

A Study on Periorbital Edema Following Postcollagen Injection

To the Editor:

Cosmetic surgeons, often equating collagen with hyaluronic acid fillers, overlook the fact that the augmentation of interstitial cells can impede lymphatic circulation. This obstruction is frequently misdiagnosed as a protein allergy resulting in suboptimal correction outcomes and diminishing patient confidence and adherence. Consequently, this article presents 4 clinical observational cases of periorbital edema treatment following collagen injections, with the aim of elucidating the primary mechanisms and preventative measures for addressing this issue.

CASE DATA

The study encompasses 4 female patients, aged between 35 and 42 years, who developed periorbital edema subsequent to collagen injections. Two instances occurred following Sunmax collagen facial injections for esthetic enhancement, while the other 2 following Filldermin collagen facial injections. Though not exclusively, the injections were administered in the periorbital region. The patients began to exhibit

symptoms of edema in 3–4 weeks after the injections, reaching their peak around 1 month later. After thorough irrigation with 10 mL of normal saline in the roof layer, a significant reduction in collagen fibrosis was observed and the swelling began to subside within 48 hours post-treatment. Three patients experienced no recurrence of symptoms, while one had a minor recurrence of periorbital edema 23 days later, which was resolved with additional treatment. Six months after the initial saline irrigation, all 4 cases had fully recovered (Figure 1).

DISCUSSION

The primary cause of periorbital edema following collagen injection is attributed to the proliferation of deep fat pad interstitial cells. This proliferation, induced by the injected material, leads to a denser, firmer fibrous network, thereby impeding lymphatic drainage.¹ Furthermore, the adherence of collagen fibers in the prezygomatic space disrupts lymphatic vessel pathways. In addition, the excessive presence of filler material may constrict circulatory systems and impedes periorbital venous return.^{2–4} While infections⁵ and immune reactions postinjection can induce swelling infrequently, limited pathological evidence support these observations.

If individuals undergoing periorbital injections with type A botulinum toxin have recently received such treatments, they are particularly vulnerable to periorbital edema due to the weakened function of the muscle pump.^{6,7} The risk of periorbital edema escalates if collagen injections are administered concurrently with these treatments, highlighting the importance of avoiding simultaneous administration.

Periorbital edema following collagen injections typically manifests approximately 20 days postinjection with its peak occurring around 1 month postprocedure. This time frame corresponds with the maximum phase of collagen regeneration,⁸ characterized by significant fibroblast proliferation, densification of the adipose interstitium, and subsequent lymphatic obstruction. This

obstruction leads to edema in both upper and lower eyelids, which may present intermittently or affect only one side, with its severity more closely associated with the extent of lymphatic blockage rather than the scope of the injection. By the 4-month mark postinjection, the formation of new lymphatic pathways often substantially mitigates periorbital edema.

The primary criterion for diagnosing periorbital edema associated with collagen injections is a history of type I collagen administration, particularly when substantial amounts of collagen are injected near the suborbicularis oculi fat and prezygomatic space.⁹ The onset of this condition is associated with the fibrosis cycle with symptoms typically emerging approximately 20 days postinjection. The edema often manifests alternately on the left and right sides or intermittently on both, without a direct correlation to the full scope of the injection.

1. Immune Response: Symptoms of type I, II, III, and IV hypersensitivity reactions differ from those observed in the discussed cases. The type IV hypersensitivity reactions characterized by delayed onset, typically occurring around 48 hours after exposure, would affect the entire injected area rather than being localized to the periorbital region. Furthermore, hypersensitivity reactions primarily involve immune cells and rarely lead to fibrosis which makes the timing, location, and histopathology inconsistent with the findings observed in the 4 patients.
2. Chronic Granulomatous Inflammation: Granulomas are primarily composed of epithelioid cells and multinucleated giant cells with lesions typically presenting as small and nodular structures measuring between 0.5 and 2 mm in diameter. However, the pathology, clinical manifestations, and disease progression associated with chronic granulomatous inflammation do not correspond with the cases presented in this study.
3. Post-traumatic Hematoma: This is characterized by a stress response

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The data sets used or analyzed during the current study are available from the corresponding author on reasonable request.

All participants signed a document of informed consent.

