



Received: October 31, 2024
Revised: December 24, 2024
Accepted: March 31, 2025

Corresponding Author:

Thongnard Kumchai, Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Bangkokthonburi University, Bangkok 10170, Thailand
E-mail: thongnard@hotmail.com

A Delayed Onset Cyst-like Lesion at the Lip after Hyaluronic Acid Filler Injection: A Case Report

Atapol Yongvikul^{1,2}, Manop Khanijou², Natthamet Wongsirichat², Thongnard Kumchai²

¹Department of Oral and Maxillofacial Surgery, Masterpiece Plastic Hospital, Thailand

²Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Bangkokthonburi University, Thailand

Abstract

Nowadays, lip augmentation has become a key component in addressing cosmetic concerns. In particular, hyaluronic acid (HA) fillers are increasingly used for this minimally invasive procedure. Generally, this procedure is well-tolerated, and major adverse events are rare. However, some delayed complications can occur following HA filler injection. Here, we report a case of a HA-related complication in a 45-year-old female patient, affecting the lower lip. Four weeks after the HA filler application, without any immediate adverse effects, a painless, well-defined border nodule occurred in the wet lip area. This cyst-like lesion was surgically identified and successfully treated with surgical excision. Clinicians should be aware that a case manifesting as a well-defined lip nodule suggests salivary gland cysts, soft tissue tumors and cysts, as well as filler-related nodules. This delayed presentation of HA-related nodule in the lower lip poses unique diagnostic and management challenges.

Keywords: filler, filler complication, hyaluronic acid, lip, mucocele

Introduction

In recent decades, lip augmentation procedures have been developed to address the growing trend of achieving ideal lips and combating signs of aging. Among the various methods available, filler injections have emerged as one of the most common and effective approaches.⁽¹⁾ The evolution of fillers has been remarkable, beginning with bovine collagen injections in the 1980s and progressing to include human collagen, hyaluronic acid (HA), calcium hydroxyapatite, poly-L-lactic acid, silicone, and other formulations.^(2,3) The ideal skin filler is expected to offer several essential characteristics. It should be biocompatible, allowing for seamless integration with the body's tissues. Moreover, it should be removable when necessary, cost-effective, hypoallergenic, have a long-lasting effect, and easy to distribute and store. In the current landscape of cosmetic procedures, HA dermal fillers stand out as a preferred choice due to their ability to meet many of these criteria. HA, regardless of its source—be it from animals, humans, or HA-producing bacteria—possesses the same molecular structure, thereby minimizing the risk of allergic or immunogenic reactions. This lack of tissue or species specificity enhances its safety profile.^(2,3) However, the rapid breakdown of original HA by hyaluronidase poses a challenge, as it has a short half-life of only 12 hours. To address this limitation, manufacturers have developed injectable HA skin fillers with enhanced longevity and durability by modifying the cross-linking chain of HA.^(2,4) These advancements have significantly extended the duration of HA fillers, allowing patients to enjoy their aesthetic benefits for longer periods with fewer maintenance treatments.

Mild pain, erythema, swelling, and bruising at the injection site are common complaints after HA injection.⁽²⁾ While these symptoms are typical and generally subsided within a short period, the procedure itself is associated with a very low rate of serious complications.⁽⁵⁾ One such severe complication, well-documented in medical literature, is blindness, which occurs when the filler is inadvertently injected into vessels around the orbits, such as the supraorbital vessels. The high pressure at the needle's end, coupled with a bolus injection technique, can cause the product to flow backward into the ophthalmic artery, leading to central retinal artery occlusion. Additionally, other uncommon yet significant complications can arise, including vascular infarction, skin necrosis,

hypersensitivity reactions, cellulitis, abscess formation, as well as nodules and granulomas. Nodule formation, in particular, presents an intriguing challenge for clinicians. These nodules may manifest as early or delayed onset, with delayed cases occurring more than 4 weeks post-injection.⁽⁶⁾ While early nodules are relatively well-documented and managed, delayed onset nodules remain less frequently reported in medical literature.

Our case report focuses on one such instance—a delayed-onset cystic-like complication related to HA filler injection in the lower lip. This delayed presentation of a cystic-like nodule in the lower lip poses unique diagnostic and management challenges. Comprehending the effects of lip augmentation with HA fillers may enable clinicians to administer safe and effective outcomes.

