Vascular Compromise from Soft Tissue Augmentation

Experience with 12 Cases and Recommendations for Optimal Outcomes

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ABSTRACT

The popularity of soft tissue fillers is, in part, due to their favorable side-effect profile. However, serious complications can occur. The authors describe their extensive clinical experience with soft-tissue augmentation and the rare complication of vascular compromise, which can lead to necrosis and scarring. Over a 10-year period between January 2003 and January 2013, the authors observed a total of 12 cases of vascular compromise. Eight patients in their clinical practice showed evidence of vascular compromise out of a total of 14,355 filler injections (0.05%). In addition, four patients treated with an experimental particulate filler had vascular complications. All cases were examined for filler type, location of complication, risk factors, treatment, and outcomes. Although treatment plans differed for each patient in their series, all cases of vascular compromise resolved fully. The authors believe that an office-based protocol for both immediate and ongoing care—including a thorough individualized assessment and treatment plan for each patient—is critical to timely and effective resolution of side effects. They propose key recommendations for the prevention and management of vascular compromise to improve patient outcomes and reduce the risk of permanent complications.
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Injectable fillers have become an integral part of aesthetic medicine for patients who want noninvasive rejuvenation. They are used to restore volume and to smooth and efface superficial wrinkles and deep folds of the face, among other indications. Widespread use began in the 1980s with the advent of bovine collagen. Since then, use has surged so that soft tissue augmentation is the second most popular nonsurgical aesthetic procedure in North America to botulinum toxin.[1] In 2007, more than 1.5 million soft tissue filler procedures were performed in the United States, with hyaluronic acid (HA) being the most frequently used.[2] As of 2010, more than 200 types of fillers were available for soft tissue augmentation worldwide.[1]

The popularity of soft tissue fillers is in part due to their favorable side-effect profile. Adverse effects from soft tissue filler injection are generally mild and self-limited. However, there are some well-documented serious complications. The most feared and potentially serious complications are vascular in nature. Collectively referred to as vascular compromise, these complications include partial or complete interruption of vascular supply by extravascular compression, or a complete occlusion of vascular supply from intravascular injection. Subsequent necrosis and scarring are potentially permanent sequelae.[2–4]

In the authors' clinical practice, 14,355 filler injections were performed between January 2003, when they first instituted their computer database, and January 2013. Fillers that are used in their office include hyaluronic acid (HA) (Juvéderm Ultra, Ultra plus, Voluma [Allergan, Irvine, California] and Restylane [Medicis Aesthetics Inc., Scottsdale, Arizona]); poly-L-lactic acid (Sculptra, Sanofi-Aventis, Bridgewater, New Jersey); calcium hydroxylapatite (Radiesse, Merz USA, Greensboro, North Carolina); silicone oil; and collagen (Evolence Breeze, Ortho Dermatologics,

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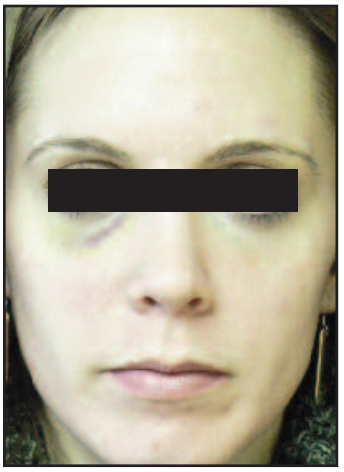
APPENDIX 1. Case summaries: filler complications, management, and outcomes

