



## CORRESPONDENCE

# Hyaluronic acid injection-induced delayed-onset foreign body granuloma

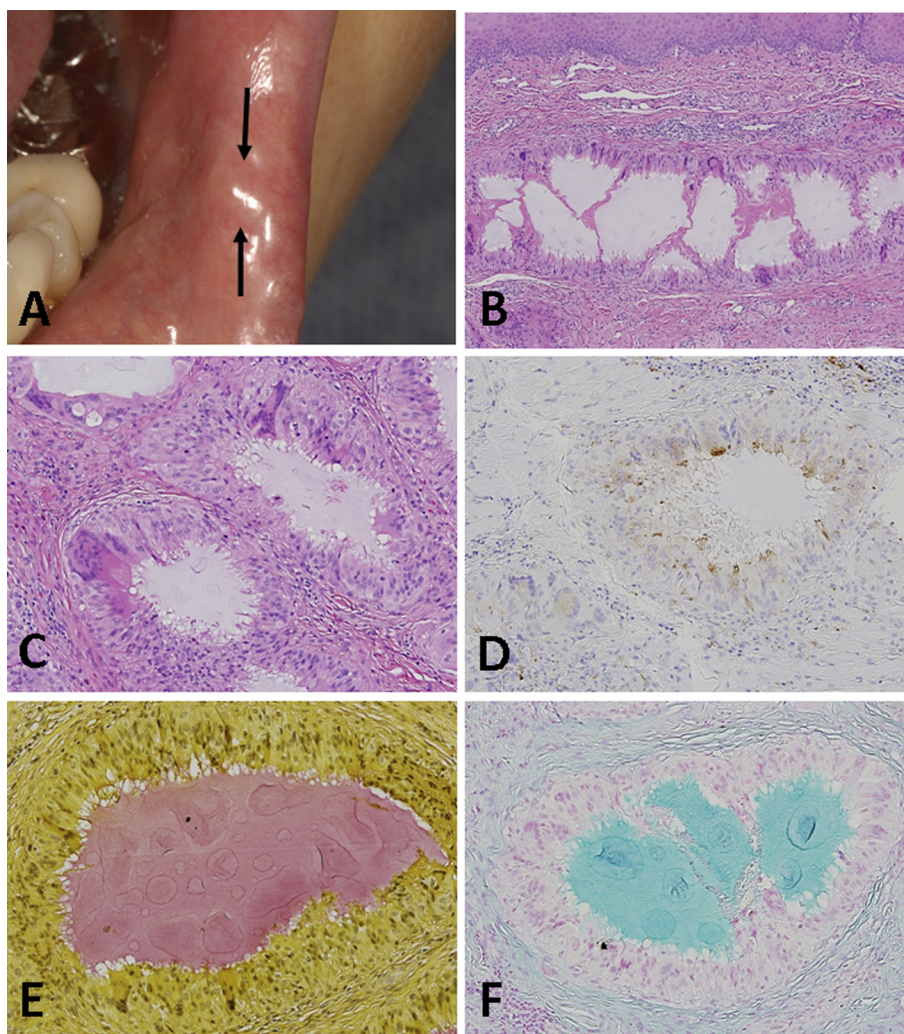


Injection of hyaluronic acids (HAs) as dermal fillers for cosmetic purpose is common and generally accepted as a safe and well-tolerable procedure. However, adverse reactions such as infection and foreign body reaction sometimes occur. Here, we report a case of delayed foreign body reaction to HA materials in a moderately distant location from the injection site.

This 73-year-old female patient complained of a swelling at the left mouth angle for 2 weeks. The patient denied all systemic diseases and drug or food allergy. A well-circumscribed submucosal nodule measuring 1.4 cm × 0.8 cm in area with firm consistency was identified at the left mouth angle (Figure 1A). No evidence of redness, local heat, or tenderness was noted. Under the impression of sialadenitis, a biopsy was performed. The biopsy specimen showed multiple various-sized duct-like structures irregularly distributed in the lamina propria, submucosa, and underlying muscle layer (Figure 1B). These duct-like structures were composed of a central pool of amorphous pale basophilic materials surrounded by aggregates of epithelioid histiocytes and multinucleated giant cells (Figure 1C). Anti-CD68 immunostain confirmed that the cells surrounding the central pool were epithelioid histiocytes and multinucleated giant cells (Figure 1D). These amorphous materials were positively stained with mucicarmine (Figure 1E) and alcian blue stains (Figure 1F) and negatively stained with periodic acid–Schiff, Gomori methenamine silver, and acid fast stains (data not shown). A foreign body granuloma was diagnosed. Although the patient did not mention a history of cosmetic injection at the initial clinical visit, it was later found that she had two injections of 1 cm<sup>3</sup> of HA (JUVÉDERM VOLUMA XC, Allergan Inc., Irvine, CA, USA) 3 months and 18 months ago,

respectively, into the nasolabial fold. Thus, an HA injection-induced delayed-onset foreign body granuloma in a moderately distant location from the injection site was further confirmed.

