

Delayed hypersensitivity reaction after hyaluronic acid filler (VCY-20)

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Abstract

Hyaluronic acid (HA) filler, a transient injectable used for rejuvenating facial treatments, has become increasingly popular over time since it doesn't require surgery. Although these procedures are generally safe, there are some application-related complications. These issues fall into three categories: reactions with early, delayed, or late onset. This case report features a 55-year-old female patient who developed widespread facial edema as a result of a delayed hypersensitivity reaction that happened after HA filler was applied.

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Introduction

Procedures involving hyaluronic acid (HA) dermal fillers for aesthetic purposes have been ranked in 2020-2021 as the second most popular nonsurgical procedure.¹ The increasing popularity of dermal fillers, particularly HA fillers, can be attributed to their efficacy and flexibility as well as their favorable safety record.²⁻⁴ Complications that arise after filler injections can be classified based on their timing in relation to the injection. These complications can be early events occurring within a few days of the treatment or delayed events occurring weeks to years after the treatment.⁵ The aim of this article is to report a case of delayed adverse reaction related to the use of HA filler (VCY-20) after microdermabrasion.

Case Report

A 55-year-old female patient, with a previous medical history of successfully treated basal cell carcinoma on the forehead through surgery four years ago and an unremarkable family history, underwent a dermatological procedure performed by her dermatologist. The procedure involved the application of hyaluronic acid VYC-20L to the malar and centofacial regions. Subsequently, one month later, she underwent microdermabrasion. Approximately five days following the microdermabrasion procedure, the patient experienced generalized facial edema and pain. Upon further inquiry, she indicated that the pain was more pronounced over the areas where the hyaluronic acid was applied. The patient denied having a fever or any other symptoms beyond those previously mentioned. Based on the patient's clinical history and physical examination, a diagnosis of delayed hypersensitivity reaction leading to edema was established. Unfortunately, diagnostic imaging, specifically ultrasound, was not available at the time of the patient's visit to the clinic.

The treatment approach involved the administration of hyaluronidase, accompanied by a single intramuscular dose of 8 mg of dexamethasone, followed by an oral course of 6 mg of oral dexamethasone every 12 hours for three days. Notably, significant improvement in the patient's condition was observed after two days of treatment, and in the subsequent days, complete resolution of the swelling and symptoms occurred.

Discussion

VYC-20L is a specific type of hyaluronic acid filler that comprises a mixture of low- and high-molecular-weight HA at a concentration of 20 mg/mL. This formulation facilitates effective crosslinking, leading to the formation of a gel with exceptional cohesive properties, increased hardness (G'), enhanced lifting capability, and prolonged *in vivo* duration. These characteristics make it particularly suitable for optimizing midface volumizing

procedures. Importantly, similar to other HA gels, VYC-20L offers the advantage of being reversible with hyaluronidase in the event of adverse reactions, providing an additional safety measure.⁶ The predominant adverse effects associated with the use of VYC-20L primarily manifest as local reactions at the treatment site, such as tenderness, swelling, firmness, and the formation of lumps or bumps.^{3,6} These effects typically resolve within a duration of two weeks or less.²⁻⁴ In a study conducted by Jones *et al.*,⁶ it was noted that two participants experienced severe delayed-onset adverse effects that required intervention. Similarly, our patient presented with a notable adverse reaction characterized by painful and widespread swelling in the centropacial region, as illustrated in Figures 1 and 2.

According to the findings of Alijotas-Reig *et al.*,⁷ most reactions associated with fillers exhibit comparable histopathological characteristics. These reactions primarily result from an inflammatory process that affects both the dermis and the underlying subcutaneous tissue. The inflammatory response is characterized by the presence of T lymphocytes, with the majority being CD4+ T lymphocytes, along with a smaller population of B lymphocytes. Additionally, a significant presence of macrophages is commonly observed, often seen engulfing particles of the injected material.

Nevertheless, Artzi *et al.*⁸ expressed uncertainty regarding whether delayed inflammatory reactions should be considered true hypersensitivity reactions. They have also stated that there could be various causes or triggers for such reactions, such as viral infections, active sinusitis, low-quality products, combinations of different products, or inappropriate techniques. Bentkover *et al.*⁹ established that phagocytosis is the main reaction occurring in the tissues in response to the appearance of any foreign body and suggested to be the main factor in determining the longevity of the fillers applied.