PATIENT	AGE	DATE OF INJECTION	FILLER* AND LOCATION	TIME OF ASSESSMENT POST-INJECTION	COMPLICATIONS	MANAGEMENT	OUTCOME
1	54	10/14/2009	1.3mL CaHA into nasolabial folds (NLF) and malar cheeks	Day 5	Violaceous reticulated painful patch to right cheek with pustules	Massage, clindamycin, intralesional triamcinolone acetonide (IL TAC)	Complete resolution
2	69	12/14/2009	1mL monophasic HA to pre-jowl sulcus, lip corners, right lateral cheek	Day 2	Violaceous reticulated painful patch to right NLF. Right upper lip pain, numbness and ecchymosis	Massage, warm compresses, patient declined treatment with hyaluronidase and prednisone	Complete resolution
3	26	01/11/2010	0.3mL CaHA to nasal dorsum	Day 4	Violaceous reticulated patch to right nasal ala	Warm compresses, conservative management	Complete resolution
4	65	06/15/2010	1mL monophasic HA to NLF	2 hours	Violaceous reticulated painful patch to left NLF	Massage, hyaluronidase	Complete resolution
5	31	11/16/2011	2mL monophasic HA to nasojugal folds	Day 5	Violaceous reticulated painful patch to right central cheek (Figure 1, left)	Massage, warm compresses, hyaluronidase	Complete resolution (Figure 1, right)
6	50	12/6/2011	2mL biphasic HA to NLF (no anesthetic)	24 hours	Violaceous reticulated painful patch to left NLF and alar crease	Massage, warm compresses, hyaluronidase, prednisone	Complete resolution
7	56	06/1/2012	1.5mL CaHA to nasal bridge and glabella	Day 4	Violaceous reticulated painful patch to forehead (Figure 2, left)	Massage, warm compresses, nitroglycerin paste, prednisone	Complete resolution (Figure 2, right)
8	58	08/1/2012	3mL CaHA to inferior NLF and malar cheeks, 0.5 cc monophasic HA to superior NLF	Immediate	Violaceous reticulated patch and blanching to left NLF (Figure 3, left)	Massage, warm compresses, nitroglycerin paste, hyaluronidase, prednisone, aspirin	Complete resolution (Figure 3, right)
9	57	08/18/2009	STUDY: Particulate experimental filler	Day 3	Violaceous reticulated painful patch and edema to right upper lip and nasolabial fold	Massage, warm compresses, nitroglycerin paste, prednisone, IL TAC	Complete resolution
10	55	03/15/2010	STUDY: Particulate experimental filler	Day 3	Violaceous reticulated painful patch to left NLF; ecchymosis to left NLF and petechiae to lip mucosa	Massage, prednisone	Complete resolution
11	38	03/15/2010	STUDY: Particulate experimental filler	Day 1	Violaceous reticulated patch, swelling, and sluggish capillary refill to left NLF; erosion on post-injection Day 6	Prednisone, fucidin 2% ointment to erosion	Complete resolution
12	36	03/16/2010	STUDY: Particulate experimental filler	Day 3	Violaceous reticulated patch, swelling, and sluggish capillary refill to left nasolabial fold	Massage, prednisone	Complete resolution

For all patients seen in the authors' office, the filler is reconstituted with 2% lidocaine and 20mg/mL, 1:200,000 epinephrine unless stated otherwise



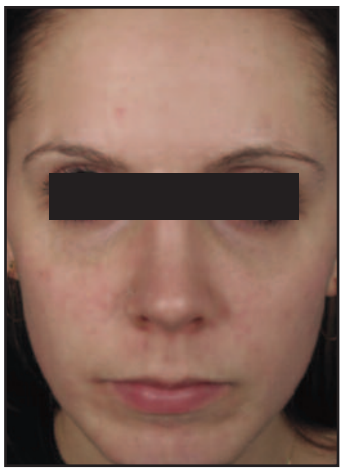
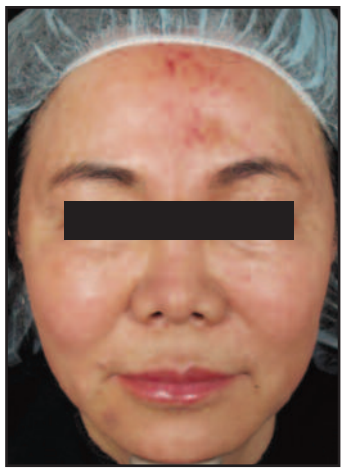


