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Case report

Factors influencing the formation of foreign body granuloma after hyaluronic acid fillers treatment. A case report and treatment protocol

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ABSTRACT

Injections of hyaluronic acid dermal fillers are minimally invasive cosmetic procedures that are generally considered safe. However, many complications have been reported in the last couple of years. The formation of foreign body granuloma is a rare side effect that usually happens weeks to months after the injection of soft tissue fillers. It is one of the most challenging when it comes to management. This study aims to report a case of foreign body granuloma formation after full face treatment with 12 ml of hyaluronic dermal fillers. A short overview of the main factors influencing granuloma formation and a treatment protocol is also presented.

INTRODUCTION

The overall appearance of people influences their emotional well-being, self-perception, and mental health. Due to the increasing demand for aesthetic procedures, cosmetic dermatology has become one of the fastest-growing branches of medicine, which offers patients a wide variety of energy-based devices, injectables, and surgical treatments for face volume restoration, beautification, and skin texture improvement. There is a wide variety of injectable filler substances on the aesthetic market nowadays. They have been developed because the injection of previous substances, such as paraffin and silicone oil, has been followed by a very high risk of late granuloma formation (1). For the last couple of years, the most frequently used products consist of either HA or microspheres composed of Polylactic acid and Calcium-hydroxylapatite. Hyaluronic acid fillers are by far the most popular dermal fillers. HA is a linear polysaccharide composed of repeating disaccharide units of glucuronic acid and N-acetylglucosamine (2). It naturally exists in the skin and plays a key role in skin hydration. Fillers based on hyaluronic acid differ depending on the degree of crosslinking, HA concentration, high and low molecular weight ratio, cohesivity, and gel hardness (3). In general, they are considered safe. Unfortunately, there are still patients who react with granuloma formation months or years after being injected. That is why a good knowledge of complication management is as crucial as good injection technique and anatomy skills to achieve the best results. Herein, a case of foreign body granuloma formation after full face treatment with HA fillers is described. The case is presented after informed consent has been given by the patient.

CASE REPORT

A 40-year-old Caucasian female patient with healthy skin, no damage in the skin barrier function, and no past medical history of skin infections, was injected with 12 ml of hyaluronic acid dermal fillers during a full-face restoration treatment, which combined both needle and cannula technique, engaging the upper, middle and lower face. This information is provided by the patient and the doctor who injected her. The products used for her face rejuvenation are made of crosslinked HA (Vycross technology) with a molecular weight of approximately 2.5 million Daltons. The crosslinking agent is 1,4-butandiol glycidyl either (BDDE), and the HA concentration in the products ranges between 17.5mg/ml to 25mg/ml (Fig. 1).

Fig. 1. *The patient before and immediately after 12 ml of HA fillers showed significant improvement in her appearance.*

The patient had no previous aesthetic treatments, no established allergies or autoimmune diseases, and was in good health up to the date of her treatment. She had her second COVID-19 booster vaccine two weeks before being injected with HA. Although she was satisfied with the overall improvement in her appearance, 14 days later, she reported periorbital edema, diffuse erythema, and pain (Fig. 2).

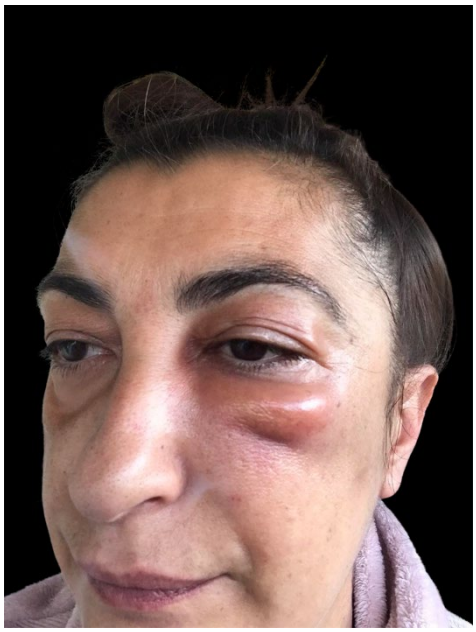

Fig. 2 *Two weeks after injecting- periorbital edema, pain, and redness.*

On the second day of the onset of the symptoms, the patient was treated with low doses of hyaluronidase (Hylasse) in combination with a systemic antibiotic, Ciprofloxacin 2x 500mg, but no significant improvement was reported. Five months later, the patient presented to our clinic with generalized edema in the periorbital region. Nodules, induration, and pain were also visible in the jawline area (Fig. 3, 4).

She reported that within a couple of months, until she came to our clinic, she went through many experts, multiple dissolving with hyaluronidase, different antibiotics, and 9 surgical incisions with no improvement of her symptoms (Fig. 5).

