

# Adverse Reaction to Hyaluronic Acid Injection Laryngoplasty: A Case Report

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**Summary: Introduction.** Injection laryngoplasty using hyaluronic acid is a safe procedure commonly performed on patients with glottic insufficiency.

**Study Design.** This is a descriptive study of a case of adverse reaction to hyaluronic acid in a patient who underwent injection laryngoplasty for the treatment of unilateral vocal cord paralysis.

**Discussion.** The patient was treated with antibiotics and corticosteroids and had a full recovery. The authors recommend close observation following injection laryngoplasty using hyaluronic acid and diligent investigation of persistent postoperative laryngopharyngeal symptoms.

**Key Words:** Injection laryngoplasty—Adverse reaction—Restylane—Vocal cord paralysis—Airway.

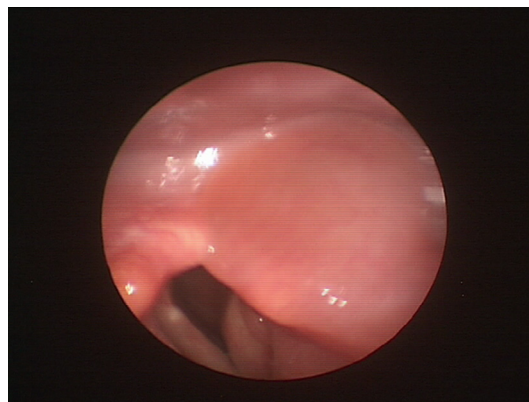
## INTRODUCTION

Injection laryngoplasty is a common therapeutic option for the treatment of glottic insufficiency. The purpose of the injection is to provide adequate glottic closure to alleviate phonatory and swallowing symptoms. The main challenges are the route of injection and the material to be injected. Many approaches have been described in the literature, and these include suspension microlaryngoscopy, the percutaneous approach, the transoral approach, and the transnasal approach. Aside from suspension microlaryngoscopy, injection is performed under local anesthetic as an office procedure.<sup>1</sup> Several injectable materials have been in use since the inception of injection laryngoplasty in 1911, with the ideal material yet to be found. The materials vary in their viscoelastic properties, inflammatory response, ease of injection, and resorption rate. Among these materials are Teflon, fat, bovine dermal collagen suspension, Radiesse, Zyplast, Zyderm, and Restylane.<sup>2</sup>

The safety and efficacy of using non-animal sourced cross-linked hyaluronic acid (Restylane) as an augmentation material has been thoroughly described in the literature. Only three cases of adverse reaction to Restylane resulting in shortness of breath have been reported.<sup>3–5</sup> The authors of this study describe one additional case of adverse reaction to hyaluronic acid in a patient with unilateral vocal cord paralysis.

## CASE REPORT

A 23-year-old woman, known to have idiopathic pulmonary hypertension, presented to the voice unit with a 6-month history of progressive hoarseness, vocal fatigue, aspiration, and dysphagia. Perceptual evaluation revealed grade 3 dysphonia with breathiness. Flexible laryngoscopy using the transnasal route showed an immobile left vocal fold in the paramedian position with incomplete glottic closure during phonation. Computerized



**FIGURE 1.** Flexible laryngoscopy showing edema at the injection site, left arytenoid, and aryepiglottic fold.

tomography angiography revealed evidence of dilated main and left pulmonary arteries with evidence of right heart dysfunction. The patient underwent injection laryngoplasty under local anesthesia using the transnasal fiberoptic approach. The left vocal fold was augmented using 0.7 cc of Restylane, small-particle stabilized hyaluronic acid (20 mg/mL). The injection was made lateral to the vocal process using a fiberoptic 19-gauge needle. The patient tolerated the procedure well, and her voice improved markedly. The patient was discharged home in good condition to be followed up in 3 weeks.

Two days following the procedure, the patient presented to the emergency department with globus sensation, dysphagia, and shortness of breath. She was afebrile with no leukocytosis. Flexible laryngoscopy revealed severe edema of the left arytenoid, false vocal fold, and aryepiglottic fold (Figure 1). The patient was promptly started on intravenous dexamethasone, inhaled racemic epinephrine, and intravenous amoxicillin-clavulonic acid. Her symptoms markedly improved a few hours later, and repeated fiberoptic laryngeal examination showed major decrease in the extent of edema. The patient was kept under monitoring for 24 hours and discharged home the next day on prednisone per os to be tapered gradually. A follow-up examination 10 days later revealed normal laryngeal examination with good closure of the glottic gap during phonation.

