

CASE REPORT



An unusual and delayed complication of hyaluronic acid filler injection: a case report

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ABSTRACT

48-year-old female with facial granulomatous nodules and fungal/bacterial infection after hyaluronic acid injection. She underwent anti-fungal/antibacterial therapy and local excision. The proposed mechanisms include inflammatory foreign body reaction and pathogen contamination. Providers must exercise caution with the use of facial fillers and demonstrate expertise in avoiding and managing potential complications.

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Filler; hyaluronic acid; adverse reaction; nasolabial folds

Introduction



Over the past two decades, facial fillers have become an increasingly popular and widely used method of facial rejuvenation [1,2]. They provide a relatively safe, non-invasive way to achieve a more youthful appearance without the risks of surgery. Hyaluronic acid fillers have become the facial filler of choice because, overall, they are safe, effective, long lasting, less immunogenic and easy to store and apply [3]. Due to the growing market and profitability, many other medical practitioners have begun to incorporate the use of fillers into their practice [4]. Although fillers provide a non-surgical approach to the restoration of volume and youthfulness to the face, they are not harmless products. This is a clinical case of hyaluronic acid injection by a non-plastic surgeon that induced an unexpected adverse reaction resulting in subsequent infection and irreversible scarring.

Case report

A 48-year-old woman presented with facial lesions ten months after injection with hyaluronic acid filler into her glabella, nasolabial folds and marionette lines performed by an outside dermatologist. Information about the exact product used and dosing was

unavailable to us. One month after the filler injection, she developed a hypersensitivity reaction consisting in facial edema, erythema, itchiness and mild fever (Figure 1). She was evaluated with computed tomography (CT) scan at an outside hospital which demonstrated preseptal cellulitis and soft tissue edema without evidence of abscess. This cellulitic reaction was treated with intravenous (IV) antibiotics and intramuscular steroids and resolved without complication. Seven months later, the patient used a brand-new suction powered facial pore cleansing device on her entire face. Thereafter, she developed enlarging ulcerated lesions only on areas previously injected with hyaluronic acid filler. The microscopic examination performed by her dermatologist revealed the presence of fungal hyphae. For this reason, the patient was referred to our institution for further management.

Upon admission, patient exhibited verrucous granuloma-like skin lesions on glabellar region, nasolabial folds and marionette lines (Figure 2(A,B)). CT face scan with IV contrast revealed abnormal cutaneous and subcutaneous heterogeneous enhancing consistent with phlegmon or early abscess formation (Figure 2(C,D)). She was treated with amphotericin B (5 mg/kg IV q24h for 2 weeks) guided by infectious disease consultants. In addition, local cultures of the lesions reported the presence of *Escherichia coli*, *Enterococcus*

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Figure 1. One month after the hyaluronic acid filler injection, patient developed a facial hypersensitivity reaction consisting in facial edema, erythema, itchiness and mild fever.

faecalis, and *Staphylococcus epidermidis*. Accordingly, vancomycin (15 mg/kg IV q12h) and meropenem (2 g IV q8h) were also added for 1 week. On post-admission day 15, we proceeded with definitive surgical debridement *via* wide local excision followed by wound care for healing by secondary intention (Figure 3(A–D)). On gross examination, the specimens appeared granulomatous in nature with liquefactive necrosis (Figure 4(A)). Final pathology reported the presence of squamous epithelium with chronic lymphohistiocytic inflammation and fibrinopurulent exudate including foreign body giant cells (Figure 4(B)). Grocott's methenamine silver (GMS) stain with adequate positive and negative controls were negative for fungal infection.

After significant clinical improvement, the patient was discharged with oral antibiotics and plans for close follow-up and future scar revision. Thus, based on culture results from intraoperative tissue samples, infectious disease team recommended doxycycline (100 mg by mouth twice a day for 14 days) and no further antifungal agents. She was seen most recently eight months post operatively. She showed no signs of ongoing infection and wounds were well healed. However, the deep scarring in the nasolabial folds has made the folds more prominent (Figure 5). This is an

