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## **Delayed hypersensitivity reaction of hyaluronic acid filler (VCY-20)**

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## **Abstract**

Hyaluronic acid filler, a temporary injectable used for rejuvenating facial treatments, has gained significant popularity over the years due to its nonsurgical approach. While these procedures are generally safe, there are certain complications associated with their application. These complications can be categorized into early-, delayed-, and late-onset reactions. In this case report, we present a 55-year-old female who experienced a delayed hypersensitivity reaction following the application of hyaluronic acid filler, resulting in generalized facial edema.

## **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 hyaluronic acid (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.

Hyaluronic acid (HA) dermal filler procedures for aesthetic purposes have consistently ranked as the second most popular nonsurgical procedure in 2020–2021 (1). The rising popularity of dermal fillers, particularly those containing hyaluronic acid (HA), can be attributed to their proven effectiveness, versatility, and favorable safety profile (2–4). Post-injection complications associated with fillers can be classified based on the timing of their occurrence relative to the injection. These complications may manifest as early events within a few days of the treatment or as delayed events emerging weeks to years after the procedure (5). The primary objective of this article is to present a case study of a delayed adverse reaction following the use of a HA filler (VCY-20) after microdermabrasion treatment.

## **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., it was noted that two participants experienced severe delayed-onset adverse effects which required intervention (6). Similarly, our patient presented with a notable adverse reaction characterized by painful and widespread swelling in the centropalpebral region, as illustrated in Figure 1A-B.

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 JH 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 JH 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 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 1C.

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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**Figure 1. A) 2 days post microdermabrasion showed centropacial swelling.**



**Figure 1. B) 2 days post initiation of treatment.**



**Figure 1. C) 4 days post initiation of treatment**