CLINICAL NOTE

Foreign Body Reaction to Calcium Hydroxylapatite Vocal Fold Augmentation

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We report a case of inflammation with foreign body cell reaction following injection of the true vocal folds (TVFs) with Radiesse (Bioform Inc, San Mateo, Calif), a synthetic calcium hydroxylapatite (CaHA) material. The patient underwent injection laryngoplasty for a 10-year history of persistent hoarseness and documented bilateral vocal fold paresis. Initial postoperative examination revealed overaugmentation with migration of the material. The material was removed in 2 successive procedures. Results of histological examination revealed the presence of chronic inflammation and foreign body giant cells (FBGCs). This is, to our knowledge, the first published case of an apparent FBGC reaction to vocal fold augmentation with Radiesse and leads us to conclude that rare CaHA rejection reactions can occur in human subjects.

Injection laryngoplasty has been available to physicians for almost a century to treat patients with glottic insufficiency. Various materials and injection sites have been attempted to augment the TVFs. Earlier approaches with paraffin[1] and bone/cartilage[2] combinations were abandoned for newer compounds such as absorbable gelation sponge (Gelfoam), fat, collagen, cadaveric dermis, and, most recently, CaHA. Teflon has become unpopular as an augmentation material owing to the high frequency of granulomas and foreign body reactions. In 2003, the Food and Drug Administration approved the use of synthetic CaHA for the augmentation of vocal folds in patients with unilateral or bilateral paresis.

The primary component in Radiesse implants is CaHA, a normally naturally occurring mineral in bone. The synthetic CaHA has been tested in animal models and has been found to be nonreactive.[3] The other component of the implant is a gel carrier, which is an aqueous formulation of sodium carboxymethyl cellulose, glycerin, and high-purity water. This is, to our knowledge, the first reported case of an FBCG reaction to Radiesse in a patient treated for glottal insufficiency.

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REPORT OF A CASE

A 46-year-old woman was evaluated for a 10-year history of hoarseness and episodic laryngeal pain. She had a history of laryngeal granulomas that required 3 surgical resections. She continued to complain of worsening hoarseness, especially during vocally intense activities such as singing. Other medical problems included gastroparesis, gastric reflux, and allergic rhinitis.

A transnasal fiberoptic laryngoscopy with videostroboscopy revealed glottal insufficiency with hyperfunctional activity of both false vocal folds. Laryngeal electromyography demonstrated bilateral thyroarytenoid and right cricothyroid muscle paresis. Suspension microlaryngoscopy was performed and 0.45 $cm^3$of Radiesse was injected into each TVF in the lateral aspect of the thyroarytenoid muscle. At the end of the operation, the anterior one third of both membranous TVFs was in apposition.

