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# Foreign body reaction to calcium hydroxylapatite after lip augmentation

Vidya Sankar, DMD, MHS; H. Stan McGuff, DDS

**S**oft-tissue volume loss is a consequence of aging, and while the quest for the fountain of youth continues, more and more people are resorting to measures that recapture a more youthful appearance. Cosmetic facial enhancement with dermal fillers is becoming common.

Ideally, injectable dermal fillers should have the following properties: biocompatibility; safety; stability at the implant site; and the ability to maintain their volume, remain pliable, induce minimal foreign body reactions and not cause foreign body granuloma.<sup>1</sup> Many dermal fillers have been used, including autologous fat, bovine collagen, paraffin, fluid silicone, polytetrafluoroethylene (Teflon, DuPont, Wilmington, Del.) and polymer and silicone particles. Problems with free-fat grafts include uneven survival, variable resorption, formation of nodules and donor-site morbidity.

For these reasons, polymer par-

## ABSTRACT



**Background.** Dentists need to be aware of soft-tissue lesions resulting from cosmetic facial/lip procedures that involve the use of injectable materials. Common side effects detected on clinical examination may include edema, bruising and noninflammatory lip nodules.

**Case Description.** A 51-year-old woman visited a dental clinic with the chief complaint of a lump on the mucosal aspect of her lower lip. She reported having noted the lesion a few weeks before seeking care at the clinic. Several weeks later, the lesion persisted and new lesions were detected. The clinician excised the initial lesion only.

**Clinical Implications.** The lip nodules were associated with a cosmetic procedure and were inflammatory in nature. This is the first granulomatous response reported as a result of injections with calcium hydroxylapatite (Radiesse, BioForm Medical, San Mateo, Calif.). Poor patient recollection of his or her medical history may result in confusion with pathological processes such as infection, neoplasia or malignancy.

**Key Words.** Calcium hydroxylapatite; side effects; dermal fillers; cosmetic procedure.

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**Figure 1.** Lip nodules (arrows) similar to the intraoral lesion that was removed from the inner aspect of the lower lip on the left side.

ticle suspension fillers are being used more often. Fillers composed of resorbable materials include collagen, hyaluronic acid, polymethylacrylate, dextran, polylactic acid substances and, in recent decades, those consisting of viscous fluids or polymer particle suspensions. These fillers have been used to correct soft-tissue defects,<sup>1</sup> as well as fill in soft-tissue volume around the lips and nasolabial region.

Common medium-term fillers—those that are resorbed after several months—include hyaluronic acid derivatives (polylactic acids and calcium hydroxylapatite [CaHA]). Resorbable fillers eventually are phagocytosed.<sup>2</sup> Permanent or nonresorbable fillers larger than 15 micrometers are encapsulated with fibrous tissue and escape phagocytosis. Frequent side effects of resorbable and nonresorbable fillers include bruising, swelling, pain and hematoma formation.<sup>3-5</sup>

We report below a soft-tissue reaction to CaHA (Radiesse, BioForm Medical, San Mateo, Calif.), an injectable filler used to cosmetically enhance the lips.

## CASE REPORT

A 51-year-old woman visited the Tertiary Care Oral Medicine Clinic at The University of Texas Health Science Center at San Antonio with the chief complaint of a lump on the mucosal aspect of her lower lip on the left side. She reported that she first noted the lesion a few weeks before coming to the clinic. She described the lesion as

having appeared first as a lump, followed by a painful so-called fever blister. When the blister resolved, the lump remained. The fever blister area indicated by the patient was on the mucosal surface of the lip. The patient had a history of similar lesions developing on the ventral surface of the tongue and buccal mucosa. She denied having a history of recurrent herpes labialis. Therefore, we presumed the lesion to be an aphthous ulcer.

On the patient's initial visit to the clinic, the clinician (V.S.) found no signs of ulceration and the patient was asymptomatic. The actual lesion was a yellow nodule measuring 6 × 3 millimeters with well-defined, irregularly shaped borders that was firm on palpation.