Figure 1. Mottled erythema to right cheek, five days post-injection (left). Resolution of vascular compromise with no sequelae, two months post-injection (right)



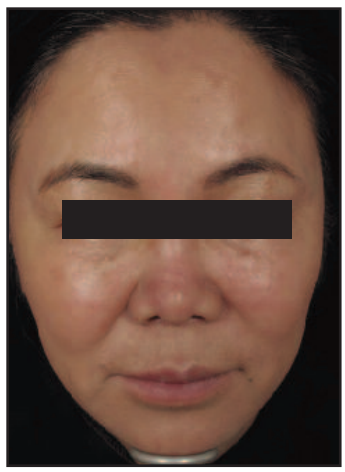
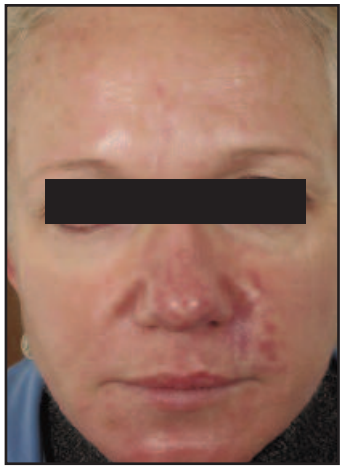


Figure 2. Mottled erythema to forehead, five days post-injection (left). Resolution of vascular compromise with no sequelae, 2.5 months post-injection (right)

Skillman, New Jersey). During this 10-year period, a total of 12 cases of vascular compromise were observed and managed, eight of which occurred in the authors' clinical practice and four in their clinical trials practice. Those cases that developed vascular compromise after soft tissue augmentation are reviewed and treatment discussed (Appendix 1).

Over a 10-year period between January 2003 and January 2013, eight patients in the authors' clinical practice showed evidence of vascular compromise out of a total of 14,355 filler injections (0.05%). They observed four cases after injection with calcium hydroxylapatite (CaHA) (out of 1,482 total injections; 0.27%), four cases after injection with volumizing monophasic HA (Juvéderm Voluma) (out of 4,321 total injections; 0.09%), and one case resulting from treatment with biphasic HA (Restylane) (out of 3,348 injections; 0.03%). One patient was treated with both CaHA and volumizing monophasic HA, and is counted in both groups (Table 1). In all cases, the injection technique was not recorded. The authors typically use a combination of antegrade and depot injection when revolumizing. In addition to the above cases in their clinical practice, in their research practice, four patients treated with an experimental particulate filler displayed evidence of vascular compromise.



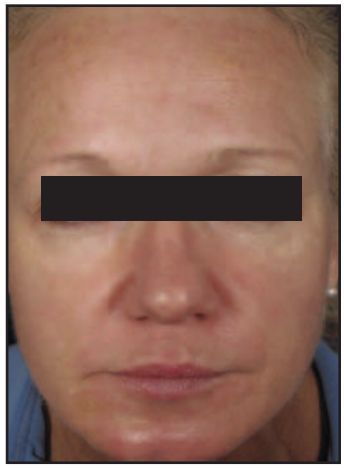


Figure 3. Dusky erythema to left nasolabial fold, five days post-injection (left). Resolution of vascular compromise with no sequelae, 3.5 months post-injection (right)

DISCUSSION

Injection of fillers is generally very well-tolerated with mild transient side effects including erythema, bruising, tenderness, and swelling lasting for a few days. Vascular compromise, occlusion, or necrosis after injection are rare, but potentially very serious adverse effects (Box 1).[3,4]