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## DISCUSSION

Hyaluronic acid is among the most commonly used substances in injection laryngoplasty.<sup>2</sup> Its ease of injection and unique properties regarding tissue regeneration, namely recruitment of fibroblasts, deposition of collagen, and improvement of the viscoelastic properties of the injected tissues,<sup>6</sup> have made it a popular injectable material. The voice outcome following injection of hyaluronic acid in the treatment of glottic insufficiency has been thoroughly described in the literature.<sup>1,4,5,7,8</sup> In a report by Song et al on 25 patients treated by percutaneous Restylane vocal fold injections, 87% reported subjective voice improvement and nine patients reported a nonsignificant improvement of voice-related quality of life.<sup>1</sup> Similarly, another study by Hertegård et al on 83 patients randomly injected with either cross-linked hyaluronan derivatives or bovine collagen revealed safety of cross-linked hyaluronan in addition to improved voice quality and vocal cord status.<sup>7</sup> In addition, Prendes et al have also reported that the long-term effect of temporary injection laryngoplasty can obviate the need for permanent medialization in a significant percentage of patients compared with an observation group who had no intervention.<sup>8</sup>

Since the early 2000s, the reports of local hypersensitivity to hyaluronic acid injection have overall decreased, thus precluding the need for pretreatment skin testing to detect hypersensitivity reactions. This has been attributed to the new nonanimal formulations made readily available in the market.<sup>9</sup> Despite these advances, adverse reactions to hyaluronic acid have been reported in the fields of dermatology, cosmetic or reconstructive medicine, and orthopedic surgery. Dermal reactions to hyaluronic acid are invariably self-limited and vary from mild erythema at the injection site to severe inflammatory response.

Laryngeal reactions to Restylane are very rare. A histologic study conducted on the vocal folds of rabbits showed that Restylane is a safe and biocompatible material but not exempted from inflammatory reactions.<sup>10</sup> Two large studies by Hertegård et al (83 and 73 patients) on the long-term efficacy and safety of cross-linked hyaluron revealed only minor temporary inflammation at the injected site in three patients 1 week after the injection.<sup>7,11</sup> It is worth noting that in these studies, only intradermal skin testing with bovine collagen was used, and in all three patients who experienced temporary inflammation, cough and hoarseness were the presenting symptoms, with no history of shortness of breath. Aside from these three minor cases of temporary inflammation that resolved without sequelae, only three cases of serious adverse reaction to hyaluronic acid resulting in shortness of breath following injection laryngoplasty have been reported in the literature.<sup>3-5</sup> In addition to the one by Shamanna et al,<sup>3</sup> there are two reports, one by Halderman et al and one by Rudolf and Sibylle.<sup>4,5</sup> In the report by Halderman et al, five patients out of 82 had adverse reaction to Restylane injection, and only one had respiratory symptoms, with laryngeal findings of edema of the false and true cords.<sup>4</sup> Similarly, Rudolf and Sibylle have reported one case out of 19 injected who had shortness of breath secondary to edema of the false cord and aryepiglottic

fold at the site of injection.<sup>5</sup> Rudolf and Sibylle's patient and our patient both had edema of the false cord that was managed successfully by corticoids therapy.

There are three possible mechanisms for the adverse reactions to hyaluronic acid. First is allergic or hypersensitivity reaction, second is an acute infection of bacterial origin that causes inflammation with fluctuant and erythematous nodules, and last but not least is an ischemic event. The ischemia may be secondary to either vascular compression by the injected material, direct injury, or injection into the vessels within the vocal fold.<sup>3</sup> In the described case, the three aforementioned mechanisms are possible given the fact that the adverse reactions occurred within 72 hours after the injection. Nevertheless, infection is less of a possibility given the fact that our patient had no systemic symptoms such as fever, malaise, or leukocytosis. An ischemic event is also less likely to be the cause in the absence of risk factors such as radiation therapy<sup>3</sup> or the presence of laryngeal findings suggestive of ischemia, namely ecchymosis, blanching, or evidence of necrosis.

## CONCLUSION

Despite the rarity of this life-threatening reaction, we recommend close postoperative follow-up of patients undergoing injection laryngoplasty using Restylane as a filling material, and diligent investigation of persistent laryngopharyngeal symptoms.

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