Dermal filling complication after hepatitis C treatment with interferon and ribavirin

Complicação de preenchimento cutâneo após tratamento de hepatite C com interferon e ribavirina

ABSTRACT

This article describes the case of a female hepatitis C patient who presented with a foreign body granuloma in the nasolabial folds and glabella five years after receiving an application of permanent dermal filler. The patient used interferon and ribavirin for treating hepatitis C for six months, and the granulomas appeared 30 days after the end of the treatment. Treatment with oral steroids was carried out, with a gradual improvement in the appearance of the skin.

Keywords: granuloma; polimetilmetacrilato; face.

RESUMO

Relata-se o caso de paciente portadora de hepatite C, com surgimento de granuloma por corpo estranho nos sulcos nasolabiais e glabela, cinco anos após submeter-se a aplicação de preenchedor cutâneo permanente. A paciente fez uso de interferon e ribavirina para tratar hepatite C durante seis meses, com o surgimento dos granulomas 30 dias após o fim do tratamento. Realizada então terapia com corticoide oral, havendo melhora gradativa do quadro cutâneo.

Palavras-chave: granuloma; polimetilmetacrilato; face.

INTRODUCTION

Cutaneous fillers play an important role in the aesthetic treatment of the signs of facial aging, including nasolabial folds, glabellar lines, nose, infraorbital region, and lips. The ideal substance to use in cutaneous fillings should be autologous, durable, non-toxic, and devoid of immunological effects. Polymethylmethacrylate is a permanent filling substance composed of non-phagocytable microspheres with an irregular surface, which can generate granulomas.

It is estimated that 3% of the world's population is infected with hepatitis C, with a relevant number of people unaware of the fact that they carry the virus (subclinical infection). The currently recommended treatment for hepatitis C includes interferon and

Case Report

Authors:

Daniela Martins Bringel¹ Lislaine Bomm² Amanda da Costa Azevedo² Roberto Souto³ John Carlos Fonseca⁴

- Dermatologist physician, Hospital Universitário Pedro Ernesto da Universidade do Estado do Rio de Janeiro (UERJ) – Rio de Janeiro (RJ), Brazil
- ² Dermatology Resident Physician, UERJ
- MSc in Dermatology Candidate, UERJ
- Associate Professor and Dermatology Preceptor, UERJ

Correspondence:

Dr. Daniela Martins Bringel R. Barão de Mesquita, 280/206 Cep: 20540-003 Tijuca - Rio de Janeiro – RJ, Brazil E-mail: danielabringel@zipmail.com.br

Received on: 19 January 2012 Approved on: 20 September 2012

This study was carried out at the Hospital Universitário Pedro Ernesto da Universidade do Estado do Rio de Janeiro (HUPE UERJ) – Rio de Janeiro (RJ), Brazil.

Financial support: None Conflict of interest: None

ribavirin. Ribavirin is a synthetic guanosine analogue that has a direct action against viral RNA; the mechanism is thought to be inhibition of virus-dependent DNA polymerase. Interferon (IFN) – more specifically the IFN-alpha – acts directly against the virus and improves the immune response by increasing the major histocompatibility complex (MHC) class I and decreasing the MHC class II. It also increases the efficiency of cytotoxicity mediated by cytotoxic T lymphocytes and inhibits the activation of T helper lymphocytes. This study presents an IFN adverse reaction case that resulted in the reactivation of the granulomatous process in a patient who had undergone cutaneous filling.

CASE REPORT

A 52-year-old female patient presented localized edema in the glabella and nasolabial folds, associated with mild erythema. She had completed a treatment for hepatitis C with pegylated Interferon and ribavirin 30 days previously. The patient reported having undergone dermal filling with polymethylmethacrylate in those sites five years before.

Dermatological examination showed hardened nodules that were not adhered to deep planes. Those nodules were arranged in strands that measured approximately 5cm in the nasolabial folds (bilateral) and 2cm in the glabella (Figures 1, 2, and 3). The soft tissue ultrasonography of the affected areas revealed echogenic plaques scattered over the subcutaneous tissue.

The diagnosis of foreign body granuloma was issued based on the patient's medical history. Initial treatment with prednisone was administered at 0.65 mg/kg/day, and a new assessment was conducted three weeks later, when a significant reduction of edema and decreased nodules size were observed. The oral prednisone was then gradually decreased (average duration of prednisone use was two months). Three months after the end of the prednisone course, the patient still sustained a reduction of nodules (Figures 4 and 5).

DISCUSSION

Dermal filling substances have been increasingly used to correct some of the alterations associated with facial aging. Substances approved for cosmetic use are: collagen-based products, autologous fat, hyaluronic acid, poly-L-lactic acid, calcium hydroxylapatite, and polymethylmethacrylate.