Case Report

We present the case of a healthy 45-year-old woman who received an application of HA on her lower lip at a local esthetic clinic. Even though IRB review is not required, this case report was prepared in accordance with the requirements of the HIPAA regulations. Four weeks after the HA filler application, without any immediate adverse effects, a painless nodule occurred at the wet zone of the lower lip opposite to teeth 32 and 33. The patient did not know the brand of the filler. She denied having lip sucking or biting habits. The lesion was a submucosal cyst-like nodule with a diameter of a centimeter (Figure 1). The patient was treated at the local clinic by hyaluronidase injection a month after the appearance of the lesion, but the lesion did not subside. Three months later, she came to our hospital reporting no change in the size of the lesion. The differential diagnosis was made: mucocele or delayed onset filler nodule. After a discussion with the patient, we decided on treatment by surgical excision of the mass under local anesthesia. The incision was made at the wet area of the lower lip, approximating to the lesion, and the mucosal flap was elevated to explore the lesion. At this point, there was a 3-millimeter dense nodule close to the swelling mucosa (Figure 2). Approximately half a cc of content was found surrounding the dense nodule. The gross feature of the semi-liquid content was translucent, gel-like substance. It is slightly cloudy in appearance and has a viscous texture (Figure 3). The nodule and HA filler-like substance were surgically removed, and the wound was closed after copious irrigation. Unfortunately,

the patient strongly declined a pathological examination of the lesion due to economic reasons.

At a month of follow-up, the lesion was grossly cured. The lip was symmetrical without swelling. The scar from surgical excision was placed on the wet lip, which was hardly visible during smiling or speaking (Figure 4).



Figure 1: A nodule at the lower lip opposite to teeth 32 and 33. The lesion was a submucosal cyst-like nodule with a diameter of a centimeter.

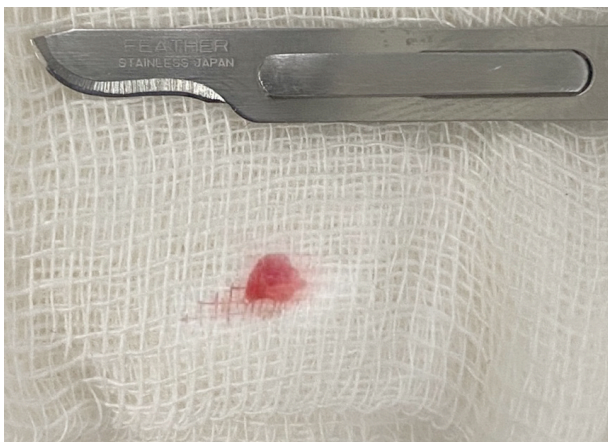


Figure 2: A 3-millimeter dense nodule was surgically removal.

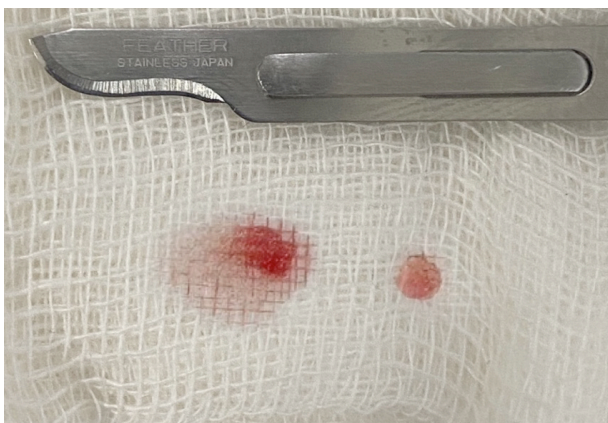


Figure 3: Approximately a half of a cc of HA filler was found underneath the dense nodule.



Figure 4: At a month of follow-up, the lesion was cured. The lip was symmetrical without swelling.

