CLINICAL VIGNETTE

Angioedema-type Hypersensitivity Reaction Following Hyaluronic Acid Dermal Filler After Recent SARS-CoV-2 Vaccination

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Introduction

Despite the continuing pandemic, demand for cosmetic procedures has remained strong, largely due to increased vaccination efforts providing patients and providers with a renewed sense of confidence against contracting the SARS-CoV-2 virus. The use of injectable hyaluronic acid (HA) dermal fillers continues to grow, with market estimates exceeding $1 billion annually.[1] Pre-market trials have revealed reassuring safety data for these products, though discussions with patients centered on potential risks are essential.[2] Providers should now also consider the impact of SARS-CoV-2 vaccination.

HA dermal fillers offer reassuring safety data; with a large review reporting an adverse event rate of just 0.06%.[3] The risk of delayed inflammatory reactions (DIR) after injection of HA dermal fillers has been reported to range from 0.02-4.25%.[1] The latter is notable given 8 recent reports of DIR in patients with HA dermal fillers following SARS-CoV-2 vaccination, in which patients received filler weeks to months prior to vaccination.[1,4]

We report a case of lip angioedema-type reaction with associated malaise and myalgia presenting hours after newly injected HA dermal filler 14 days after second dose of Moderna mRNA SARS-CoV-2 vaccine.

Case Presentation

A 48-year-old woman with history of asymptomatic Hashimoto's thyroiditis controlled without medication, melasma treated with systemic tranexamic acid, and asthma with as needed inhaler use, presented to our outpatient dermatology clinic in February 2021 for soft tissue augmentation. This was her second treatment with HA dermal fillers, having previously received 0.7 cc of Juvederm Ultra in the upper and lower lips and 1 cc of Juvederm Voluma in the malar cheeks 16 months prior. She had no immediate or delayed-onset complications after these initial treatments. Three days prior to this visit, the patient tested negative for SARS-CoV-2. At the visit, 0.5 cc of Restylane Silk was injected into the upper and lower mucosal lips, and 2 cc of Restylane Refyne was injected into the malar cheeks. She had received the second dose of the Moderna SARS-CoV-2 vaccine 14 days prior. The patient tolerated the procedure well with no immediate complication (Figure 1a).

Six hours after HA dermal filler treatment, the patient felt progressive tightening of her upper and lower lips. Photographic evaluation revealed angioedema of the mucosal lips, especially the upper lip (Figure 1b). Concurrently, the patient also reported bilateral calf pain and spasms along with generalized malaise, replicating symptoms she experienced after the second dose of the Moderna SARS-CoV-2 vaccine.

The patient was immediately started on cetirizine 10 mg twice daily, and oral corticosteroids were also prescribed, but the patient deferred. Twenty-four hours after injection, the patient reported lip swelling was increased, and myalgia and malaise persisted (Figure 1c). As such, the patient started Medrol dose pack while continuing cetirizine 10 mg twice daily. Within 1 day, the patient reported modest improvement in lip swelling along with resolution of myalgia and malaise. Lip angioedema resolved after day 7 of oral corticosteroids, at which time antihistamines were also stopped (Figure 1d).

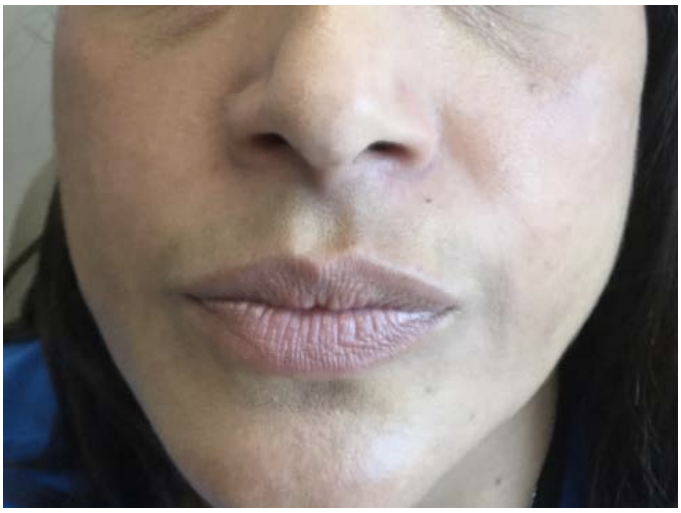

Figure 1a. Frontal view of the lips at baseline before injection.

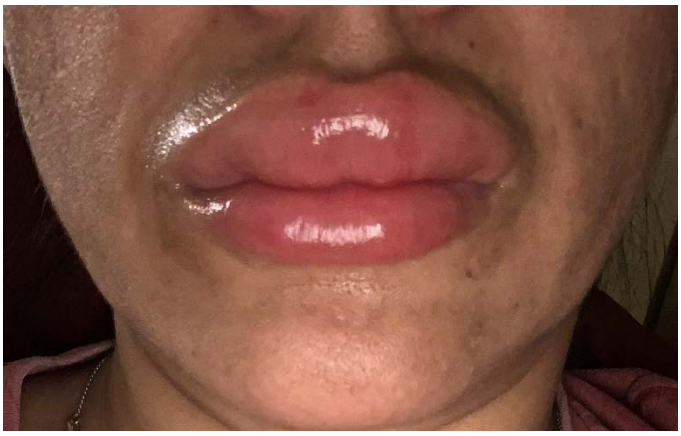

Figure 1b. Prominent angioedema-type swelling affecting the upper greater than lower mucosal lips present 6 hours after dermal filler injection.