Polymethylmethacrylate comes in the form of synthetic microspheres with a diameter of $40\text{-}60\mu\text{m}$, vehiculated in a suspension medium that may be non-protein or crystalloid collagen. The product has a permanent nature, with only the vehicle being absorbed. According to the vehicle used, there are different commercial versions, such as Artecol, Metacril, and PMMA. The 4-8 μ m microspheres are susceptible to phagocytosis, yet are not conveyed to the lymph nodes or distant organs. Larger microspheres (of 20, 40, and 100 μ m) are encapsulated by connective tissue. Histological examinations after implantation of the product show multiple fibroblasts, the microencapsulation of each microsphere, and small foreign body reaction. The injected product stimulates neocollagenesis and neovascularization according the pattern typical of foreign body reaction.



Figure 1: Nodule in the nasolabial



Figure 2: Nodule in the nasolabial fold



Figure 3: Nodule in the glabella

Filling complication in hepatitis C 273



Figure 4: Reduction of the nodule in the glabella 21 days after treatment



Figure 5: Reduction of the nodule in the nasolabial fold 21 days after treatment

Complications can occur in the form of allergic reactions, hypertrophic scars, telangiectasia, and granulomas, which usually appear 6-24 months after the injection of the filler.

According to the literature, the formation of foreign body granuloma occurs in 0.01% to 2.5% of applications.³⁻⁵ Passy and colleagues reported the existence of two types of granulomatous complications: the applicator's lack of technical skills and product-related problems.⁶ The formation of nodules and inflammatory responses are cyclical. Treatment can be carried out with intralesional application of triamcinolone 5-fluoracil, oral corticosteroids, or allopurinol. It is often necessary to remove the product surgically.^{7,8} The expected response to the use of cutaneous fillers is a weak granulomatous reaction. IFN and other immunostimulant medications can lead to the exacerbation of such a preexisting chronic inflammation, which has been obser-

ved in patients with sarcoidosis triggered b y the use of IFN.89

Based on the literature review, the authors conclude that treatment for hepatitis C exacerbated the patient's previous low-grade chronic inflammation, which was manifested in facial edema and nodules in the sites where the cutaneous filler had been applied, which responded favorably to oral corticosteroids.¹⁰

Hepatitis C is currently a serious public health problem in Brazil and in the world due to the great number of infected people – who are often asymptomatic for many years until they develop a chronic form of the disease, with the onset of cirrhosis and hepatocarcinoma. Many individuals only become aware they are infected when donating blood or undergoing clinical admission exams for professional reasons. The large number of carriers that does not know they are infected perpetuates the disease. Therefore, it is important to test for hepatitis C prior to dermal filling, since the treatment of that disease can entail exacerbate the granulomas and, as directed by the Brazilian Ministry of Health, that type of filling is contraindicated in patients with hepatitis C.¹¹

REFERENCES

- Talarico S, Hassun KM, Monteiro EO, Parada MOB, Buratini LB, Arruda L, et al. Avaliação da segurança e eficácia de novo preenchedor à base de ácido hialurônico no tratamento dos sulcos nasogenianos e contornos dos lábios. Surg Cosmet Dermatol.2010;2(2):83-6.
- Caramez C, Diacomo CG, Schmitd L, Santos L, Lupi O. Alterações dermatológicas na hepatite C. Rev Bras Clin Med. 2010;8:53-8.
- Ersek R. Bioplastique at 6 years: clinical outcome studies. Plast Reconstr Surg. 1997;100(6):1570-74.
- Christensen L, Breiting V, Janssen M, Vuust J, Hogdall R. Adverse reactions to injectable soft tissue permanent fillers. Aesthetic Plast Surg. 2005;29(1):34-48.
- Salles AG, Lotierzo PH, Gemperli R, Besteiro JM, Ishida LC, Gimenez RP, et al. Complications after polymethylmethacrylate injections:report of 32 cases. Plast Reconstr Surg. 2008;121(5):1811-20.
- Lemperle G. Complications from Artecoll are treatable. Aesthetic Surg J 2003;23(6):469-70.
- Passy S. Procedimentos estéticos ancilares: Parte II Metacrill. In: Rejuvenescimento facial: cirurgia videoendoscópica e procedimentos ancilares. Rio de Janeiro: Revinter;2003. p.280-91.
- Conejo-Mir JS, Sanz Guirado S, Angel Muñoz M. Adverse granulomatous reaction to Artecoll treated by intralesional 5-fluorouracil and triamcinolone injections. Dermatol Surg. 2006;32(8):1079-81.
- Reisberger EM, Landthaler M, Wiest L, Schröder J, Stolz W. Foreign body granulomas caused by polymethylmethacrylate microspheres: successful treatment with allopurinol. Arch Dermatol. 2003;139(1):17-20.
- Fischer J, Metzler G, Schaller M. Cosmetic permanent fillers for tissue augmentation. A new contraindication of interferon therapies. Arch Dermatol. 2007;143(4):507-10.
- 11. Ministério da Saúde. Manual de tratamento da lipoatrofia facial. 2009. p.1-45.