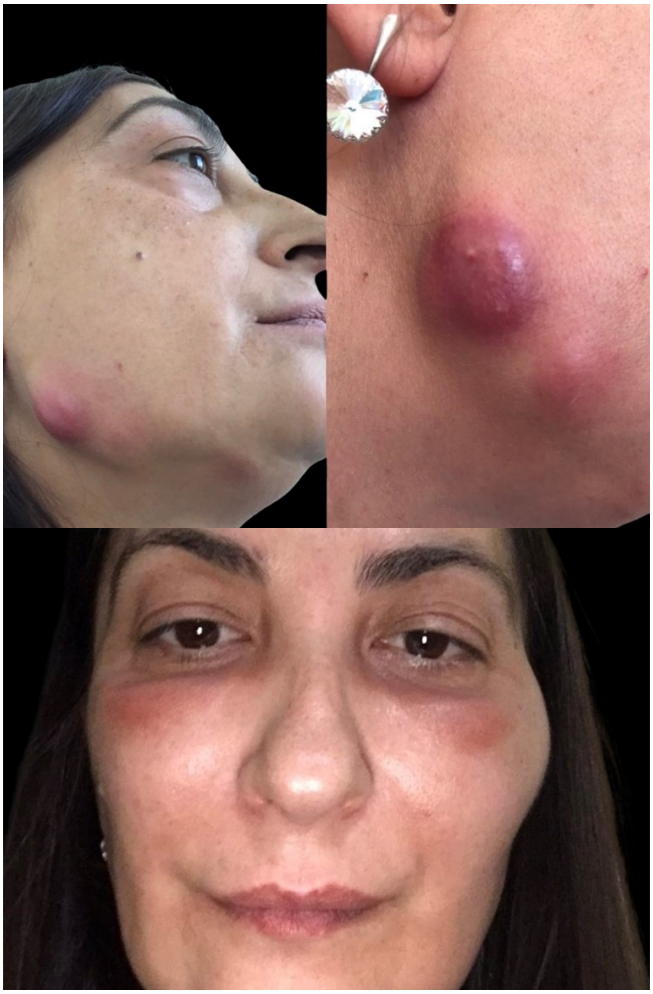

Fig. 3, 4. *Five months post-treatment. Generalized edema and painful nodules in the lower face.*

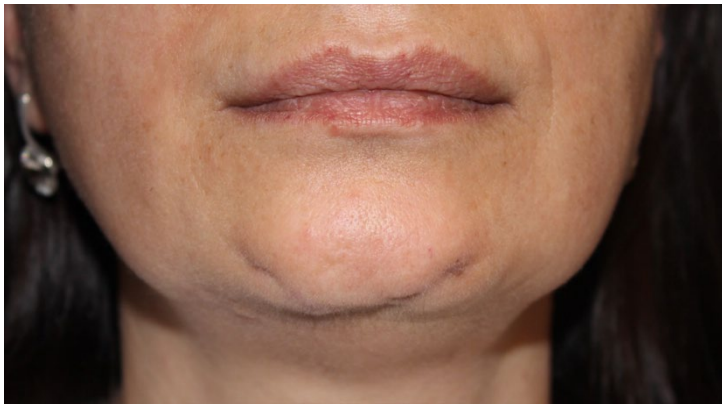

Fig. 5. *Scars left from surgical incisions.*

As the correct clinical and histological diagnosis is crucial for successful complication management, a 3mm punch biopsy was obtained from a nodule in the lower face. It revealed a deep dermal infiltrate of multinuclear giant cells, neutrophils, and epithelioid cells, proving the foreign body granuloma diagnosis (Fig. 6).