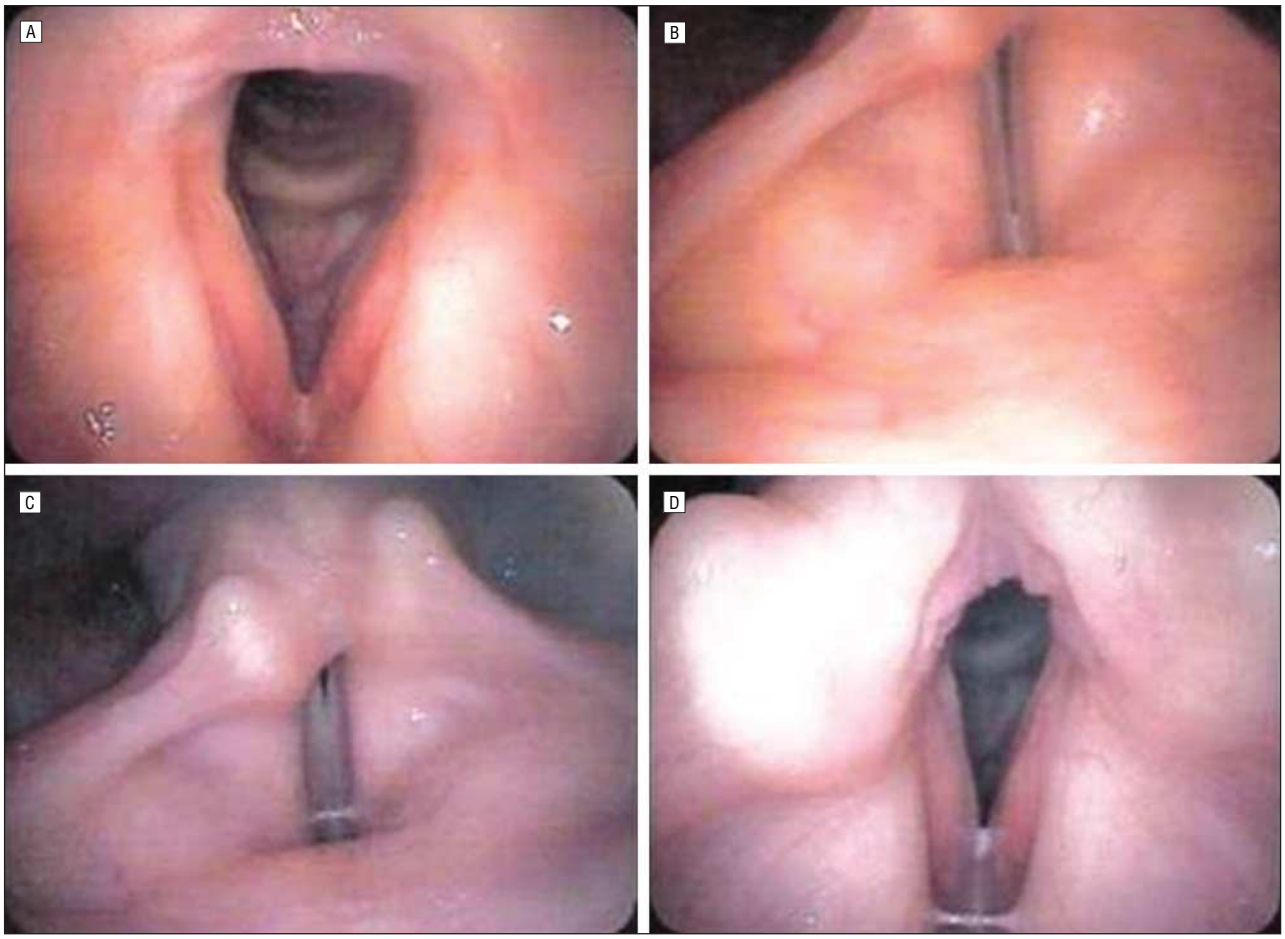

Figure 1. Laryngoscopy 1 week following Radiesse (synthetic calcium hydroxylapatite; Bioform Inc, San Mateo, Calif) implantation demonstrates overaugmentation of the true vocal folds.

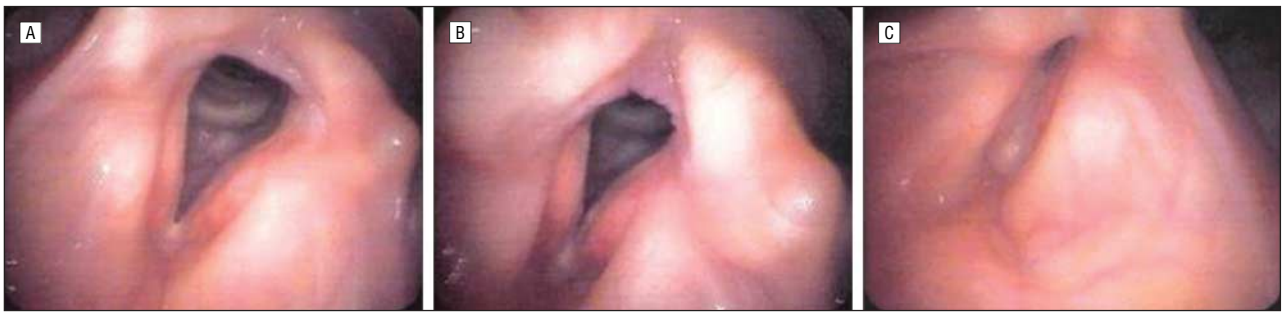

Figure 2. Three weeks following injection laryngoplasty there is erythema and calcium hydroxylapatite migration.

The patient complained of severe laryngeal pain and aphonia lasting 36 hours after her initial surgical procedure. At her 1-week postoperative visit, transnasal fiberoptic laryngoscopy showed overaugmentation of both TVFs with mucosal erythema (**Figure 1**). Three weeks postoperatively, the patient complained of persistent hoarseness without improvement. The transnasal fiberoptic laryngoscopy with videostroboscopy revealed migration of the Radiesse material into the upper lateral aspect of the vocal folds and severe vibratory restriction of both vocal fold mucosae (**Figure 2**).

