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CASE REPORT

Calcium hydroxylapatite associated soft tissue necrosis: A case report and treatment guideline

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Summary We present an uncommon case of nasal alar and facial necrosis following calcium hydroxylapatite filler injection performed elsewhere without direct physician supervision. The patient developed severe full-thickness necrosis of cheek and nasal alar skin 24 h after injections into the melolabial folds. Management prior to referral included oral antibiotics, prednisone taper, and referral to a dermatologist (day 3) who prescribed valacyclovir for a presumptive herpes zoster reactivation induced by the injection. Referral to our institution was made on day 11, and after herpetic outbreak was ruled out by a negative Tzanck smear, debridement with aggressive local wound care was initiated. After re-epithelialization and the fashioning of a custom intranasal stent to prevent vestibular stenosis, pulsed dye laser therapy was performed for wound modification. The patient healed with an acceptable cosmetic outcome. This report underscores the importance of facial vasculature anatomy, injection techniques, and identification of adverse events when using fillers. A current treatment paradigm for such events is also presented.

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Introduction

Injectable fillers are a common, minimally invasive approach in the early treatment of facial aging due to volume depletion. Use of calcium hydroxylapatite (CHA) has grown in popularity following FDA approval in 2006 to improve moderate to severe wrinkles. Radiesse (Merz Aesthetics, San Mateo, CA) is the CHA approved for aesthetic applications in the United States, and is composed of 25–45 μm spheres suspended in a carboxymethylcellulose carrier. Therapeutic results can be expected to last a year or more, depending on injection location. CHA must be injected at the dermal-subcutaneous border. If injected superficially CHA can lead to nodule formation and induration. Use of CHA filler in areas with a thinner dermis, such as the nasal dorsum and tear troughs, increases the risk of inadvertent product show through the skin. Many practitioners have noted that CHA seems to expand during the first 5 min following an injection, resulting in a transient discomfort noted by some patients. Other common adverse events related to filler injection include tenderness, local erythema, and bruising. In a recent 5-year review assessing soft tissue fillers, CHA was associated with the greatest risk of complications (2.6%), which include cellulitis, tissue necrosis, and nodule formation.[1] More severe, but less common complications include herpes zoster reactivation, arterial embolization leading to infarction, temporary blindness and oculomotor palsy.[2,3] The most feared complication is vascular compromise and tissue necrosis. Although adequate data is not available to quantify the risk of necrosis with CHA fillers, smaller studies estimate this incidence to correlate with the known 0.001% incidence of collagen or hyaluronic acid fillers.[4–6] The glabellar region is most notoriously at risk for tissue necrosis following filler injection due to its reliance on the supratrochlear blood supply. Similarly, there have been recently reported cases of nasal alar necrosis following both CHA and hyaluronic acid injection.[7] We present a recent case of soft tissue necrosis of the melolabial and nasal ala region that was not accurately identified, leading to delay in therapeutic intervention and increase in patient morbidity.

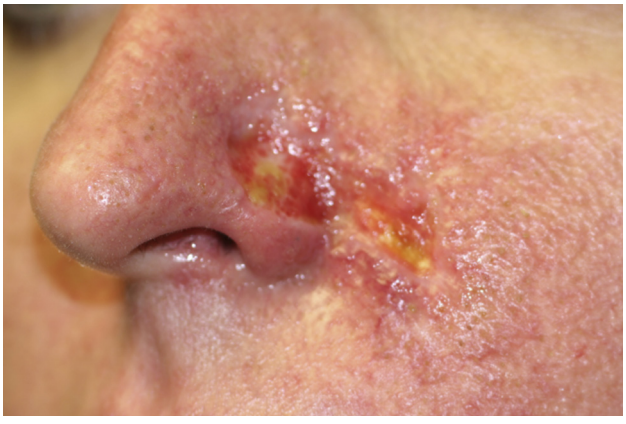


Figure 1 Necrosis, diffuse inflammation, and fibrinous exudate were apparent upon presentation to our institute on day 11 following the filler injection.

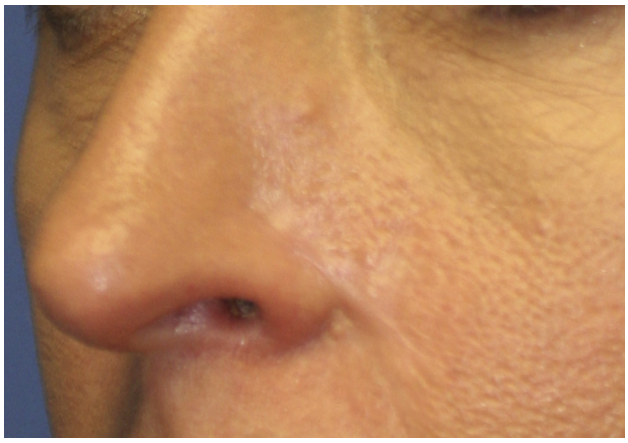


Figure 2 Appearance of the infarcted area after complete healing and treatment with pulsed dye laser. Photograph was taken 4 months after the offending injection.

