

Hyaluronidase injection for upper eyelid lumps secondary to hyaluronic acid filler injection: three case reports

Pricila Tien Yan Wang, Andre Ma, Hunter Kwok-Lai Yuen

Department of Ophthalmology, Hong Kong Eye Hospital, Hong Kong SAR, China

Correspondence and reprint requests:

Prof Hunter Kwok-Lai Yuen, Department of Ophthalmology, Hong Kong Eye Hospital, Hong Kong SAR, China.

Email: hunterklyuen@gmail.com

Abstract

Hyaluronic acid dermal filler is effective in treating upper eyelid retraction in thyroid eye disease. We report on three cases of hyaluronidase injection to treat upper eyelid lumps or edema secondary to hyaluronic acid filler injection.

Key words: Dermal fillers; Graves ophthalmopathy; Hyaluronic acid; Hyaluronoglucosaminidase; Restylane-L

Introduction

Upper eyelid retraction is the most common sign of thyroid eye disease (TED) and leads to exposure keratopathy and aesthetic issues. Hyaluronic acid (HA) injection is an increasingly popular treatment but is associated with edema. Hyaluronidase, an enzyme that degrades HA, can treat HA-related complications such as dermal filler-related swelling; however, its use for upper eyelid retraction filler-related swelling is limited. We report on three cases of hyaluronidase injection to treat upper eyelid lumps or edema secondary to HA filler injection. We also reviewed the literature regarding potential complications of HA dermal fillers for upper eyelid retraction.

Case presentations

Patient 1

In May 2020, a 55-year-old woman with TED presented with bilateral upper eyelid retraction. Her marginal reflex distance 1 was 5 mm in the right eye and 4 mm in the left eye. Her right upper eyelid retraction was initially managed with three Botox injections (each given at 3-month intervals), but the response was suboptimal. In February 2022, the patient received a Restylane-L (lidocaine-containing HA dermal filler) injection: 0.5 mL in the right upper eyelid and 0.2 mL in the left upper eyelid. Nine months later, she complained of a persistent lump in both upper eyelids (**Figure 1**). At 36 and 40 months after the Restylane-L injections, she received a total of 75 and 150 IU/mL, respectively, of hyaluronidase injections in her bilateral upper eyelids. The lumps subsided gradually.

Patient 2

In February 2023, a 54-year-old woman with TED presented with bilateral upper eyelid retraction. Her marginal reflex distance 1 was 7 mm in the right eye and 8 mm in the left eye. For each eye, upper eyelid retraction was treated with three 40 mg subconjunctival triamcinolone injections, each given at a 1-month interval. However, there was residual retraction and mild lagophthalmos in the left eye. In

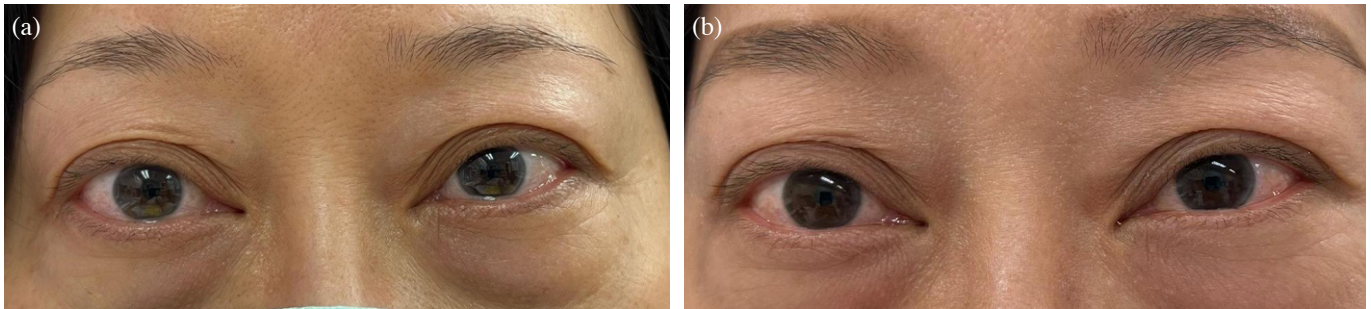


Figure 1. Patient 1: (a) mild swelling of both upper eyelids secondary to hyaluronic acid filler injection and (b) decreased swelling after hyaluronidase injection.