Mechanisms leading to tissue necrosis are not fully understood. It is felt there must be extra- and intravascular factors. Extravascular causes result from compression of the vessel from the injectable filler. Secondary inflammation and edema can further put pressure on the vessels leading to decreased skin perfusion. Intravascular causes are direct injection of the filler into the vasculature causing obstruction and damage to the wall of the blood vessels.[5] Compression of the vessel from filler typically occurs immediately after injection. It can occasionally present later if there is pressure from the filler and subsequent post-injection swelling.[6] Embolization of filler material has also been reported following HA injection. This presentation may be immediate and has also been reported with a delayed presentation at six hours post-injection.[7]

Typically, the first indication of vascular damage after filler injection is painless blanching. This can be subtle and may go unnoticed. Over the next couple of days, progression to a painful, violaceous, reticulated patch may occur. A necrotic eschar may develop on top of an ulcer with subsequent scar formation. Treatment should be instituted at first sign of this complication to prevent necrosis and scarring.[2,8]

TABLE 1. Risk of vascular compromise in the authors' clinical practice

FILLER	TIME FRAME EVALUATED	NUMBER OF PATIENTS WITH EVIDENCE OF VASCULAR COMPROMISE	NUMBER OF FILLER INJECTIONS OVER TIME FRAME	PERCENTAGE WITH COMPLICATION IN GROUP (%)
Total fillers injected in clinical practice	Jan 2003–Jan 2013	8	14,355	0.05
CaHA*	Jan 2004–Jan 2013	4	1,482	0.27
Volumizing monophasic HA*	Feb 2009–Jan 2013	4	4,321	0.09
Biphasic HA	Jan 2003–Jan 2013	1	3,348	0.03

*One patient with evidence of vascular compromise was treated with both CaHA and volumizing monophasic HA, and is counted in both groups

BOX 1. Adverse effects from soft tissue augmentation

Early (occurring up to one week after injection)
- **Injection site reactions (bruising, swelling, erythema)**
- **Infections**
- **Nodules/asymmetry**
- **Hypersensitivity**
- **Vascular compromise**

Delayed (occurring weeks to years after injection)
- **Infection**
- **Granuloma formation**
- **Biofilm formation**

***Adapted from Glashofer MD, Flynn TC. Complications of temporary fillers. In: Carruthers J, Carruthers A. *Soft Tissue Augmentation*. Toronto: Elsevier Saunders; 2013:179–187.**

Historically, the glabella has been the most commonly reported site of necrosis. This area is a watershed site with limited collateral circulation. Small-caliber vessels branch out from the supratrochlear arteries.[9,10] In previous reports with injection of Zyplast (Allergan, Inc.), 50 percent of tissue necrosis occurred in the glabellar area.[11] The nasolabial fold is another high-risk site. The embryonic fusion planes at the alar groove may not allow for accommodation of filler volume and the angular artery can be compromised.[2] Rare, but extremely dangerous complications can occur with injection of fillers, including blindness. Lazzeri et al[12] reviewed the literature and reported on 32 cases of transitory or permanent blindness following fat injection or aesthetic injections of other materials including fillers. In another case series, Park et al[13] reported on 12 cases of retinal artery occlusion following injection into high-risk sites, such as the glabellar region and nasolabial folds.

To the authors' knowledge, this is one of the largest case series published on vascular compromise with cutaneous complications secondary to soft tissue augmentation. In this series, the authors observed vascular compromise from three different commercially available fillers and an experimental particulate filler. These fillers were all placed in a deeper plane for their volumizing properties. Of note, the authors did not observe any cases of vascular compromise from fillers placed more superficially to efface rhytides.

Patients treated with CaHA and volumizing monophasic HA in the authors' clinical practice were injected using a 28-gauge (G), ¾-inch needle. The biphasic HA was injected using a 29G, ½-inch needle. The particulate experimental filler was injected using a 27G, 1½-inch needle. Pertinent patient risk factors that may have contributed to complications include a prior rhinoplasty in a patient who developed evidence of occlusion at the nasal ala after treatment with CaHA and a positive smoking history in a patient treated with both CaHA and volumizing monophasic HA (Table 2).

