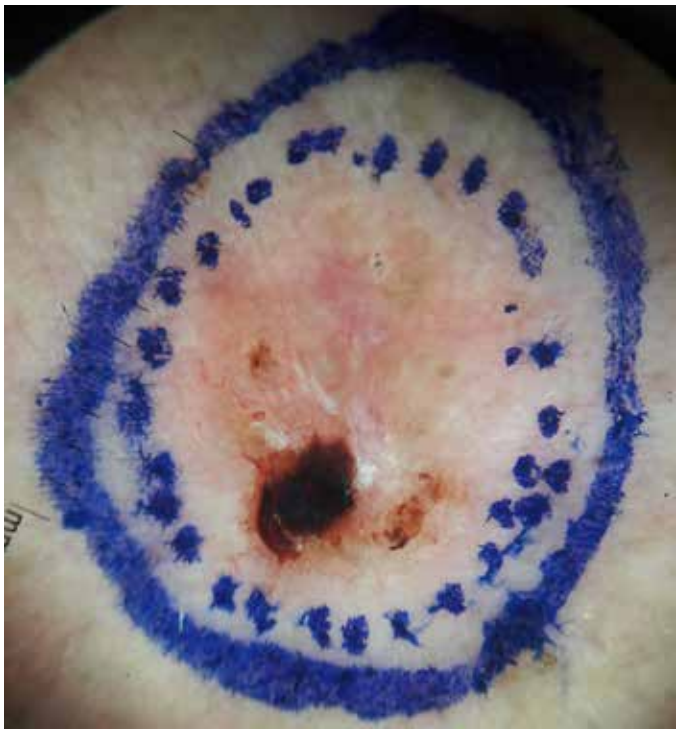

Figure 2: Dermoscopy of the lesion with polarized light: presence of arboriform vessels on the entire surface, ulceration in the lower left quadrant, and bright white structures in the center (10x magnification)

DISCUSSION

There is a consensus that BCC incidence is increasing, both in the elderly and in young non-syndromic patients. Individuals under 40 years already account for more than 5% of diagnoses,[2] and the hypotheses for this phenomenon are not elucidated.

Greater cumulative exposure to ultraviolet radiation, time available for leisure, unprotected sun exposure, culture of tanning, ozone depletion (2% in the last 20 years), ethnic heritage, and skin phototype (phototypes I and II, for example) are probably the factors that most contribute to the BCC increased incidence.[2,3,4]

Young patients have more lesions on the trunk, superficial subtype, which are more associated with this type of exposure.[5] The habit of sunbathing is linked to five times higher risk of developing BCCs in the trunk.[2,5] The reported patient had a lesion on the face, solid nodular subtype, different from the young people's profile described in the literature.

Genetic factors are associated with the disease's appearance in young people, especially among syndromic cases, such as xeroderma pigmentosum and basal cell nevus syndrome. Sporadic cases also originate from genetic changes. The literature describes that between 30% and 75% of sporadic cases are associated with the patched hedgehog gene mutation. However, other genetic alterations are also described.[4,5]

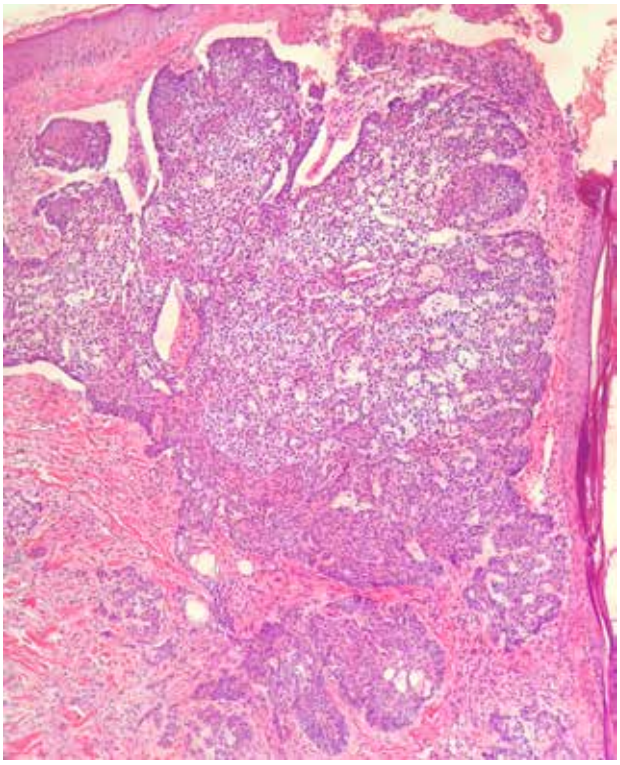

Figure 3: Detail of histopathological examination of the piece with neoplastic arrangement of basaloid cells with palisade arrangement at the periphery, peritumoral retraction, and infiltration to the reticular dermis (hematoxylin & eosin staining)

