

Images in Allergy

Masquerader of Lip Angioedema After Lip Injection

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A 27-year-old woman with specific antibody deficiency who was receiving immunoglobulin replacement therapy, with complex congenital heart disease (tetralogy of Fallot, pulmonary atresia, and major aortopulmonary collaterals), with group I pulmonary hypertension and resolved Cushing syndrome resulting from prior chronic steroid treatment, presented urgently with acute lip angioedema.

In July 2020, she began to notice that the upper lip was swollen. Later, the lower lip became swollen as well (Figure 1). When she presented to the clinic through telehealth 12 days later, the lower lip was more swollen than the upper lip (Figure 2). She denied having shortness of breath, recent trauma, infection, new medication, urticaria, or rash. She was not taking an angiotensin-converting-enzyme inhibitor and had stopped most medications one by one for a few days without relief. The swollen lip was not responding to high-dose antihistamines. There was no family history of angioedema or personal history of thyroid or autoimmune problems, and she was not pregnant.

While the patient had a virtual physical examination, she was found to have four indurated painful nodules in the inner lower and upper lips (Figure 2), which were inconsistent with angioedema. She had received four lip injections with a soft tissue filler (JUVÉDERM VOLBELLA XC, a hyaluronic acid gel, Allergan plc, Coolock, Dublin, D17 E400, Ireland) 4 months earlier. The locations of these nodules corresponded to the hyaluronic acid injection sites. Lip mucosal biopsy revealed granulomatous mucositis with eosinophilic infiltrates and the presence of hyaluronic acid deposits (Figure 3). It was concluded that she had developed a delayed granulomatous hypersensitivity reaction to the filler and was given the diagnosis of lip pseudo-angioedema. Oral steroid therapy was considered after lip biopsy, but she preferred not to take it

owing to her prior history of secondary Cushing syndrome. The lip swelling eventually resolved spontaneously without scarring within 2 weeks. We recommended against new hyaluronic acid injections.

Many conditions can mimic angioedema, and the increasingly popular cosmetic procedure of filler material injections can pose new clinical challenges. Careful evaluation including a history of prior lip injections and a physical examination is important to diagnosis and treatment. Mucosal biopsy may be performed but is not required for diagnosis. There are several ways to classify filler adverse reactions (eg, severity, nature). Complications can also be categorized by timing, and in fact the timing will often determine the management approach. Common classifications include early (0-14 days after injection), late (14 days to 1 year), and delayed (more than 1 year). Whereas early complications often present as an infection or an acute inflammation, late and delayed complications may result from granuloma formation. In this case, the patient had a noninfectious, late-onset, inflammatory nodule (granuloma on biopsy).¹ Management of hyaluronic acid-induced granulomas may include intralesional hyaluronidase injection to reverse its effects and oral or intralesional steroids with or without intralesional 5-fluorouracil. In some cases, laser excision may be used. Antihistamines are ineffective. With 2.6 million soft tissue filler injections a year,² we anticipate that allergists may encounter more patients with this type of pseudo-angioedema.

REFERENCES

1. Graivier MH, Bass LM, Lorenc ZP, Fitzgerald R, Goldberg DJ, Lemperle G. Differentiating nonpermanent injectable fillers: prevention and treatment of filler complications. *Aesthet Surg J* 2018;38(suppl 1):S29-40.
2. American Society of Plastic Surgeons. Plastic Surgery Statistics Report. 2018. Available from: <http://www.plasticsurgery.org>. Accessed September 15, 2020.

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FIGURE 1. Patient developed swelling of the lips that mimicked angioedema.



FIGURE 2. Presence of two indurated painful nodules in the inner lower lip (black arrows).

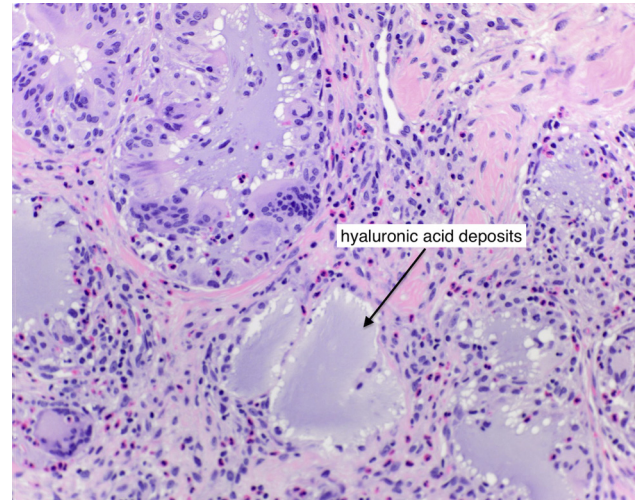


FIGURE 3. Histiocytes and histiocytic giant cells joined by eosinophils surrounding pale blue homogeneous material (hyaluronic acid deposits shown with black arrow); hematoxylin and eosin; magnification 400 $\times$.