Four weeks following initial surgery, the patient underwent suspension microlaryngoscopy with examination under anesthesia. Findings included injected mucosa in the upper lateral surface of both TVFs with marked firmness to palpation. Approximately 60% of the material was carefully dissected from surrounding skeletal muscle fibers and removed through bilateral lateral macroflaps. Results of histological examination revealed an FBGC reaction.

Approximately 4 weeks after the subtotal removal of the Radiesse, the patient's dysphonia, odynophonia, and vocal fatigue persisted. The transnasal fiberoptic laryngoscopy revealed continued erythema of the vocal folds and migration of the material (**Figure 3**). Suspension microlaryngoscopy was repeated with total removal of the material through bilateral lateral macroflaps. Once again, findings on histological analysis demonstrated skeletal muscle

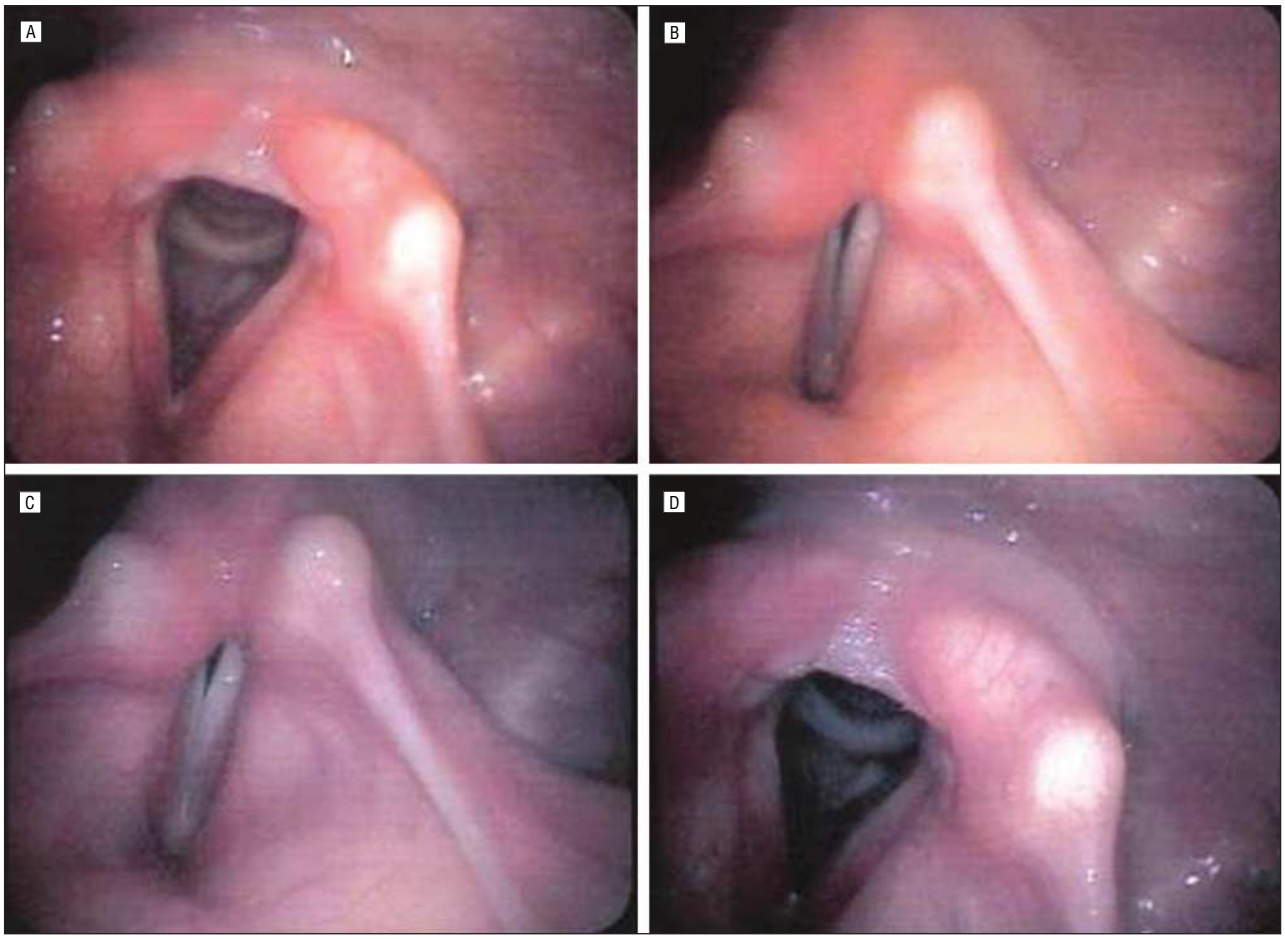

Figure 3. Calcium hydroxylapatite migration and erythema persist 8 weeks after Radiesse (synthetic calcium hydroxylapatite; Bioform Inc, San Mateo, Calif) injection and 4 weeks after its subtotal removal.

with FBGC and chronic inflammation (**Figure 4**).

COMMENT

To our knowledge, this is the first documented case of an FBGC reaction to synthetic CaHA in the TVFs. Previous experimental research with this material in animal models failed to identify foreign body reactions to this material.[3] We postulate 2 theories regarding FBGC reaction to CaHA. In an investigation studying mice with a deleted osteopontin gene, scientists discovered more FBGCs surrounding an implant.