Figure 4: Immediate postoperative appearance with sliding flap for closure of a surgical defect

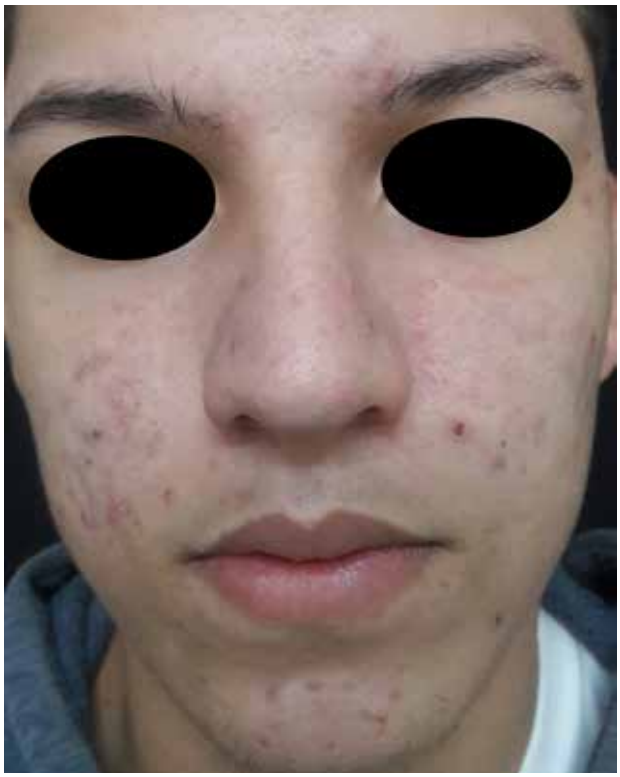

Figure 5: Scar appearance six months after surgery

There is a theory that the sebum layer would act as a barrier to ultraviolet rays protecting the skin and preventing the appearance of BCC. Thus, oily and acne-prone skin would present higher protection and a lower incidence of BCC.[6] This theory does not fit our case, as the reported patient had oily skin and acne, which may have confused the general practitioner and the patient, delaying the diagnosis.

Men are more affected than women in a 2:1 ratio and with a higher number of lesions, probably due to greater sun exposure.[4]

CONCLUSIONS

The increase in the incidence of this cancer in the younger population can represent growth in all age groups, especially its occurrence in the future older adults, as individuals with a history of BCC are at increased risk of another tumor's appearance. In five years, approximately 40% of patients will have another BCC lesion.[7]

As it is increasingly common, it is essential to advance this diagnosis in younger age groups. It would help to avoid delays in diagnosis, such as what happened to our patient who treated the facial lesion for two years as acne. It is crucial to institute preventive sun protection care from early childhood, as they are essential to reduce the future risk of developing BCC.

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AUTHORS ' CONTRIBUTION:

Karina Bittencourt Medeiros | ORCID 0000-0001-8202-6711

Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; data collection, analysis, and interpretation; critical literature review.

Guilherme Athanasio Shwetz | ORCID 0000-0003-2157-6116

Approval of the final version of the manuscript; active participation in research orientation; critical revision of the manuscript.

Graziela Junges Crescente Rastelli | ORCID 0000-0002-4235-1410

Data collection, analysis, and interpretation; active participation in research orientation.

Case Reports

Authors:
Rogerio Nabor Kondo[1]
Fabiana de Mari Scalone[1]
Luciana Rigolin Mazoni Alves[1]
Ricardo Hirayama Montero[1]

[1] Department of Internal Medicine, Dermatology Service, do Hospital Universitário Regional do Norte do Paraná da Universidade Estadual de Londrina, Londrina, Paraná (PR), Brazil.