The patient had no known drug allergies or history of adverse drug events. Her social history was significant for smoking one pack of cigarettes per day for the previous 25 years. The patient's medical history was pertinent for depression, for which she was receiving bupropion (Wellbutrin, GlaxoSmithKline, Philadelphia) treatment. Her medical history was otherwise unremarkable.

The patient returned six weeks later for a biopsy. At that visit, the clinician detected two new 2- to 3-mm lesions on the right and left vermilion borders of the lower lip (Figure 1). At this visit, the patient amended her medical history to include previous injections of cosmetic fillers; however, she thought that the lesion on the left side of the lip preceded the cosmetic injection. We later confirmed with the nurse who performed the procedure at the patient's physician's office that the material used for the cosmetic procedure was CaHA (Radiesse).

After anesthetizing the left side of the lower lip, the clinician made a 1-centimeter superficial incision along the mucosal aspect of the lip, thus exposing the lesion. The overlying mucosa and connective tissue appeared normal, and the clinician performed an excisional biopsy via blunt dissection. The lesion was attached to the surrounding connective tissue. The excised mass was pale yellow with a rubbery consistency.

**ABBREVIATION KEY.** CaHA: Calcium hydroxylapatite.

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**Fillers composed of resorbable materials have been used to correct soft-tissue defects, as well as fill in soft-tissue volume around the lips and nasolabial region.**  
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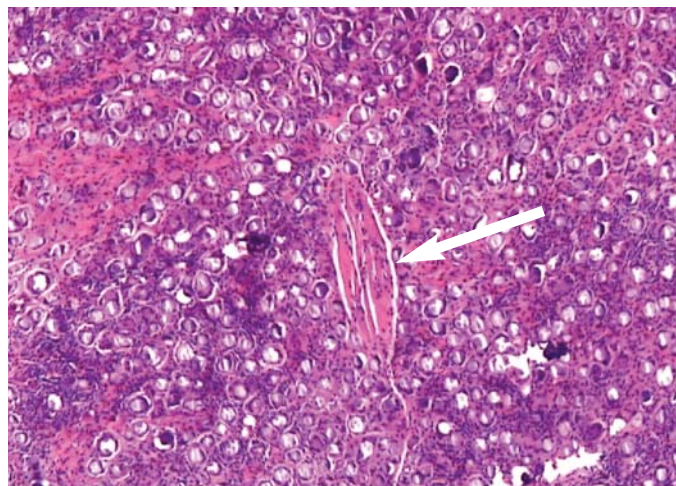
The final histologic diagnosis was the presence of a foreign material along with a florid foreign body giant cell reaction of the soft tissue, chronic inflammation and fibrosis. We also found evidence of chronic sclerosing sialadenitis. The foreign material was not birefringent under polarized light (Figures 2 and 3).

## DISCUSSION

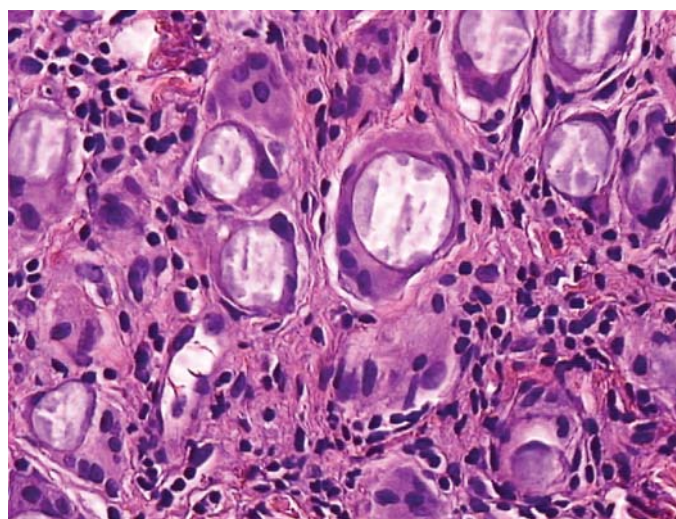
Radiesse is marketed as a next-generation injectable filler used in various cosmetic, reconstructive and therapeutic applications to augment and contour folds, depressions and defects of the facial area. This dermal filler is made of CaHA microspheres suspended in a gel carrier. The microspheres form a scaffold through which the body's own collagen grows, and this growth is what produces the desired long-term effect. The visual improvement is immediate and intended to last one year or longer. According to a November 2005 company press release, the product had been used in more than 150,000 procedures worldwide.<sup>6</sup>

