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A Case of Foreign-Body Granuloma of the Glabella due to Polyacrylamide Filler and an Intractable Ulcer after Skin Biopsy: An Immunohistochemical Evaluation of Inflammatory Changes

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Key Words

Foreign-body granuloma · Immunohistochemical evaluation · Inflammatory change · Polyacrylamide filler

Abstract

Introduction: Polyacrylamide hydrogel has been considered a safe and biocompatible soft tissue filler, and it has been widely used in cosmetic procedures. However, recent studies have revealed some complications with polyacrylamide filler injections. ***Case Report:*** We present the case of foreign-body granulomas of the glabella, which subsequently formed an infectious ulcer 3 years after a polyacrylamide injection. An immunohistochemical evaluation of the foreign-body granulomas was performed in order to study the relationship between foreign-body granulomas and immune response. ***Conclusion:*** We believe that our analysis of foreign-body granulomas 1 and 3 years after a filler injection may contribute to revealing the mechanism of chronic and intractable infections after filler injections.

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Introduction

Soft tissue augmentation is increasing in popularity as a result of increased interests in facial contouring, breast augmentation, and cheek reshaping [1]. In aesthetic and reconstructive surgery, facial soft tissue augmentation is performed using several biomaterials. Among them, polyacrylamide hydrogel is widely used in cosmetic procedures as a filler material [2]. It is of note, however, that polyacrylamide hydrogel may not be safe or biocompatible [1–4]. Here, we describe a patient who developed foreign-body granulomas on her glabella after an injection of polyacrylamide gel. We also present the results of an immunohistochemical analysis.

Case Report

A 57-year-old woman was referred to our hospital with a 3-month history of swelling of her glabella. The patient stated that the swelling had become rigid and indurated. Examination revealed a tumor of the glabella (fig. 1a). The tumor was 2 cm in diameter and was not well demarcated; it was skin colored and caused no redness, pain, or heat. The patient's medical history was unremarkable, with no previous cosmetic interventions. An ultrasound examination of the tumor revealed hypoechoic deposits predominating in the subcutaneous tissue of the glabella and dorsum of the nose (fig. 2). A skin biopsy was performed for diagnostic purposes. Examination of the specimen revealed granulomas consisting of histiocytes and foreign-body giant cells with patchy infiltration of lymphocytes and fibroblasts. Amorphous materials were embedded in the giant cells (fig. 1c). We asked the patient again if she had received a cosmetic filler injection. She finally admitted that she had had a polyacrylamide gel injection in the glabella 1 year before. We diagnosed her with foreign-body granulomas of the glabella due to polyacrylamide filler.

As there remained a slight induration along the surgical scar, the patient was started on oral tranilast (300 mg per day) and hydrocortisone butyrate 0.1% ointment for 4 months, which resulted in no improvement. The treatment was discontinued, and the tumor was observed without treatment. One year later, the tumor became swollen and red (fig. 1b). We performed an incisional biopsy for diagnosis and again found foreign-body granulomas with diffuse infiltration of lymphocytes and neutrophils (fig. 1d). After the biopsy, the surgical incision did not close despite suturing, and an ulcer formed on the patient's glabella, which became red and infected with purulent discharge. Although she was treated with cefdinir (300 mg per day) and sulfadiazine silver cream, the ulcer persisted for 5 months and still remained unhealed.

Discussion

Implantation of biomaterials elicits a foreign-body reaction consisting of monocyte adhesion, differentiation to macrophages, and subsequent macrophage fusion to form foreign-body giant cells. Lymphocytes transiently appear at the implant site during the inflammatory response and influence macrophage behavior directly and indirectly with monocytes, macrophages, and foreign-body granuloma cells; however, the lymphocyte response to biomaterials remains unclear [5]. There is a possibility that giant cell formation is stimulated by a Th1 response via interleukin (IL)-2 and interferon-γ, whereas a Th2 response downregulates foreign-body granulomas by limiting the number of effective

macrophages and decreasing the number of giant cells as a result of increased IL-4, IL-5, and IL-6 expression [6]. Using CD4, CD8, and CD68 staining, we conducted an immunohistochemical analysis of the foreign-body granulomas in order to evaluate the relationship between T cells and foreign-body granulomas. In two different specimens that were excised before and 1.5 years after the excisional biopsy, CD4-positive lymphocytes infiltrated more than CD8-positive lymphocytes, especially around amorphous structures and hair follicles (fig. 1e–h), which may be consistent with the above explanation. In addition, CD68-positive macrophages surrounded amorphous structures in the dermis (fig. 1i, j).

In our case, the surgical incision formed an infectious ulcer 3 years after the filler injection. We believe that bacteria were introduced during the injection procedure and formed a persistent and intractable infection on the glabella by forming a biofilm [7–10]. Previous reports put forth that infection may occur late after an injection and may be related to immune responses [8, 9]. Although we did not examine whether the infiltrating T cells were effector T cells or regulatory T cells, persisting effector T cells can become exhausted and function inefficiently in situ [11]. Although it is limited to a single case and issues remain to be addressed in the future, our immunohistochemical analysis of foreign-body granulomas 1 and 3 years after a filler injection may contribute to revealing the mechanism of chronic and intractable infections after filler injections.