Correspondence:
Av. Ayrton Senna da Silva, 1055 - sala 1205- Gleba Fazenda Palhano
86050-460 Londrina (PR)
E-mail: kondo.dermato@gmail.com

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Autologous fat transplantation: a good option for treatment to facial deformity after head trauma

Lipoenxertia autóloga: uma boa opção para tratamento de deformidade facial após traumatismo craniano

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ABSTRACT

Correcting facial deformities is still a significant challenge for the dermatological surgeon. The therapeutic options may vary depending on the etiology, location, costs, and attending physician's experiences of the. Although some studies have shown controversies regarding the results of using autologous fat transplantation (AFT) to treat facial depression, we report a case with good aesthetic results after two sessions of AFT in a male patient with a depressed facial fracture after head trauma.

Keywords: Transplantation; Transplantation, Autologous; Subcutaneous fat; Skull fracture, depressed

RESUMO

Corrigir deformidades na face ainda é um grande desafio para o cirurgião dermatológico. As opções terapêuticas podem variar conforme a etiologia, a localização, os custos e a experiência do médico-assistente. Apesar de alguns trabalhos demonstrarem controvérsias quanto aos resultados do uso de lipoenxertia autóloga (LA) para tratamento de depressões na face, relatamos um caso com bom resultado estético, após duas sessões de LA, em paciente masculino com afundamento facial após traumatismo craniano.

Palavras-chave: *Fratura do crânio com afundamento; Transplante; Transplante autólogo; Gordura subcutânea*

INTRODUCTION

Depending on the facial deformity and its etiology, it is possible to use several methods, from less invasive ones (such as botulinum toxin[1] and filling with hyaluronic acid[2]) to more complex surgeries (such as silicone implants or acrylic resin prostheses[3]). Autologous fat transplantation (AFT) is a surgical alternative, especially in cases of lipodystrophy.[4-10]

We report a case of a patient with complaints of depressed facial scars (Figure 1) after a head injury, which is considered ideal for AFT for treatment, with satisfactory aesthetic results. Although this technique has cost-benefit advantages, the literature describes the unpredictability of the results due to the possibility of absorption with consequent loss of volume and the need for new uses. [5,6,7]

This case report aims to demonstrate this technique's effectiveness, low cost, easy performance, and patient and surgical team's good satisfaction level.

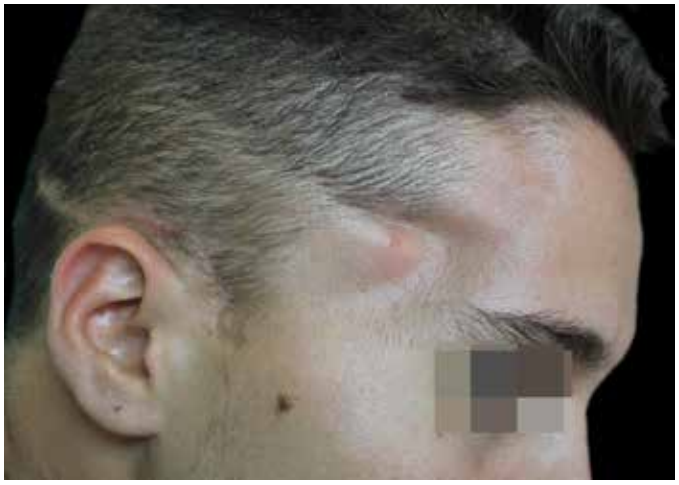

Figure 1: Right frontal deformity

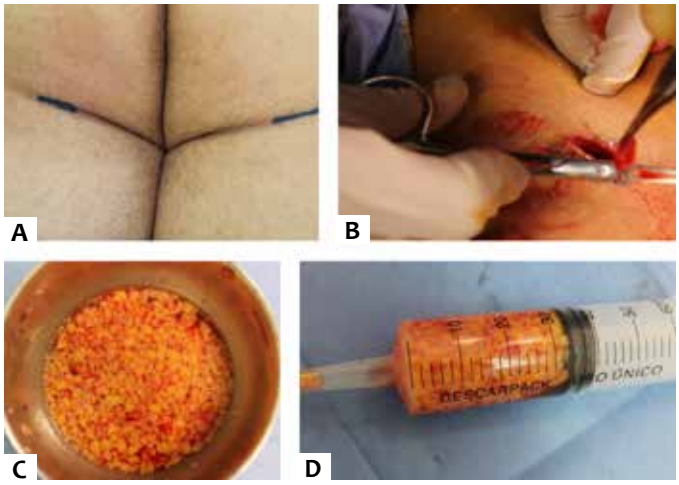

Figure 2: A - Marking on the infra-gluteal fold. **B.** Removal of adipose tissue. **C.** Fragmented adipose tissue. **D.** Urological syringe filled with fat