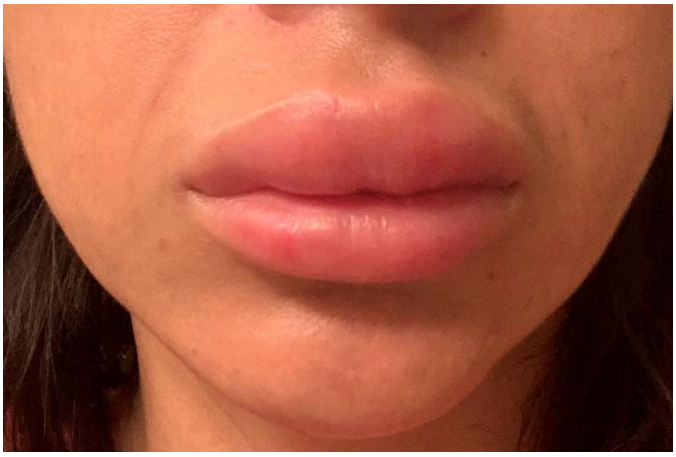

Figure 1c. Angioedema-type swelling persisted 24 hours status post dermal filler injection.

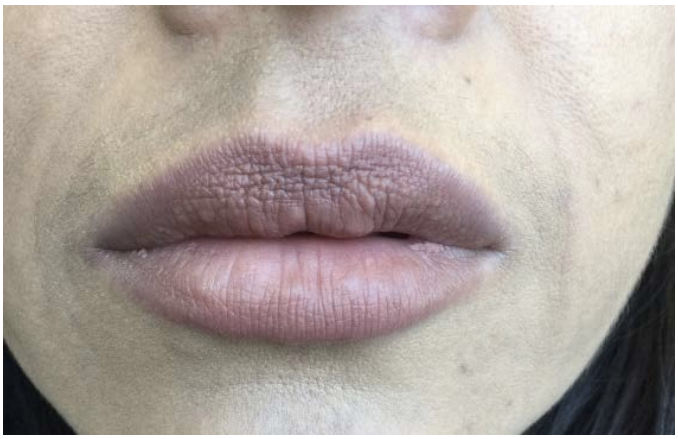

Figure 1d. The patient's swelling resolved with return to normal at 1-week status post dermal filler injection.

Discussion

Injection of HA dermal fillers is increasingly popular for aesthetic facial enhancement. As seen in clinical practice, lip swelling is expected after injection but is generally mild and self-limited. Systemic symptoms such as malaise or myalgias are not expected. Multinational data on NASHA fillers revealed that when these rare complications present, edema, erythema, and tenderness last, on average, for 4 days.[3]

Our patient's angioedema presented with concurrent malaise and myalgia, which mimicked her experience 2 weeks prior following the second dose of the Moderna vaccine. We postulate that continued immune activation from recent vaccination heightens immune surveillance. In the post vaccination setting, there is a plausible higher likelihood of immune detection of the HA dermal filler as a neoantigen, resulting in a subsequent inflammatory cascade.

The Pfizer and Moderna mRNA vaccines' phase I trials measured antibody response 2 weeks after the second dose, suggesting ongoing antibody formation.[5] More data about antibody formation from the phase III trials will better clarify the immunologic response. In addition, the extent and duration of her angioedema-type hypersensitivity occurred after injection of just 0.5 cc of HA dermal filler.

Given existing data and understanding of the body's response to SARS-CoV-2 vaccination, pre-treatment discussion with patients seeking HA fillers would benefit from inclusion of planning around SARS-CoV-2 vaccination to accompany review of risks, benefits, and screening for dental procedures and herpes simplex virus.[2] While our findings and previously reported cases of DIR following vaccination occurred in the setting of mRNA vaccines, caution should also be exercised in the setting of modified adenovirus vaccines.

As seen in prior reports of DIR following SARS-CoV-2 vaccination with angioedema-like presentations, our patient improved rapidly with oral corticosteroids. Previously reported cases of DIR were treated with hyaluronidase injection, oral antihistamine, oral corticosteroids, oral antibiotics (e.g., doxycycline and nitrofurantoin), intralesional 5-fluorouracil, and lisinopril, the latter of which resulted in resolution of angioedema within 1 to 3 days with 5 to 10 mg administration.[1,2,4]

Conclusion

We report a case of localized angioedema-like hypersensitivity reaction with concurrent systemic myalgia and malaise in the setting of HA dermal filler administered 2 weeks after the second dose of SARS-CoV-2 mRNA vaccination. While we hypothesize her reaction being correlated with her recent vaccination and the use of Restylane NASHA gel filler, less likely contributing factors to this patient's immediate adverse reaction may include a DIR 2 weeks after vaccination related to her prior Juvederm filler or her underlying autoimmune disease. Vaccinated patients should not be precluded from dermal fillers. However, providers should discuss with recently vaccinated patients the potential risk of reactions to HA dermal filler injections. We recommend that patients be screened for recent SARS-CoV-2 vaccination and informed of possible reactions before being treated with HA dermal fillers. If angioedema-type hypersensitivity reaction were to present,

treatment options include corticosteroids, antihistamines, or possibly lisinopril, with the expectation of resolution.

Disclosures: There are no conflicts of interest in this study, and no authors have any disclosures.

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