Case report

The patient was a 41-year-old woman with a past medical history of rhinoplasty surgery, septal perforation, and multiple prior dermal filler injections to the melolabial folds, who received CHA injections to both melolabial folds with extension to the alar-facial creases. A nurse at a local "med spa" performed the injection without direct physician supervision. Approximately 24 h following the injection, the patient noted swelling and skin changes to her left alar crease. She initially sought treatment at the spa and was treated for presumptive infection with ciprofloxacin and prednisone taper. On post-injection day 3, the patient

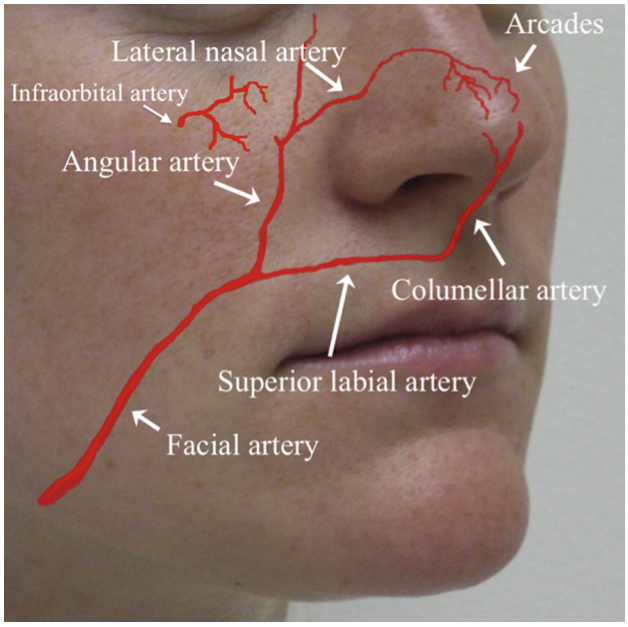


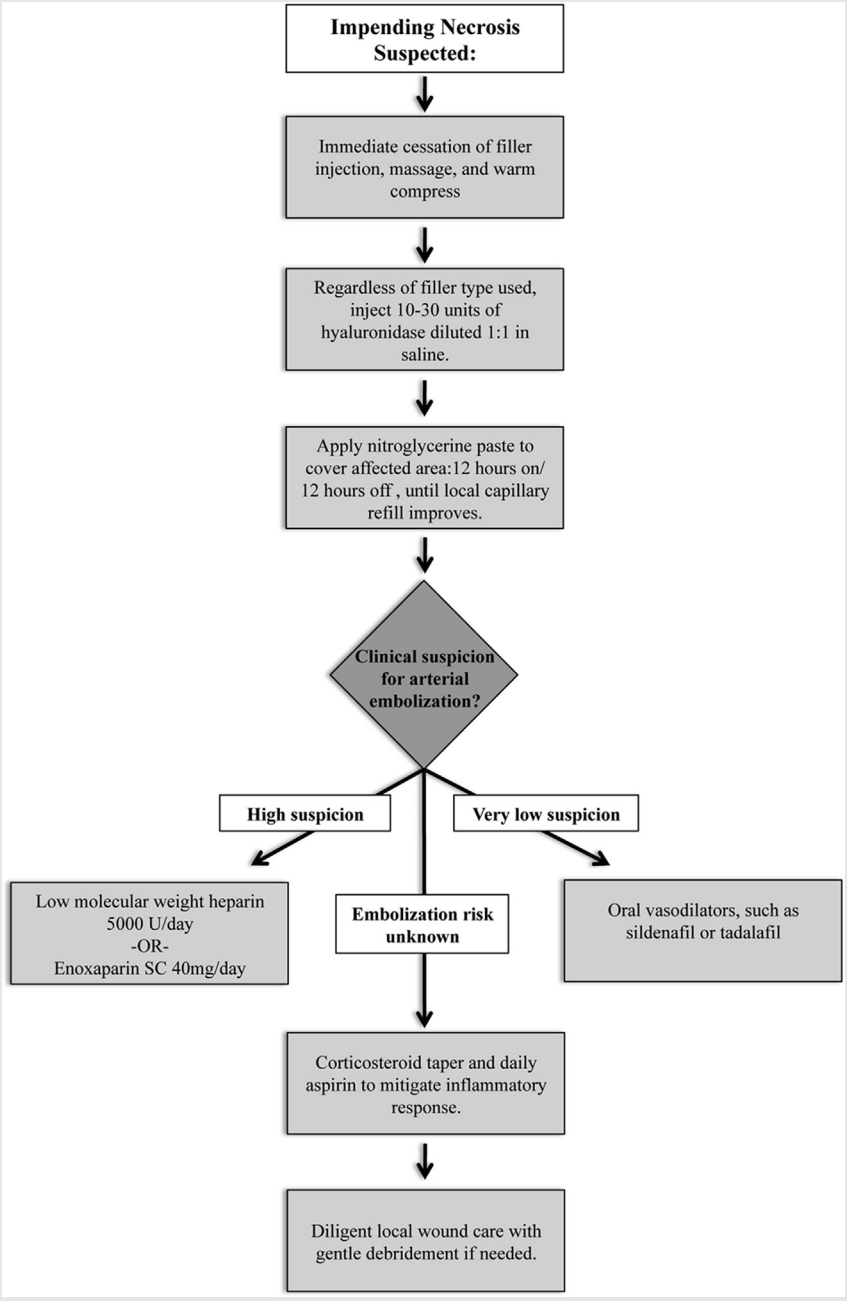
Figure 3 Native vascular anatomy to the nasal ala. Although the infraorbital and dorsal nasal arteries provide some redundancy, the nasal alar region receives most of its blood supply from the angular artery.