Discussion

Lips, in particular, have historically been a significant feature of the face, contributing to overall attractiveness and a youthful appearance. The lower lip lies between the mouth and the mentolabial sulcus. The sharp demarcation between the colored edge of the lip and surrounding skin is called the vermillion border. The vermillion is a transition layer between the outer, hair-bearing tissue and the inner mucous membrane. The skin of the vermillion is made up of three to five cellular layers and is much thinner compared to the skin on the rest of the face.^(7,8) Therefore, lip augmentation procedures aimed at enhancing fullness and promoting a youthful look are frequently sought after in aesthetic medicine. Lip enhancement techniques are classified into surgical and nonsurgical procedures.⁽¹⁻³⁾ One surgical procedure, the triple V-Y augmentation technique⁽⁹⁾, is performed without the use of dermal fillers or implants and aims to expand the vermillion by advancing the labial mucosa forward. Other surgical options for lip augmentation exist as well.⁽¹⁰⁾ Surgical lip implants and autologous fat transfer are used only rarely.⁽¹¹⁾

The injection of dermal fillers is the most popular nonsurgical procedure performed to increase the volume and improve the shape of the lips.⁽¹²⁾ Semi-permanent dermal fillers—such as calcium hydroxyapatite and poly-L-lactic acid—and permanent fillers are not preferred for lip augmentation because they have an increased risk of irregularity and nodule formation. Hyaluronic acid filler is one of the most commonly used products for lip enhancement.¹¹ HA injections are generally safe with a very low risk of severe adverse reactions, though complications such as skin necrosis, infection, allergic reactions, visual impairment, and nodules or granulomas can occur. Based on a review of lip complication in 17 reported cases,⁽¹³⁾ nodules may develop early or delayed after injection, with an incidence of 0.1 to 1.0%. When the HA nodule

occurred at more than 4 weeks, the nodule is diagnosed as delayed type.⁽⁶⁾ These nodules can be inflammatory, resulting from the body's foreign-body response, or non-inflammatory, typically caused by improper filler placement. Inflammatory nodules may appear days to years after injection, while noninflammatory ones often appear immediately. HA is typically temporary and resorbable, minimizing foreign-body effects, accordingly many non-inflammatory nodules resolve with observation, massage, or hyaluronidase.^(5,6)

However, diagnosing lip nodules can be challenging since patients may not report their history of filler injections, which could have been performed weeks, months, or even years prior. A broad range of potential diagnoses commonly includes abscesses, sialadenitis, mucocele, benign salivary gland neoplasms, or malignancy.^(14,15) Infections can present early or late in the clinical course and are more commonly associated with single nodules. Involvement of multiple sites suggests a foreign-body granulomatous response more likely. Cases presenting as well-defined lip nodules suggest salivary gland tumors or cysts, such as mucocles, as well as soft tissue tumors and cysts. Timely and accurate diagnosis of these masses is crucial, as they may mimic neoplasms, which is particularly important given the generally older age group of these patients. Differential diagnoses were summarized in the table 1.

In 2020, Phillip-Dormston⁽⁶⁾ provided the management of delayed-onset nodules caused by HA filler. For the inflammatory group, the management starts with non-steroidal anti-inflammatory drugs combined with antihistamines and antibiotics, hyaluronidase, intralesional steroid injection, intralesional laser, and intralesional radiofrequency. If an abscess or fluctuation is present, surgical intervention with incision and drainage may be required for resolution. For non-inflammatory nodules, small or inconspicuous lesions can often be managed conservatively with observation. Hyaluronidase can be administered when the lesion is visible. This guideline was developed for filler-related HA nodules, but in our patient, the lesion was differentially diagnosed as mucocele and an HA-related nodule. We decided on treatment by excision and filler evacuation. A key limitation of this report is the absence of pathological confirmation. However, the author posits that the lesion likely originates from HA filler, based on its distinct gross features and the patient's history of HA filler injection in the affected area.

Conclusions

Practitioners should be aware that a case manifesting as a well-defined lip nodule suggests salivary gland cysts, soft tissue tumors and cysts, as well as filler-related nodules. This delayed presentation of HA related nodule in the lower lip poses unique diagnostic and management

Table 1: A summary of differential diagnoses for cystic-like lesions and related lesions at the lips.