METHODS

A 15-year-old man, student, had a motorcycle crash, with a consequent head injury and frontal, parietal, and temporal bone fractures on the right side. He underwent neurosurgical interventions, such as bone graft and insertion of a platinum plate, to correct depressed scars and fractures. After days of induced coma and intensive care, the patient evolved without motor sequelae at hospital discharge (only local paraesthesia) but with aesthetic deformity (he referred to a local depressed scar) that bothered him. He was 16 years old when he underwent neurosurgery for dermatological assessment.

As it was only an aesthetic correction, the mother and the patient were informed about the procedure. They signed the Patient Photo Release and Informed Consent forms.

The patient remained with the bandages for 24 hours. We prescribed sulfamethoxazole and trimethoprim tablets 400/80 mg[2] every 12 hours for ten days.

Technique Description:

I - Removal of fat tissue (Figure 2)

a) Patient in a horizontal position;

b) Marking of the bilateral infra-gluteal fold (donor site);

c) Asepsis with 10% topical polyvinyl iodine from the donor site;

d) Placing of surgical drapes;

e) Infiltration of the donor site using 2% lidocaine with vasoconstrictor;

f) Linear incision with blade size 15;

g) Removal of fat tissue with Adson forceps and iris scissors and insertion of the material in a vat with saline;

h) Fractionation of fat tissue with iris scissors into smaller fragments for better aspiration of the contents in the urological syringe;

i) Primary wound closure using 4.0 mononylon, single stitches, from the donor site;

II - Fat grafting (Figure 3)

a) Marking the area to be filled;

b) Anesthetic infiltration using 2% lidocaine with a vasoconstrictor surrounding the marked area;

c) 6 mm incision, using blade size 15 on the upper parts of the demarcated areas (at 12 hours);

d) Local skin detachment using a tentacle, through the incisions, in the plane above the skull (in this case), up to the previously delimited area;

e) Using a urological syringe (60 ml), fat is injected through the incision until it fills the detached cavity;

f) Incision suture with 5.0 mononylon, single stitches;

g) Local cleaning with saline;

h) Occlusive dressing with gauze.

Figure 3: A - Marking the area to be filled. **B.** Incision with blade size 15 and local detachment using tentacle

Figure 4: Immediate postoperative

RESULTS

The patient responded well in the immediate postoperative period, without infection of the surgical sites or hemorrhages. Six months after the intervention, he presented good aesthetics and no functional impairment of the face, although partial resorption of local fat occurred (Figure 5). We recommended a second AFT with the consent of the patient and his mother.

The second intervention was conducted without complications. After nine months, the patient presented a very good aesthetic result (Figure 6).

DISCUSSION

The correction of facial deformities, whatever their etiology, is still a significant challenge for the dermatological surgeon. In more straightforward cases, such as post-traumatic chin deformities, botulinum toxin can be used.[1] However, for lipodystrophy or depressed facial scars, autologous fat grafting (AFT), hyaluronic acid, or poly-L-lactic acid are recommended.[2] For cases of cartilage and bone loss, acrylic resin prostheses can be used.[3]