[4] Alternatively, artificial material rejection has been linked to prior sensitization during exposure to a similar compound. Before injection laryngoplasty, this patient had several orthopedic surgeries necessitating synthetic material implantation. As such, the artificial joint implants could have served as an immunogenic agent in our patient.

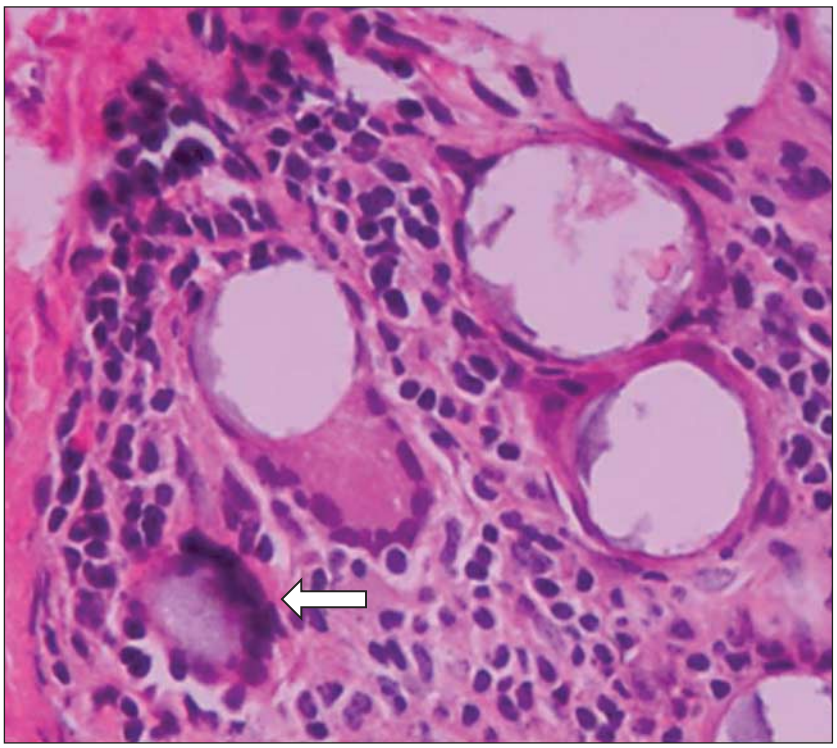

Figure 4. A robust chronic inflammatory infiltrate is present with numerous foreign body giant cells (arrow) engulfing the foreign, crystalline material (hematoxylin-eosin, original magnification ×100).

Verbal reports indicate that CaHA produces a mild inflammatory infiltrate that resolves in animal models.[5] Foreign body giant cells have been identified on histological inspection. These verbal reports contradict the evidence available previously.[3] These findings suggest that some subjects can develop an inflammatory reaction to CaHA.

Other than CaHA, there are other materials available for medialization procedures, including Silastic and Gore-Tex. Silastic has been used for several years in patients and has been shown to be biocompatible. Early animal models showed that a fibrous capsule surrounds the implant and the implant produces a minimal inflammatory response with predictable consistency.[6] Similar results, but with the presence of some FBGCs, were found in animal studies that used Gore-Tex.[7]

In conclusion, physicians should be aware of the potential for an inflammatory response with FBGC reactions as a rare complication to CaHA injections in the TVFs.

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