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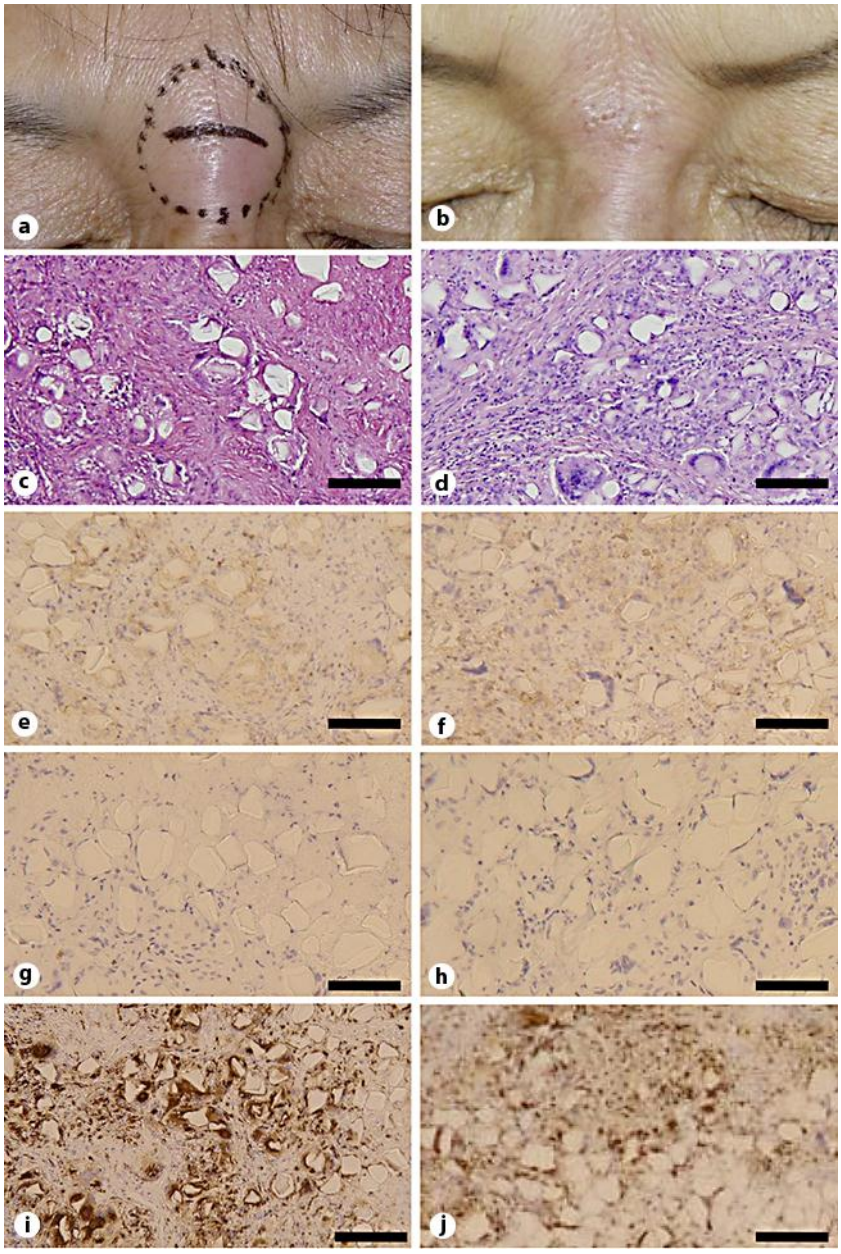

Fig. 1. Clinical and histological findings. **a**, **b** Clinical appearance. **c–j** Histological findings. **c**, **d** Hematoxylin and eosin staining. **e**, **f** CD4. **g**, **h** CD8. **i**, **j** CD68. These findings were observed before (**a**, **c**, **e**, **g**, **i**) and after (**b**, **d**, **f**, **h**, **j**) biopsy. Bars = 10 μm (**c–j**).

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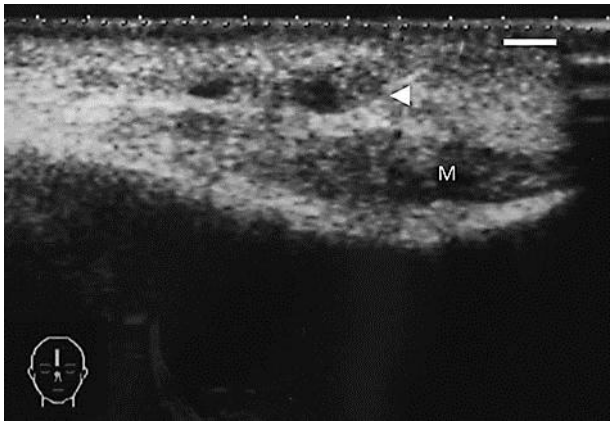

Fig. 2. Ultrasound examination of the glabella demonstrates the low echoic area (arrowhead) above the frontal muscle (M). Bar = 1 mm.