Subcutaneous injection of different dermal fillers for cosmetic soft-tissue augmentation has become popular. Although these dermal fillers are generally thought to be safe, a variety of adverse reactions including infection, allergy, and foreign body reaction have been reported.<sup>1</sup> The complications associated with the dermal filler injection may be of immediate, early (within days), or delayed (after weeks to years) onset. Among these complications, delayed reactions usually result in diagnostic problems because of long-standing durations and the distance between the swelling and previous filler injection site. HA is a natural polysaccharide present in the body and has been considered as immunologically inert. Because of the biocompatibility and temporary duration of approximately 6–9 months, HA is not commonly associated with many long-term adverse reactions. JUVÉDERM VOLUMA XC is a cross-linked HA filler produced by *Streptococcus equi* bacteria, formulated to a concentration of 20 mg/mL in a physiologic buffer. HA injection-induced early onset complications including swelling, erythema, and nodule formation are common and reported in 62–71% patients, however, the delayed-onset complications such as foreign body granuloma are rare.<sup>1</sup> It is also worthwhile to mention that the HA filler may migrate to a distant site to form a foreign body granuloma similar to this case. Surgical excision remains the only effective treatment of choice. Immunostains can be used to identify specific cells in various lesions.<sup>2–5</sup> In this study, anti-CD68 stain was used to confirm that the cells surrounding the HA pool were histiocytes and multinucleated giant cells.



**Figure 1** Clinical, histopathological, and immunostained photographs of a hyaluronic acid (HA) injection-induced foreign body granuloma. (A) Clinical photograph of the lesion showing a well-circumscribed nodule in the left mouth angle (arrows). (B, C) Histopathological microphotographs of the lesion revealing multiple duct-like structures composed of a central pool of amorphous pale basophilic materials surrounded by aggregates of epithelioid histiocytes and multinucleated giant cells in the lamina propria, submucosa, and underlying muscle layer (hematoxylin and eosin stain; original magnification: B, 10 × and C, 20 × ). (D) Immunohistochemical stain showing CD68-positive epithelioid histiocytes and multinucleated giant cells surrounding a lumen-like structure (original magnification: 20×). (E) Mucicarmine and (F) alcian blue stains demonstrating the pink- and blue-stained HA materials in the lumen-like structures (original magnification: 20×).

### Conflicts of interest

The authors have no conflicts of interest relevant to this article.

### References

1. Ledon JA, Savas JA, Yang S, Franca K, Camacho I, Nouri K. Inflammatory nodules following soft tissue filler use: a review of causative agents, pathology and treatment options. *Am J Clin Dermatol* 2013;14:401–11.
2. Chen J-C, Chang Y-K, Chiang W-F, Lu D. Palatal diffuse large B-cell lymphoma masquerading as an infiltrative bony mass. *J Dent Sci* 2013;8:98–9.
3. Lu S-Y, Lin C-F, Huang S-C. Metastatic oral malignant melanoma transformed from pre-existing pigmented lesions in mandibular gingiva: report of an unusual case. *J Dent Sci* 2013;8:328–32.
4. Wu Y-C, Wang Y-P, Chang JY-F, Chiang C-P. Langerhans cells in lining epithelia of epidermoid cysts. *J Dent Sci* 2013;8:448–50.
5. Chen H-M, Wu Y-C, Wei L-Y, Chiang C-P. Metastatic hepatocellular carcinoma of the anterior palatal gingiva. *J Dent Sci* 2014; 9:202–4.

Chih-Huang Tseng  
Graduate Institute of Clinical Dentistry, School of  
Dentistry, National Taiwan University, Taipei, Taiwan

Yi-Ping Wang  
Graduate Institute of Clinical Dentistry, School of  
Dentistry, National Taiwan University, Taipei, Taiwan

Department of Dentistry, National Taiwan University  
Hospital, College of Medicine, National Taiwan University,  
Taipei, Taiwan

*Graduate Institute of Oral Biology, School of Dentistry,  
National Taiwan University, Taipei, Taiwan*

Hsin-Ming Chen

*Graduate Institute of Clinical Dentistry, School of  
Dentistry, National Taiwan University, Taipei, Taiwan*

*Department of Dentistry, National Taiwan University  
Hospital, College of Medicine, National Taiwan University,  
Taipei, Taiwan*

*Graduate Institute of Oral Biology, School of Dentistry,  
National Taiwan University, Taipei, Taiwan*

Julia Yu Fong Chang\*

*Graduate Institute of Clinical Dentistry, School of  
Dentistry, National Taiwan University, Taipei, Taiwan*

*Department of Dentistry, National Taiwan University  
Hospital, College of Medicine, National Taiwan University,  
Taipei, Taiwan*

*Graduate Institute of Oral Biology, School of Dentistry,  
National Taiwan University, Taipei, Taiwan*

\*Corresponding author. Department of Dentistry, National  
Taiwan University Hospital, College of Medicine, National  
Taiwan University, Number 1, Chang-Te Street, Taipei  
10048, Taiwan.

*E-mail address: [jyfchang@ntu.edu.tw](mailto:jyfchang@ntu.edu.tw) (J.Y.F. Chang)*

Received 26 January 2015  
Available online 30 July 2015