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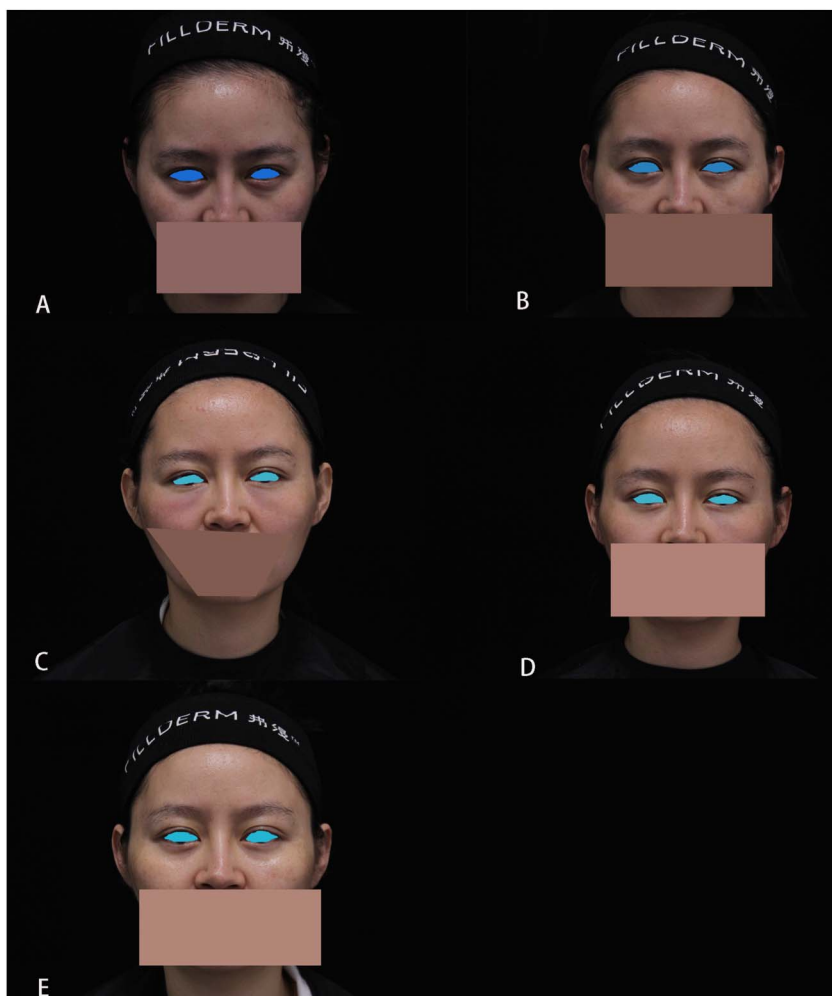


FIGURE 1. Case data on periorbital edema after collagen injection. Preoperative; 1 week postoperative; during edema onset; 2 weeks after treatment; long-term after treatment.

with a predictable timeline where peak swelling typically occurs at 48 hours and usually subsides within a week. This distinct timeline distinguishes it from the onset cycle of periorbital edema following collagen injections.

A detailed preoperative evaluation of the individuals seeking cosmetic enhancement is essential. Factors to consider include (1) preexisting periorbital swelling; (2) a history of hyperlipidemia,¹⁰ hyperglycemia, or renal disease¹¹; (3) advanced age accompanied by significant changes in skin texture¹²; (4) plans for concurrent collagen and botulinum toxin treatments; and (5) sensitive skin or preexisting rosacea.

Identifying these risk factors can help in mitigating the likelihood of edema following periorbital collagen injections.

The primary treatments for periorbital edema are normal saline and triamcinolone irrigation. Normal saline irrigation considered the first-line treatment aims to alleviate edema by dispersing collagen accumulations. While it is generally safe and effective, its success may vary across individuals and symptom severity. In more severe cases or when initial treatments fail, triamcinolone irrigation serves as an alternative. However, cautious use of triamcinolone is advised due to potential side effects, such as skin thinning or pigmentation changes,¹³ necessitating avoidance of high doses or frequent applications. If edema recurs after 1 month, another irrigation session may be necessary. The use of oral immunosuppressants and antihistamines is discouraged.

Preventing periorbital edema post-collagen injections involves several strategies. Optimizing injection

techniques to avoid critical areas can significantly lower complication risks, requiring a deep understanding of facial anatomy and proficient technical skills. In addition, personalized treatment plans based on comprehensive patient assessments can further reduce complications especially in individuals with certain health conditions. Finally, avoiding simultaneous treatments with other volumizing fillers and type A botulinum toxin is recommended to decrease the chances of developing periorbital edema.

In future research, it is imperative to further investigate how various types and sources of collagen impact the risk of edema. In addition, extended follow-up studies are essential for comprehending the long-term effects of collagen injections and the potential for delayed complications. Given the physiological diversity among individuals, there is

a necessity for the development of more personalized treatment and prevention approaches. There is a pressing need for improvement in physicians' abilities to select appropriate collagen types, execute precise injections, and manage complications efficiently. This underscores the significance of enhanced training for medical professionals particularly in patient evaluation and injection techniques.

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