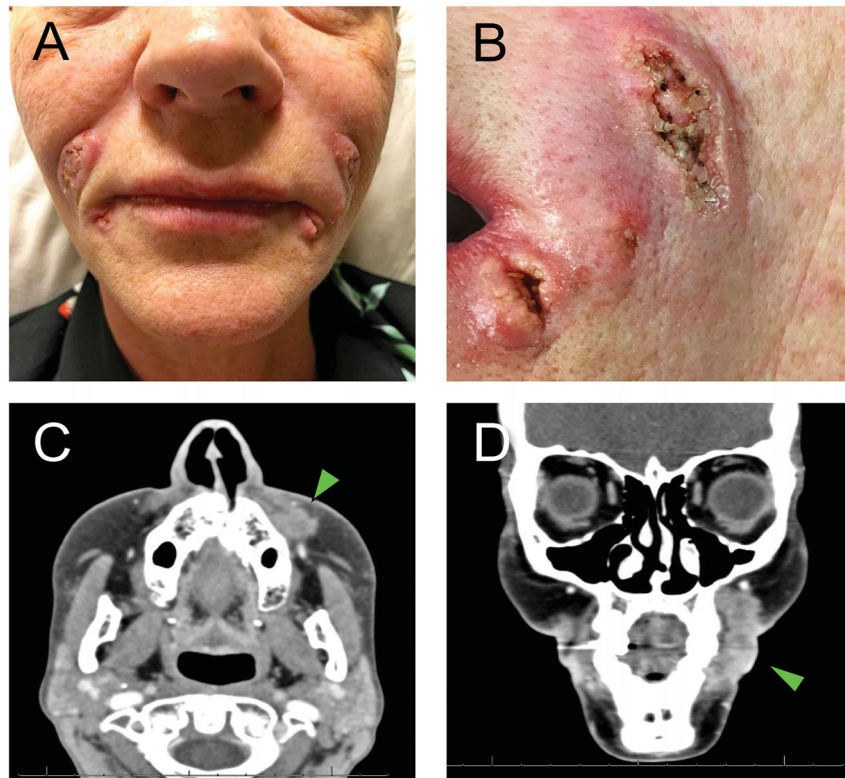


Figure 2. A. Verrucous ulcerative skin lesions on nasolabial folds, marionette lines and glabella region (not shown). B. Detail of the lesions on the left side of the face. C and D. Arrowheads show the abnormal heterogeneous enhancing soft tissue extending along the lateral left maxilla (1.6 cm AP by 1.0 cm transverse by 2.6 cm craniocaudal dimensions).

aesthetic concern for the patient, but in an attempt to avoid direct excision or reinjection of foreign material locally, we have discussed alternatives which include laser of the affected area and partial scar revision.

Discussion

The most common filler complications include bruising, swelling, over- or under-volumization, and, more concerning, infection, vascular occlusion, and blindness [5]. This case, in contrast, represents an unusual delayed inflammatory and infectious complication.

It is unclear what caused our patient's ulcerative lesions. She had a complex presentation with multiple factors that contributed to the progression of her facial lesions. Based on her presentation and review of the literature, we hypothesize that she initially had an allergic type reaction. Even though the CT report attributed the event as preseptal cellulitis, she had other areas of inflammation at other injection sites as demonstrated in the photograph and a pattern mimicking angioedema (Figure 1). Subsequently, the aggressive suction-assisted pore cleansing of the face could potentially create microscopic epidermal

abrasions leading to inadvertent inoculation of pathogenic agents. Interestingly, she developed delayed inflammatory foreign body reaction lesions only in those areas where the hyaluronic acid filler was previously injected. In this regard, although the patient claims impeccable technique by the injecting provider, it is not possible to eliminate suboptimal technique at the time of injection. Accordingly, *Mycobacterium* facial infections due to the topical application of non-sterile ice prior to the filler injection has been described [6,7]. In addition, the patient states that the stock of fillers at her provider's office was investigated without any evidence of contamination. This finding is consistent with several reports about the sterility of partially used hyaluronic acid fillers [8,9].

There have only been few reports of similar complications in the literature, and this is the only case exhibiting all three features: allergic, inflammatory, and infectious [5-7,10-12]. The potential underlying mechanisms for this rare unexpected course of hyaluronic acid filler injection include: 1) immediate and delayed hypersensitivity reactions, and 2) granuloma formation mediated by either inflammatory foreign body reactions or bacterial biofilm aggregation.