Condition	Key features	Clinical presentation	Treatment
Abscess	Infection, localized swelling, redness, warmth, and/or pain	Single nodule, tenderness, history of trauma or infection	May require surgical drainage
Sialadenitis	A form of inflammation of salivary gland, often due to obstruction	Lip swelling with pain, sometimes the patient has fever	Antibiotics, Drainage rarely needed
Mucocele	Cystic lesion with fluid-filled, caused by a blockage of duct or tear of the gland	Soft, bluish nodule; often associated with trauma (e.g., lip biting, bracket irritation)	Surgical removal
Benign tumor	Non cancerous lesion included benign of salivary gland, lipoma or fibroma	Firm and painless nodule with slow growing	Excision
Malignancy	Hard, fixed nodule, irregular borders, lymphadenopathy	Rapidly growing, painful, with possible ulceration or bleeding	Urgent biopsy for a diagnosis
Hyaluronic acid filler Nodule	Its distinct features and the patient's history of HA filler injection	Well defined, firm and non tender	Observation, massage, hyaluronidase injection; if unresolved, surgical removal

challenges. Despite its rarity, understanding and recognizing such complications are essential for providing optimal patient care and ensuring timely intervention to mitigate potential adverse outcomes.

Funding

No funding to declare.

Acknowledgments

None

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used ChatGPT-4 to refine and correct certain parts of the English grammar. After using this tool the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

References

- Cooper H, Gray T, Fronek L, Witfill K. Lip augmentation with hyaluronic acid fillers: a review of considerations and techniques. *J Drugs Dermatol*. 2023;22(1):23-9.
- Monheit GD, Coleman KM. Hyaluronic acid fillers. *Dermatol Ther*. 2006;19:141-50.
- Brandt FS, Cazzaniga A. Hyaluronic acid gel fillers in the management of facial aging. *Clin Interv Aging*. 2008;3:153-9.
- DeLorenzi C. Complications of injectable fillers, part I. *Aesthet Surg J*. 2013;33:561-75.
- Trinh LN, McGuigan KC, Gupta A. Delayed granulomas as a complication secondary to lip augmentation with dermal fillers: a systematic review. *Surg J (N Y)*. 2022;8(1):e69-e79.
- Kroumpouzos G, Harris S, Bhargava S, Wortsman X. Complications of fillers in the lips and perioral area: Prevention, assessment, and management focusing on ultrasound guidance. *J Plast Reconstr Aesthet Surg*. 2023;84:656-69.
- Moore KL, Dalley AF. *Clinically Oriented Anatomy*. 4th ed. Lippincott Williams & Wilkins; 1999.
- Hennekam RC, Cormier-Daire V, Hall JG, Méhes K, Patton M, Stevenson RE. Elements of morphology: standard terminology for the nose and philtrum. *Am J Med Genet A*. 2009;149A(1):61-76.
- Obradovic B, Obradovic M. Triple V-Y vermilion augmentation of the upper lip. *J Craniofac Surg*. 2015;26(8):e736-e738.
- Maloney BP, Truswell W 4th, Waldman SR. Lip augmentation: discussion and debate. *Facial Plast Surg Clin North Am*. 2012;20:327-46.
- Mannino GN, Lipner SR. Current concepts in lip augmentation. *Cutis*. 2016;98:325-9.
- Landau M. Lip augmentation and rejuvenation using Dermicol-P35 30G: personal experiences from my clinic. *Aesthet Surg J*. 2009;29(3 Suppl):S12-S15.
- Alcântara CEP, Noronha MS, Cunha JF, Flores IL, Mesquita RA. Granulomatous reaction to hyaluronic acid filler material in oral and perioral region: a case report and review of literature. *J Cosmet Dermatol*. 2018;17(4):578-83.
- Carlos-Fabuel L, Marzal-Gamarra C, Martí-Álamo S, Mancheño-Franch A. Foreign body granulomatous reactions to cosmetic fillers. *J Clin Exp Dent*. 2012; 4(4):e244-e247.
- Jham BC, Nikitakis NG, Scheper MA, Papadimitriou JC, Levy BA, Rivera H. Granulomatous foreign-body reaction involving oral and perioral tissues after injection of biomaterials: a series of 7 cases and review of the literature. *J Oral Maxillofac Surg*. 2009;67:280-5.