developed soft tissue necrosis and was seen by a dermatologist who prescribed valacyclovir for a presumptive herpes zoster reactivation induced by the injection. On post-injection day 11, the patient was referred to our institution. On presentation, frank tissue necrosis, diffuse inflammation, and fibrinous exudate were observed. Gentle debridement was performed revealing a partial thickness tissue loss (Figure 1). An aggressive daily local wound care regimen was implemented and daily wound debridement was performed. During this time herpes zoster reactivation was ruled out with a Tzanck smear. The wound was then allowed to heal by secondary intention and a custom intranasal acrylic resin stent was fashioned to reduce the risk of cicatricial vestibular stenosis. Finally, on post-injection day 74, pulsed dye laser therapy was utilized to reduce scarring and hyperpigmentation. The patient healed with an acceptable result and declined additional scar revision surgery (Figure 2).

Discussion

Although rarely reported, nasal alar tissue necrosis is a known complication of injectable filler use. Tissue necrosis

Table 1 Management strategy for impending tissue necrosis associated with injection of CHA dermal filler.



can result from direct embolization of vasculature with filler material or from compression of local vasculature by the filler product. The complication described in this case represents an insult to the distribution of the angular branch of the facial artery (Figure 3). The patient had undergone prior nasal surgery and it is likely that her native vascular anatomy had been altered, leaving her nasal alar region dependent on arcades from the superior labial and infraorbital arteries. Given the delayed onset of symptoms (approximately 24 h), arterial embolization is less likely versus vascular compression. While excluded in this case, it is important to consider an acute herpetic reactivation which can mimic impending tissue necrosis.[2] Given the significant morbidity and deformities associated with soft tissue necrosis, we advocate the consideration of this worst-case scenario to prevent any delay in therapeutic interventions.

To prevent filler associated tissue injury, a complete understanding of facial vascular anatomy is necessary. In our practice, we inject only with a moving needle in a retrograde fashion and avoid large bolus injections in areas near known vascular landmarks. We also use microcannulas for product placement to reduce the incidence of common, transitory adverse events as well as vascular cannulization or injury.[8] Microcannulas are highly flexible, have a round blunted tip, and employ a side port for the actual injection of filler material. Their flexibility and lack of the sharp bevel tip inherent in traditional needles make the risk of arterial puncture with microcannulas much less likely. Further, we feel that product placement is more accurate as a cutting needle tip creates a plane of injection while a microcannula follows the natural anatomic tissue planes.