Figure 2. Patient 2: (a) a nodule on the lateral side of the left upper eyelid secondary to hyaluronic acid filler injection and (b) complete resolution of the nodule immediately after hyaluronidase injection.

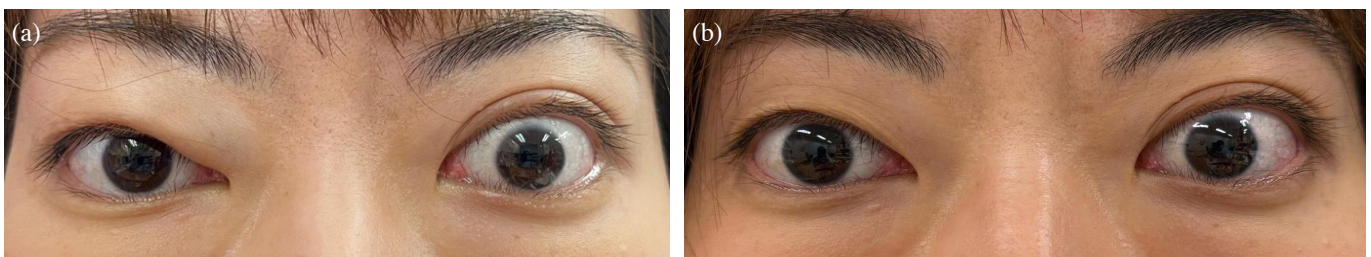


Figure 3. Patient 3: (a) swelling on the medial side of the right upper eyelid secondary to hyaluronic acid filler injection and (b) decreased swelling after hyaluronidase injection.

February 2024, she received a Restylane-L injection (dose unknown) in her left upper eyelid. Five months later, she had swelling with a firm nodule on the lateral side (**Figure 2**). Further 8 months later, she received a hyaluronidase injection (90 IU/mL) in the left upper eyelid, and the nodule resolved immediately.

Patient 3

In June 2021, a 29-year-old woman with TED presented with upper eyelid retraction and proptosis in her right eye. Her marginal reflex distance 1 was 5 mm in the right eye and 2 mm in the left eye. The upper eyelid retraction was treated with three 40-mg subconjunctival triamcinolone injections, each given at a 1-month interval, but the response was suboptimal. She then received Restylane-L injections in December 2021 (dose unknown) and March 2022 (1 mL). There was a swelling after the second injection, which persisted despite a subconjunctival triamcinolone injection 12 months later (**Figure 3**). In April 2025, she received a hyaluronidase injection (150 IU/mL) in the right upper eyelid, and the swelling resolved.

Discussion

TED is a common autoimmune condition that can lead to visual impairment. Inflammation and fibrosis of orbital tissues can lead to eyelid retraction, exophthalmos, and double vision. Eyelid retraction occurs in up to 90% of Caucasian patients with TED,¹ causing exposure keratopathy and cosmetic issues.

Eyelid retraction in TED can be caused by the enlargement and fibrosis of the levator palpebrae superioris, scarring between the levator aponeurosis and surrounding soft tissues, increased sympathetic stimulation of Müller's muscle, and overaction of the levator muscle to counteract the ipsilateral tight inferior rectus muscle.² Traditional treatments include pulse intravenous methylprednisolone, blepharotomy, and mullerectomy. Recently, minimally invasive techniques such as HA dermal filler injections have been explored to correct eyelid retraction. HA can both weaken the levator muscle and add load to the upper eyelid. It is commonly injected in the subconjunctival levator-Müller plane (0.2 to 0.5 mL per injection).³

There are four main types of dermal fillers: HA, calcium hydroxyapatite, poly-L-lactic acid, and polymethylmethacrylate. HA is the most popular. It is a glycosaminoglycan polysaccharide found in skin, connective tissue, and synovium, and has very low immunogenicity.⁴ Its anionic properties can attract water and increase volume to provide structural support. HA fillers have been approved to treat facial wrinkles, whereas Restylane, Belotero, and Juvederm are used for upper eyelid retraction. Nonetheless, HA is associated with localized swelling, infection, granuloma formation, and vascular compromise.