Adverse events reported in published trials generally were mild, consisting of ecchymosis, edema, erythema, pain and pruritus.<sup>7</sup> Lip nodules develop in about 12.4 percent of patients undergoing lip augmentation and in 3.7 percent of those receiving radial lip lines.<sup>5</sup> In addition, Godin and colleagues<sup>3</sup> reported temporary visible product nodularity in up to 33 percent of patients. However, the duration of this temporary effect has not been defined. Sustained nodules may develop as a result of injecting the material too superficially in the connective tissue and/or injecting too much material.<sup>3</sup> These superficial nodules are removed by unroofing the area over the injected material with an 18-gauge needle.

Lemperle and colleagues<sup>1</sup> demonstrated histologically that Radiesse microspheres are packed and surrounded by fibrin fibers and by little cellular tissue. As the lesions age, the implants (that is, the injected material) are surrounded by a fine fibrous capsule, and single microspheres are encapsulated by a thin fibroblastic stroma with flattened cells. Specifically, until now, no granulomatous formations have been reported with this product.<sup>5</sup> Because Lemperle and colleagues<sup>1</sup> observed few macrophages, the CaHA likely is degraded enzymatically rather than by being phagocytosed. These results have been seen in human forearm test sites.<sup>1</sup> We were unable to locate any reports of reactions in oral mucosal tissue.



**Figure 2.** Hematoxylin-eosin–stained section showing diffuse soft-tissue deposition of globular foreign material focally surrounding skeletal muscle fibers (arrow). A foreign body giant cell response is evident with chronic inflammation and interspersed areas of fibrosis (original magnification  $\times 4$ ).



**Figure 3.** Hematoxylin-eosin–stained section showing globular deposits of amorphous material with surrounding foreign body giant cells, chronic inflammation and interspersed collagen fibers (original magnification  $\times 25$ ).

The results of the biopsy in this case differ from those reported elsewhere in that the lesions histologically consisted of diffuse deposition of round amorphous foreign material with a surrounding multinucleated foreign body giant cell response, patchy chronic inflammation and fibrosis. The associated soft-tissue elements included fibrocollagenous connective tissue, skeletal muscle, vascular channels, peripheral nerve fibers and minor salivary glands. The minor salivary gland lobules displayed a patchy interstitial lymphoplasmacytic chronic inflamma-

tory infiltrate, with multiple lobules exhibiting acinar atrophy, interstitial fibrosis, ductal ectasia and inspissated secretions. The formation of multinucleated foreign body giant cells may have been unique to our patient, or it may be that oral tissues react differently from the way skin reacts when exposed to this filler. The type of filler material cannot be determined definitively on a histologic basis.

### CONCLUSION

This case is unique in that the cosmetic filler injection resulted in a foreign body reaction not reported previously as a side effect of using this product. It is not uncommon for nodules to develop after cosmetic fillers are injected within the soft tissues in the head and neck. In this case, development of the nodule in a submucosal intra-oral location was the result of the material's being placed too deep rather than too superficially. As cosmetic procedures become more common, dentists should question patients about any cosmetic procedures they may have undergone and include

them in the differential diagnosis. However, despite a clinical history of having received cosmetic injections, any patient with a persistent mass lesion should undergo a biopsy to rule out neoplasm or another pathological process. ■

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