If impending necrosis is suspected, or even considered, prompt treatment is absolutely mandatory (Table 1). The downside for taking action in a circumstance without vasculature injury is minimal in comparison to the case example given. Current recommendations include immediate cessation of filler injection, prompt massage with the intent to mechanically distribute the filler away from local vasculature, application of a warm compress, and prompt use of topical nitroglycerin paste to encourage vasodilation.[9] The minimal amount of nitroglycerin paste needed to cover the affected area should be reapplied daily, 12 h on and 12 h off, until local capillary refill times improve. We recommend the use of 10—30 units hyaluronidase (Vitrase, ISTA Pharmaceuticals, Irvine, CA) diluted 1:1 in saline, regardless of the type of filler used.[10] Hyaluronan is a known mediator of early inflammation, and hyaluronidase has been shown to reduce edema and tissue necrosis in the setting of myocardial infarction.[11] Anecdotally, hyaluronidase has been used successfully via the same presumptive mechanism to mitigate inflammation and edema in cases of necrosis related to dermal filler injection, even those using CHA. Daily aspirin and a corticosteroid taper are used to decrease the inflammatory component of the vascular injury. If available, hyperbaric oxygen can also be utilized to promote tissue oxygenation. If vascular compression rather than filler embolus is suspected, consider the additional use of oral vasodilators such as sildenafil or tadalafil. There is some concern that the use of vasodilatory agents in the case of known arterial cannulization may further push filler material into the tissue capillary bed, leading to complete vascular occlusion and worsening necrosis. If filler embolization is suspected, low molecular weight heparin or enoxaparin may be useful to reduce further thrombus formation and minimize the extent of necrosis.[12]

Conclusion

To prevent injectable associated tissue necrosis a complete understanding of vascular anatomy, filler properties and indications for use, as well as knowledge of the patient's complete medical history is mandatory. In the circumstance of impending necrosis, early identification and the use of appropriate vasodilatory, anti-inflammatory, and antimicrobial therapies is paramount to improve tissue survival and optimal wound healing. Consideration of an infectious or herpetic presentation should be made, but not at the sacrifice of addressing vascular compromise. Finally, custom prosthetics, such as an intranasal stent, are useful in reducing soft tissue retraction and stenosis.

Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.bjps.2013.08.008.

References

1. Daines SM, Williams EF. Complications associated with injectable soft-tissue fillers: a 5-year retrospective review. *JAMA Facial Plast Surg* 2013;**15**:226—31.
2. Sires B, Laukaitis S, Whitehouse P. Radiesse-induced herpes zoster. *Ophthal Plast and Reconstr Surg*;**24**:218—9.
3. Sung MS, Kim HG, Woo KI, Kim Y-D. Ocular ischemia and ischemic oculomotor nerve palsy after vascular embolization of injectable calcium hydroxylapatite filler. *Ophthal Plast and Reconstr Surg*;**26**:289—91.
4. Bass LS, Smith S, Busso M, McClaren M. Calcium hydroxylapatite (Radiesse) for treatment of nasolabial folds: long-term safety and efficacy results. *Aesthet Surg J* 2010;**30**:235—8. The American Society for Aesthetic Plastic Surgery.
5. Narins RS, Jewell M, Rubin M, Cohen J, Strobos J. Clinical conference: management of rare events following dermal fillers—focal necrosis and angry red bumps. *Dermatol Surg* 2006;**32**:426—34. Official Publication for American Society for Dermatologic Surgery [et al.].
6. Hanke CW, Higley HR, Jolivette DM, Swanson NA, Stegman SJ. Abscess formation and local necrosis after treatment with Zyderm or Zyplast collagen implant. *J Am Acad Dermatol* 1991;**25**:319—26.
7. Grunebaum LD, Bogdan Allemann I, Dayan S, Mandy S, Baumann L. The risk of alar necrosis associated with dermal filler injection. *Dermatol Surg* 2009;**35**(Suppl. 2):1635—40 official publication for American Society for Dermatologic Surgery [et al.].
8. DeJoseph LM. Cannulas for facial filler placement. *Facial Plast Surg Clin North Am* 2012;**20**:215—20 vi—vii.

9. Cohen JL. Understanding, avoiding, and managing dermal filler complications. *Dermatol Surg* 2008;**34**(Suppl. 1):S92—9 official publication for American Society for Dermatologic Surgery [et al.].
10. Dayan SH, Arkins JP, Mathison CC. Management of impending necrosis associated with soft tissue filler injections. *J Drugs Dermatol JDD* 2011;**10**:1007—12.
11. Maroko PR, Hillis LD, Muller JE, et al. Favorable effects of hyaluronidase on electrocardiographic evidence of necrosis in patients with acute myocardial infarction. *New Engl J Med* 1977;**296**:898—903.
12. Schanz S, Schippert W, Ulmer A, Rassner G, Fierlbeck G. Arterial embolization caused by injection of hyaluronic acid (Restylane). *Br J Dermatol* 2002;**146**:928—9.