Understanding the causes of swelling and corresponding management strategies is crucial to optimize outcomes and patient safety. Immediate post-injection swelling typically resolves within 72 hours.⁵ Vasodilation-triggered episodic edema, particularly following infraorbital filler injection, can occur secondary to exercise or heat or alcohol exposure.⁶ Prevention involves educating patients to avoid these triggers.

Delayed swelling due to type IV hypersensitivity can occur days to months after injection. Approximately 0.5% of cases experience delayed-onset nodules after HA-based facial dermal fillers, with a median onset time of 4 months.⁷ These cases were successfully treated with intralesional corticosteroids and hyaluronidase. Granulomatous inflammation can cause firm nodular swelling and is usually associated with redness and pain. Chronic, painless, persistent swelling in the lower eyelids and malar region after filler injection has also been reported. In a study of 120 patients, 18 reported 'fluid build-up' in the malar region after HA filler injection in the orbital rim hollow and cheek.⁸ It was speculated that the persistent edema might be related to impaired lymphatic drainage. Another study reported five cases of recurrent lower eyelid edema after HA injections.⁹ The underlying pathophysiology might involve the relatively fluid-impermeable midface osteocutaneous septa and immune-mediated lymphatic damage, causing lymphedema. Gradual filler dissolution is recommended through serial low-dose hyaluronidase injections combined with synchronous fractionated radiofrequency microneedling, enabling incremental filler breakdown with simultaneous soft-tissue contraction.⁹

There are only a few reports of the use of dermal fillers for upper eyelid retraction in TED. One study reported mild complications such as mild upper eyelid lumpiness on downgaze (23.5%), which improved but persisted over time.¹⁰ Our patients with upper eyelid swelling secondary to HA filler injection were successfully managed with hyaluronidase injection.

Hyaluronidase, a soluble enzyme that degrades HA by hydrolyzing β -1,4-N-acetylglucosaminidic bonds,¹¹ is effective for managing HA-based filler complications, particularly in aesthetic medicine.^{12,13} Hyaluronidase is a rapid and safe method for managing eyelid edema following

tear-trough augmentation with HA fillers.¹⁴

There is no standardized guideline for dosage. The usual practice for treating uncomplicated nodules or swelling is 5 IU of hyaluronidase for every 0.1 mL of HA (20 mg/mL).¹⁵ In vivo degradation of cross-linked, highly cohesive HA fillers requires 30 IU of hyaluronidase.¹⁶ A cross-linked filler (Juvederm Voluma, 20 mg/mL) requires even higher hyaluronidase doses for effective dissolution: >20 IU per 0.2 mL of filler.¹⁷ Dermal fillers with greater hydrophilicity and cross-linking require higher or repeated doses of hyaluronidase.

To reduce the risk of swelling, injections should be administered slowly and evenly, avoiding bolus injection. Clinicians should exclude any underlying allergies, rosacea, or history of filler-related swelling. A low-viscosity, low-hydrophilic HA filler (eg, Restylane-L) can reduce the risk of eyelid swelling. HA should be injected subconjunctivally into the levator plane to weaken the levator muscle, with a fanning and retrograde threading technique. Volume per injection should be minimized and individualized to avoid overcorrection and tissue distension. Patients should be warned to avoid massaging the injection area and exposure to heat and alcohol. Light cold compression can be applied to any swelling.

Contributors

All authors designed the study, acquired the data, analyzed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an editor of the journal, HKLY was not involved in the peer review process. Other authors have disclosed no conflicts of interest.

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Data availability

All data analyzed in this study are available from the corresponding author upon reasonable request.

Ethics approval

The patients were treated in accordance with the tenets of the Declaration of Helsinki. The patients provided written informed consent for all treatment and procedures and for publication.

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