One of the potential differential diagnoses considered in this case was edema secondary to filler injection. Kim *et al.*¹⁰ explain that this adverse effect is typically categorized as an early complication of the procedure, characterized primarily by swelling, ecchymosis, and erythema. Swelling, which was observed in our patient, and ecchymosis can occur simultaneously at the time of injection, and it is important to note that they usually resolve spontaneously. The management of symptoms can be aided by the application of cold compresses with gentle pressure, as suggested by Kim *et al.*¹⁰ Immediate post-injection erythema is considered a normal and temporary occurrence; however, if it persists for several days or longer, it may indicate a hypersensitivity reaction.

The characteristics of friction-induced skin damage are influenced by various factors, including the type of friction (static or dynamic), the magnitude of force applied (low or high), and the properties of the surface involved, such as the body location, moisture level, and coefficient of friction. Clinically, friction-induced skin damage presents with visible signs such as lichenification, hyperpigmentation, erythema, scaling, fissuring, blister formation, ulceration, and persistent alterations.¹¹

In the case of our patient, despite the application of cold compression post-procedure, the pain and swelling did not improve and did not resolve spontaneously within the expected timeframe for these complications. This factor helps to rule out these potential differential diagnoses and raises suspicion of a hypersensitivity reaction.

Epidermal fillers, being foreign substances to the body, can trigger a type of edema in the deeper layers of the skin known as angioedema. Angioedema is characterized by localized edema with a sudden onset, affecting submucosal tissues and deep skin layers. It can be mediated by bradykinin or histamine and may occur alone or in conjunction with chronic urticaria.¹² Several case

reports have documented facial angioedema associated with the use of hyaluronic acid fillers, with favorable responses observed following treatment with antihistamines alone or in combination with corticosteroids.¹³ To rule out angioedema from our list of differential diagnoses, we considered the time of appearance, as angioedema typically occurs within the first 24 hours of exposure. In our patient's case, the edema started after one month of hyaluronic acid injection and 96 hours after the microdermabrasion procedure. Additionally, the patient's clinical history is relevant, as she had no previous episodes of angioedema, nor did any members of her family. Furthermore, the physical examination did not reveal any swelling of the mucous membranes in the upper respiratory tract or gastrointestinal system, which are typically associated with angioedema.¹⁴

Based on these criteria, we can exclude angioedema as a differential diagnosis for our patient's reaction, as it aligns more with the characteristics of early appearance hypersensitivity reactions rather than delayed ones. Hyaluronidase is an enzyme that effectively degrades hyaluronic acid derived from various sources. It has been proposed as a treatment for hyaluronic acid-related granulomas, and there are reports in the literature indicating its efficacy in some cases.¹⁵

Alijotas-Reig *et al.*⁷ state that oral corticosteroids are nowadays the most employed systemic treatment for adverse reactions to filler applications. They mention that no cases of treatment



Figure 1. Two days post microdermabrasion showed centropacial swelling.



Figure 2. Two days post initiation of treatment.



Figure 3. Four days post initiation of treatment

resistance have been reported thus far when medium to high doses of prednisone (0.5 to 1 mg/kg/day) are administered to manage complications associated with the adverse effects of fillers. In our patient's case, we incorporated hyaluronidase along with corticosteroids as part of the therapeutic approach. Significant improvement was observed on the sixth day following the initiation of treatment, as depicted in Figure 3.

In our specific case, the diagnostic resources of diagnostic ultrasound and a pathologist were not accessible at the clinic during the patient's visit. Therefore, the diagnosis was primarily based on the clinical examination and assessment of symptomatology, utilizing the diagnostic criteria for the main differential diagnoses. It is important to highlight that when feasible and available, diagnostic ultrasound should be performed by a skilled clinician to provide valuable assistance in the diagnostic process.

Conclusions

While complications associated with epidermal fillers have been documented in the literature, delayed-onset complications are relatively rare and encompass a wide range of signs and symptoms, including induration, erythema, and edema. Due to the infrequent occurrence of these complications, a standardized treatment algorithm has not been established. However, there are reports in the literature where the use of hyaluronidase and steroids has proven effective in resolving delayed-onset complications efficiently. These treatment modalities have shown promise in addressing such complications, providing valuable insights into their management.

This case report serves to highlight the successful management of a delayed hypersensitivity reaction presenting as generalized facial edema. By sharing this case, we aim to promote early detection of similar complications and potentially improve patient prognosis. We underscore the importance of not overlooking the utilization of diagnostic tools such as ultrasound and skin biopsy whenever they are accessible. These resources can provide valuable information for accurate diagnosis and informed treatment decisions.

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