Ossification and Migration of a Nodule Following Calcium Hydroxylapatite Injection

Victor Zhu, MD; Eric L. Cole, MD

PRACTICE **POINTS**

- Calcium hydroxylapatite filler can migrate and form nodules in distant locations from the original injection site.
- Practitioners of calcium hydroxylapatite fillers should be aware of the potential for nodule migration to avoid costly, time-consuming, and invasive referrals and procedures.

To the Editor:

Calcium hydroxylapatite is an injectable filler approved by the US Food and Drug Administration for moderate to severe rhytides of the face and the treatment of facial lipodystrophy in patients with HIV.¹ This long-lasting filler generally is well tolerated with minimal side effects; however, there have been reports of nodules or granulomatous formation following injection of a calcium hydroxylapatite filler that appeared ossified on radiographic imaging. We highlight this rarely reported phenomenon to increase awareness of this complication.

A 72-year-old woman presented to our clinic with a mass on the left cheek. The patient had a history of treatment with facial fillers but no notable medical conditions. She initially received hyaluronic acid injectable gel dermal filler twice—3 years apart—before switching to calcium hydroxylapatite injections twice—4 months apart—from an outside provider. One month after the

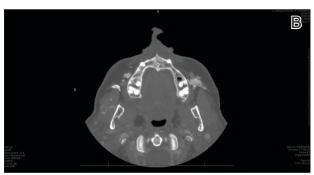
second treatment, she noticed a mass on the left cheek and promptly returned to the provider who performed the calcium hydroxylapatite injections. The provider, who had originally injected in the infraorbital area, stated it was unlikely that the filler would have migrated to the mid cheek and referred the patient to a general dentist who suspected salivary gland pathology. The patient was referred to an oral and maxillofacial surgeon who suspected the mass was related to the parotid gland. Maxillofacial computed tomography (CT) revealed heterotopic ossification vs myositis ossificans, possibly related to the recent injection. The patient was eventually referred to the Division of Plastic Surgery, Department of Surgery, at the University of Texas Medical Branch (Galveston, Texas) for further evaluation. Physical examination revealed a 2×1-cm firm, mobile, nontender mass in the left cheek in the area of the buccinator muscles. The mass did not express any fluid and was most easily palpable from the oral cavity. Radiography findings showed that the calcium hydroxylapatite filler had migrated to this location and formed a nodule (Figure). Because calcium hydroxylapatite fillers generally last 12 to 18 months, we opted to observe the lesion for spontaneous resolution. Four months later, the patient presented to our clinic for follow-up and the mass had reduced in size and appeared to be spontaneously resolving.

We present a unique case of a migrating nodule that occurred after injection with calcium hydroxylapatite, which led to concern for neoplastic tumor formation. This complication is rare, and it is important for practitioners

From the Division of Plastic Surgery, Department of Surgery, University of Texas Medical Branch, Galveston. The authors report no conflict of interest.

Correspondence: Eric L. Cole, MD, Division of Plastic Surgery, Department of Surgery, University of Texas Medical Branch, 301 University Blvd, Galveston, TX 77555-0724 (elcole@utmb.edu). doi:10.12788/cutis.0635







A-C, Computed tomography of the maxillofacial axial regions showed high-attenuation linear streaks and nodules of similar signal intensity as bone, signifying injected calcium hydroxylapatite.

who inject calcium hydroxylapatite as well as those who these patients may be referred to for evaluation to be aware that migrating nodules can occur. This awareness can help reduce unnecessary referrals, medical procedures, and anxiety.

Calcium hydroxylapatite filler is composed of 30% calcium hydroxylapatite microspheres suspended in a 70% sodium carboxymethylcellulose gel. The water-soluble gel rapidly becomes absorbed upon injection; however, the microspheres form a scaffold for the production of newly synthesized collagen. The filling effect generally lasts 12 to 18 months.1

Calcium hydroxylapatite, similar to most fillers, generally is well tolerated with a low complication rate of 3%. Although nodule formation with calcium hydroxylapatite is rare, it is the most common adverse event and encompasses 96% of complications. The remaining 4% of complications include persistent inflammation, swelling, erythema, and technical mistakes leading to overcorrection. 1 Migrating nodules are rare; however, Beer 3 reported a similar case.

Treatment of calcium hydroxylapatite nodules depends on differentiating a cause based on the time of onset. Early nodules that occur within 1 to 2 weeks of the injection usually represent incorrect positioning of the filler and can be treated by massaging the nodule. Other more invasive techniques involve aspiration or injection of sterile water. Late-onset nodules have shown response to corticosteroid injections. For inflammatory nodules of infectious origin, antibiotics can be useful. Surgical excision of the nodule rarely is required, as most nodules will resolve spontaneously, even without intervention.^{1,2}

Radiologic findings of calcium hydroxylapatite appear as high-attenuation linear streaks or masses on CT (280-700 HU) and as low to intermediate signal intensity on T1- or T2-weighted sequences on magnetic resonance imaging. Oftentimes, calcium hydroxylapatite has a similar radiographic appearance to bone and can persist for 2 years or more on radiographic imaging, longer than they are clinically visible.4 The nodule formation from injection with calcium hydroxylapatite can mimic pathologic conditions such as miliary osteomas, myositis ossificans, heterotrophic/dystrophic calcifications, and foreign bodies on CT. Our patient's CT findings of high attenuation linear streaks and nodules of similar signal intensity to bone were consistent with those previously described in the radiographic literature.

Calcium hydroxylapatite fillers have a good safety profile, but it is important to recognize that nodule formation is a common adverse event and that migration of nodules can occur. Practitioners should recognize this possibility in patients presenting with new masses after filler injection before advocating for potentially invasive and costly procedures and diagnostic modalities.

REFERENCES

- 1. Kadouch JA. Calcium hydroxylapatite: a review on safety and complications. J Cosmet Dermatol. 2017;16:152-161.
- Moulinets I, Arnaud E, Bui P, et al. Foreign body reaction to Radiesse: 2 cases. Am J Dermatopathol. 2013;35:e37-40.
- Beer KR. Radiesse nodule of the lips from a distant injection site: report of a case and consideration of etiology and management. J Drugs Dermatol, 2007;6:846-847.
- Ginat DT, Schatz CJ. Imaging features of midface injectable fillers and associated complications. AJNR Am J Neuroradiol. 2013;34:1488-1495.