Eight patients experienced vascular compromise at the nasolabial fold or lip, two at the malar cheek, one at the nasal ala, and one at the glabella. The anatomic sites most commonly affected were at increased risk for vascular occlusion including the nasolabial folds where the angular artery or lateral nasal artery can be occluded and the glabellar region where there is minimal collateral circulation.[14–16]

The incidence of vascular complications in the authors' clinical practice was 0.05 percent. This is higher than the 0.001 percent reported in the literature with injection of collagen and HA fillers; however, it is difficult to make a direct comparison because the data includes newer synthetic fillers that are designed to be injected in a deeper plane in addition to HA fillers. It has been reported that the rate of vascular complications secondary to soft tissue

TABLE 2. Filler used and complication by site, underlying risk factors, and needle size

FILLER	CASE #	LOCATION OF COMPLICATION	RISK FACTORS	NEEDLE SIZE
CaHA	1	Cheek		28G, ¾ inch
	3	Nasal ala	Previous rhinoplasty	
	7	Forehead		
CaHA and volumizing monophasic HA	8	Nasolabial fold	Smoker	28G, ¾ inch for both
Volumizing monophasic HA	2	Nasolabial fold/lip		28G, ¾ inch
	4	Nasolabial fold		
	5	Cheek		
Biphasic HA	6	Nasolabial fold		29G, ½ inch
Experimental particulate filler	9	Nasolabial fold/lip	Study patient	27G, 1½ inch
	10	Nasolabial fold/lip	Study patient	
	11	Nasolabial fold	Study patient	
	12	Nasolabial fold/lip	Study patient	

augmentation is rising.[17] This could parallel the rise in filler treatments performed or more likely reflects a shift in the paradigm from two-dimensional to a three-dimensional revolumization.

PREVENTION

There are a number of preventative strategies that can reduce the risk of occlusion. The key strategies the authors' group has implemented are outlined in Box 2.

Preventative measures include taking a detailed history to assess for previous treatment with fillers or cosmetic surgeries in the area to be treated. Choosing a reversible HA filler allows for treatment with hyaluronidase and possible reversal of vascular occlusion if used early.[5] It is important to be cautious when injecting high-risk anatomic areas, such as the glabella or nasolabial folds.[2,14,15] Aspirating before injecting if possible and using low volumes of product in two or more treatment sessions reduces the risk of vascular occlusion.[10,12] Other measures to reduce vascular complications include injecting with a small gauge needle,[2,12] injecting slowly,[12,18,19] and use of the cannula technique.[14]

TREATMENT

It is important to recognize that the management of vascular compromise from soft tissue fillers is not based on a large body of evidence. A treatment protocol has been developed at the authors' office to be implemented if vascular complications are suspected (Box 3).

If blanching occurs while injecting, immediately discontinue the injection and begin warm compresses. The authors suggest application for 10 minutes every one to two hours. This encourages quick vasodilation to restore blood supply to the area.[4,15] Massage of the treated area should be instituted.[20] A nerve block may be necessary to facilitate vigorous massage. In the authors' experience, massage can dramatically, albeit temporarily, reverse the blanched or dusky appearance of the skin and should be repeated regularly for several days to improve the likelihood of tissue viability.