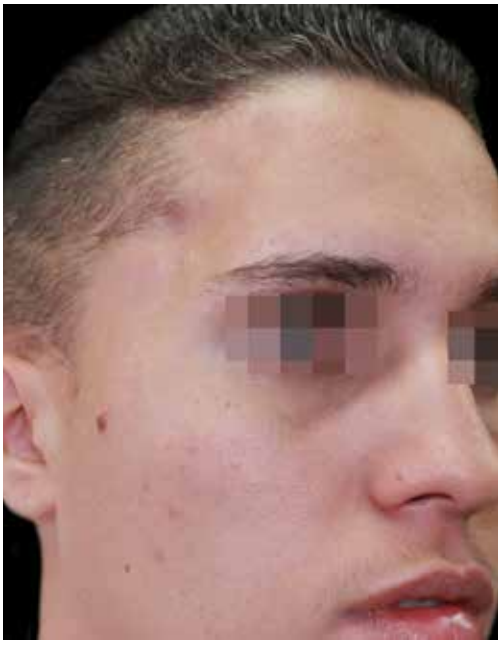

Figure 5: Six months after the first intervention

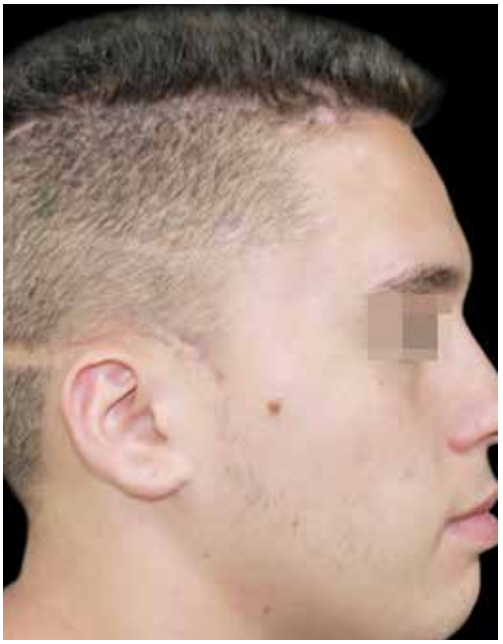

Figure 6: Nine months after the second intervention

AFT is very interesting in correcting facial deformities, considering that the adipose tissue is relatively abundant on the skin surface, has an ideal texture and modeling, in addition to an almost zero tissue rejection index. [6,8,10]Although it has been proposed since the end of the 19th century, some studies present controversies regarding the procedure given the effectiveness of the results.[6,8] The hypothesis for no improvement would be fat absorption or low tissue viability transferred.[6]

With the neurosurgery team's permission, in the case of an aesthetic procedure, we opted to perform the AFT in the present case, considering the low cost, tissue rejection rate, and risk of complications.

The patient evolved with good aesthetic results, and after six months of the first surgery (Figure 5), there was a significant improvement in the local depressed scar. Even so, we conducted a second intervention to correct the possible absorption of some areas. Nine months later, the patient achieved an excellent result (Figure 6). Some studies have also noticed a significant improvement with AFT, especially after the second intervention. [5,6]

This study hypothesizes that the procedure's effectiveness is higher on the second session due to the remaining adipocytes' presence from the first intervention. It hinders the absorption of this new injected fat tissue and, somehow, also stimulates fibroblasts.

Another therapy option is poly-L-lactic acid (PPLA). PPLA is a biocompatible, resorbable, and immunologically inert polymer. Its mechanism of action consists of the stimula-

tion of fibroblasts in their subclinical inflammatory response. It can be used in cases of facial deformities, including plates and screws. [2,6] We opt for not using it due to the extent of the depressed scar, costs, and risk of papules, nodules, and granulomas formation.

Although some studies have shown controversial results, the AFT technique used in the case has proved to be entirely satisfactory. The deformity that the patient called "sinking" was solved and provided an improvement in his self-esteem.

CONCLUSION

AFT is a technique that is easy to perform, well-tolerated, has low cost, and presents good cosmetic results (Figures 5 and 6).

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AUTHORS ' CONTRIBUTION:

Rogerio Nabor Kondo | ORCID 0000-0003-1848-3314
Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; active participation in research orientation; intellectual participation in propaedeutic and/or therapeutic conduct of studied cases; critical literature review; critical revision of the manuscript.

Fabiana de Mari Scalone | ORCID 0000-0002-5050-8246
Approval of the final version of the manuscript; study design and planning; preparation and writing of the manuscript; critical literature review; critical revision of the manuscript.

Luciana Rigolin Mazoni Alves | ORCID 0000-0003-4865-4110
Approval of the final version of the manuscript; preparation and writing of the manuscript; critical literature review; critical revision of the manuscript.

Ricardo Hirayama Montero | ORCID 0000-0001-8148-1026
Approval of the final version of the manuscript; preparation and writing of the manuscript; critical literature review; critical revision of the manuscript.

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