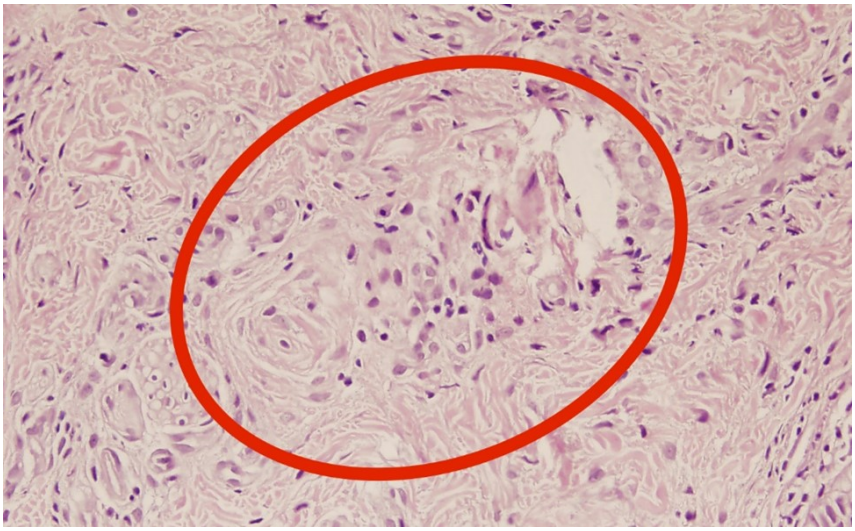

Fig. 6. *Histology of Foreign Body Granuloma.*

The bacterial swab proved negative. From the laboratory findings- high ESR and CRP- 5 months after being injected with HA. Clarithromycin 500mg plus Moxifloxacin 400mg twice daily for 10 days were introduced to her treatment plan. A combination of intralesional steroid (0.3ml of 10mg/ml triamcinolone + 0,2 ml 2% Lidocaine +0,5ml of saline) and Hyaluronidase (5-30 Units per 0.1ml of HA- to reduce the substrate) showed fast improvement in the following 2 weeks. Bleomycin and 5-Fluorouracil are also therapeutic options but are not always easy to find in some countries. Immunomodulators like Cyclosporine have been used, but there is not enough data on this treatment. Incisions, drainage, and fat grafts should not be considered first-choice options because of the possible incomplete removal or scar formation. The patient showed significant improvement and no complaints on 2, 4, and 6-month follow-up. There were no visible erythema and swelling. However, some volume loss was visible due to the multiple dissolving sessions (Fig. 7).

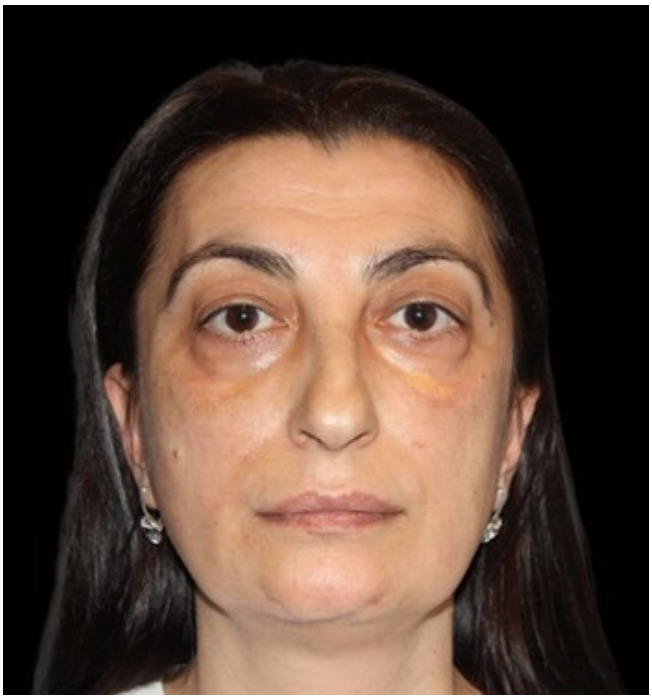

Fig. 7. *Two-month follow-up shows significant improvement.*

DISCUSSION

There are three main groups of complications depending on the time of onset. Early complications usually happen within a few days after the procedure. They include edema, pain, bruising, hypersensitivity reactions, asymmetry, lumps, and vascular occlusion. Most of them are normal physiological reactions to the injection of foreign substances and disappear independently (4). Late side effects happen two to six weeks post-injection and include late allergic reactions, chronic inflammation, infection, and hypertrophic scars. Delayed reactions (biofilms and granuloma formation) happen months to years after treatment with soft tissue fillers and tend to be unpredictable. Foreign body granuloma is a chronic, inflammatory reaction that entraps a foreign body to prevent its migration. The reaction occurs due to the immune system's inability to degrade or phagocytose foreign body material (5) enzymatically. The incidence of FBG after filler injections ranges from 0,02-0,4% (6). Unfortunately, its pathogenesis remains unknown. Different substances cause different clinical and histological types of foreign body granuloma. Hyaluronic acid usually causes cystic granulomas that may evolve into a sterile abscess. Permanent injectable fluids such as silicone might form edematous granulomas, and particulate products like polylactic acid may form sclerosing granulomas, which may remain for several years if not treated right (1). Several factors might influence the formation of foreign body granuloma after injectables. These are the particle size and surface and the impurities of the products. A larger volume injected in one injection point and repeated injections increase the risk of granulomas. There is much controversy regarding whether bacterial biofilm is one of the reasons for FBG formation, and many publications support the idea that if steroid intralesional injections help in the treatment of granuloma, bacterial biofilm cannot be a factor for granuloma formation. Since the COVID-19 pandemic started, many cases of delayed inflammatory reactions to dermal fillers after COVID-19 vaccination have appeared in literature and remain a big diagnostic challenge; most present cases of hypersensitivity reactions, swelling, and pain. Theoretically, hyaluronic acid-based fillers could act as adjuvants that enhance an antigen-specific immune response, particularly in individuals with risk factors of previous vaccine reactions, allergies, or urticaria (7). Although more data is needed to confirm the relation between delayed inflammatory reactions to fillers and the COVID-19 vaccine, more and more

studies show that immune system triggers influence these delayed complications and that foreign body granulomas have become more common since COVID-19 (8).

CONCLUSION

Hyaluronic acid-based filler injections are one of the top five most frequently used minimally invasive procedures these days. As their usage increases, so does the incidence of complications. The delayed side effects like granuloma formation are the most challenging ones because of their unknown pathogenesis. That is why gathering information and building the right treatment protocols is very important for aesthetic practitioners, especially in the era of COVID-19 when more and more cases of immune reactions to dermal fillers are being observed.

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