If the complication occurs with an HA filler, hyaluronidase is recommended.[19] Hyaluronidase works to break down and hydrolyze hyaluronic acid. One can consider skin testing to evaluate risk of allergy.[7] Dayan et

BOX 2. Authors' key prevention strategies

- Before injecting, a detailed history should be obtained including any previous cosmetic procedures or surgeries. Exercise caution in the setting of nasal augmentation post-rhinoplasty
- The injector should be well-trained and have a firm understanding of the facial vascular anatomy and the depth at which the filler should be implanted
- Choosing a reversible filler (HA filler) increases the likelihood of resolution without sequelae as hyaluronidase can be used to remove the product
- Using the cannula technique may reduce risk of vascular compromise
- Extreme caution should be observed when injecting filler in anatomically sensitive areas such as the glabellar region and nasolabial folds
- In high-risk areas, use low volumes of product in two or more treatment sessions
- Inject product slowly. Discontinue the injection immediately if blanching occurs
- Use a smaller gauge needle if practical
- If possible, aspirate before injecting to ensure filler is not placed in the intravascular space

BOX 3. Authors' key treatment strategies

- Warm compresses, 10 minutes every 1–2 hours
- Vigorous massage, nerve block if necessary, no epinephrine
- Hyaluronidase if filler is HA filler
- Consider topical nitroglycerin paste 2%. Can be applied as frequently as every 1–2 hours initially. Once at home, patient can apply up to 3 times a day to the affected area provided he/she does not develop symptoms of dizziness
- Consider administering aspirin, 325mg under tongue immediately and 81mg daily thereafter
- Consider oral prednisone 20–40mg daily for 3–5 days
- Consider hyperbaric oxygen
- Follow patient daily until improvement. Provide him/her with clear written instructions about management at home and contact phone numbers

al[17] proposed treating impending necrosis with 10 to 30 units of hyaluronidase regardless of the filler type, including for non-HA fillers. Hyaluronidase has been shown to have edema-reducing benefits and theoretically reduces occluded vessel pressure.[16] Some authors have experience canalizing an occluded vessel and injecting hyaluronidase with immediate reversal of signs of occlusion.

Nitroglycerin paste application can allow for more significant vasodilation.[4,14,15,17] The authors have used topical 2% nitroglycerin paste applied initially every one to two hours. This can be continued at home three times per day providing the patient does not experience dizziness. This treatment recommendation is controversial because it may cause superficial shunting of blood and disruption of deeper vascular supply or may allow further migration and compromise blood flow downstream in the case of particulate fillers.

Aspirin is used to block platelet aggregation and has moderate anti-inflammatory properties. It can help prevent blood clotting within a partially occluded vessel.[14,15] The authors suggest a dose of 325mg under the tongue immediately and 81mg daily thereafter.

Oral prednisone, 20 to 40mg daily, for three to five days is recommended. Oral corticosteroids prevent further vascular compromise by decreasing the inflammatory component of the injury.[14]

Treatment with hyperbaric oxygen can be considered. It has the potential to deliver oxygen deep into the skin to keep tissues viable. Its use is controversial though and the risks, benefits, and inconvenience must be weighed when considering this treatment.[14,17]

Other treatments outside of the authors' protocol have been recommended. Low molecular weight heparin has been used to prevent thrombosis and embolization.[4] Drugs designed for treatment of erectile dysfunction, such as sildenafil and tadalafil, have been utilized; these medications cause smooth muscle relaxation, dilation of the blood vessels, and increased blood flow.[14]

If necrosis does occur, diligent wound care is critical.[9] Treatment of the resulting scar may involve silicone gel sheeting and intralesional triamcinolone acetonide. Long-term scar management can include dermabrasion, surgical excision, or laser resurfacing.[4]

While the exact treatment plan differed for each patient in the authors' series, the end result for all patients was full resolution of symptoms. The authors believe that a thorough individual assessment and treatment plan should be instituted for each patient. Having an office-based protocol for both prevention and treatment of vascular-related complications is critical to timely and effective

resolution of side effects. Immediate and ongoing care ensures optimal outcomes and decreases the risk of permanent complications.

SUMMARY

With the increased use of soft tissue augmentation for revolumization, it is imperative to be aware of potential complications. Vascular compromise is one of the most serious side effects. Herein the authors report on their extensive collective experience with soft tissue augmentation and describe 12 cases of vascular compromise. They propose key recommendations for prevention and management of this side effect to improve patient outcomes.

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