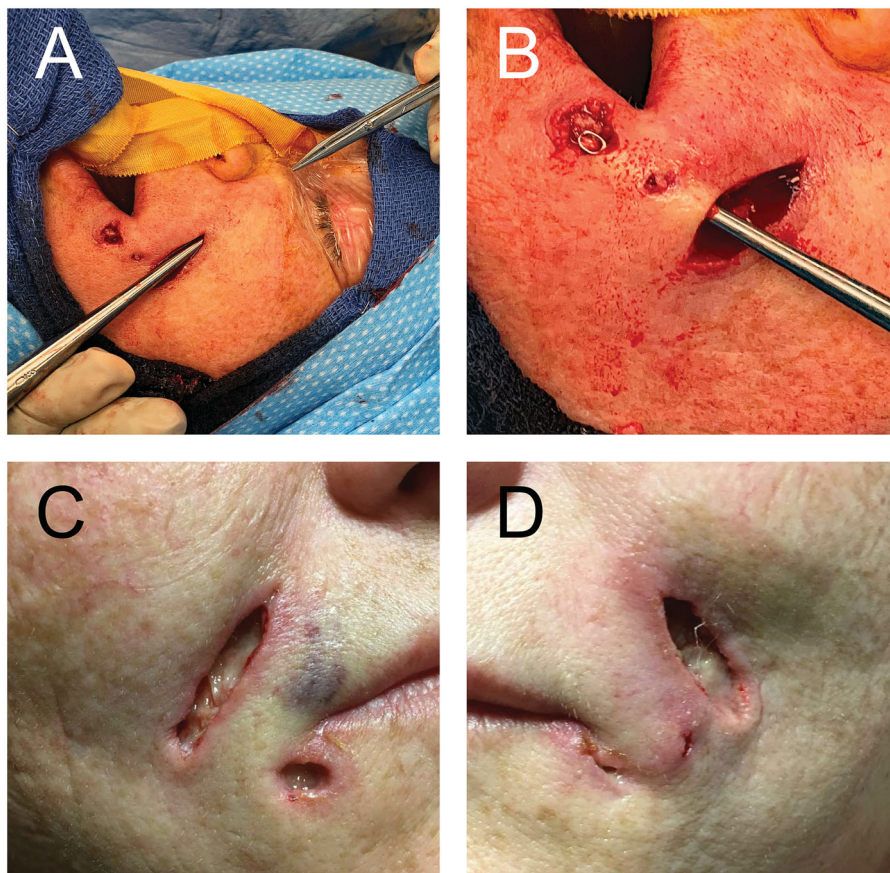


Figure 3. A and B. Intraoperative images showing the communication between nearby lesions and extension up to the infraorbital rim. C and D. Postoperative wounds that healed with regular dressing by secondary intention.

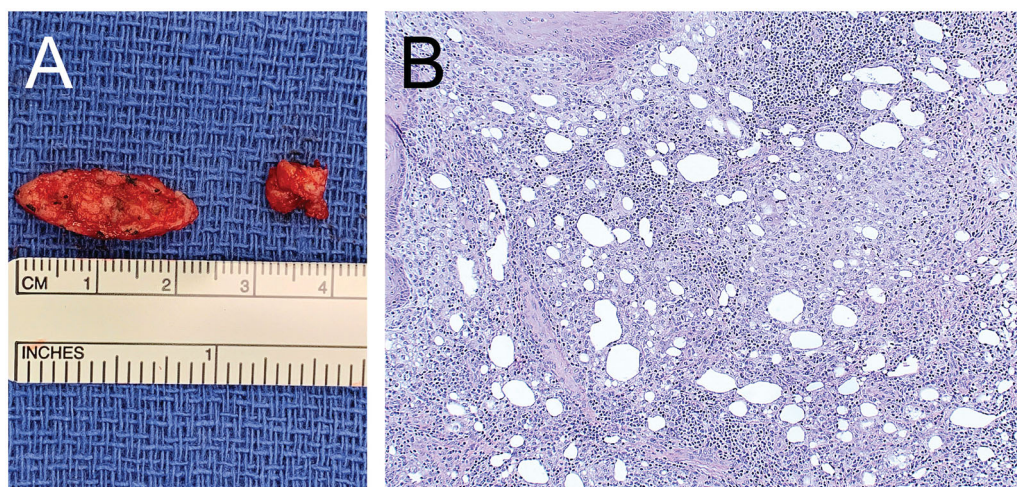


Figure 4. A. Intraoperative image showing the specimens from the left nasolabial fold and left marionette line. B. Hematoxylin-eosin stain showing lipogranulomas with granulomatous inflammation within the connective tissue stroma (20× magnification).



Figure 5. Eight months after surgical excision of verrucous skin lesions. Patient showed no signs of ongoing infection and wounds are well healed. Deep scarring in the nasolabial folds has made the folds more prominent.

Several authors have described in detail type I histamine and IgE mediated hypersensitivity reactions as well as delayed type IV T-cell mediated hypersensitivity reactions as unusual complications of hyaluronidase injection [13,14]. The former can be seen in rare cases that rapidly progress to angioedema [5,10,13–17].

In our patient, the clinical assessment of the lumps as well as their subsequent pathologic examination (Figures 2 and 4) support the diagnosis of granulomatous formation. It seems that the initial injection of filler triggers a physiologic foreign body reaction as a result of an influx of inflammatory cells [5–14,16,18]. However, when there is a failure of effective phagocytosis of such inflammatory cells, the original self-limited response can progress to a severe inflammatory

granulomatous process [10,13]. The underlying mechanism that induces this adverse transformation is currently not well understood [13]. Such reactions may be also triggered by formation of bacterial biofilms which have similar presentation and are equally difficult to treat [10,19].

As final contributing factor in our case, the patient was transferred to our institution with diagnosis of fungal infection. Although no fungal growth was obtained in additional cultures after admission, appropriate treatment was established following the recommendation of infectious disease colleagues.

Ultimately, the combination of antibacterial and antifungal systemic treatments along with surgical excision eradicated any ongoing infection without further complication.

Conclusion

In summary, we report an unusual progression of rare complications of hyaluronic acid injection in a single patient. This type of cases requires a multidisciplinary approach with a combination of systemic and surgical management [13,15]. It is also important to emphasize the need for awareness and caution when injecting facial fillers as well as expertise in avoiding and managing potential complications.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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