

# Complication of Soft Tissue Fillers: Prevention and Management Review

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## ABSTRACT

The use of dermal fillers has increased manifold over the past decade, which has been attributed to the ever-increasing need of the population to look young. Fillers have become quite popular both among patients and treating physicians due to their quick and quite predictable results. Filler injection is a safe procedure in the hands of an experienced provider using appropriate technique. Nevertheless, various adverse effects to fillers have been reported that range from mild injection site complications, such as pain and bruising, to severe complications, like tissue necrosis, retinal artery occlusion, and infections. The esthetic provider should be aware of and be able to quickly recognize such complications, and be confident in managing them. In this article we highlight the various adverse effects noted with the use of fillers and discuss prevention and management.

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## INTRODUCTION

The injectable cosmetic treatments including fillers have become highly popular in recent years. Fillers are safe in the hands of an experienced provider but can be associated with side effects. Although the incidence of adverse effects to filler injection is low, the significant increase in the number of such procedures has led to an increased number of reported complications.

Fillers can be classified into permanent and biodegradable. Although these types have a similar percentage of adverse events in the first 12 months after filler injection, permanent fillers can result in severe side effects even several years after placement.<sup>1</sup>

These authors recommend use of certified fillers, which may vary from country to country. Silicone, for instance, has never been certified and should be banned for esthetic purposes.

## COMPLICATIONS

A wide range of complications have been noted with the use of fillers, which vary from mild injection site reactions to granulomas and severe hypersensitivity reactions (Table 1). Rohrich and colleagues classified filler related complications as early, late, and delayed, on the basis of timeframe of appearance as less than 14, 14 days to 1 year, and more than 1 year, respectively.<sup>2</sup>

TABLE 1.

Complications of Fillers	
Early Complications	Delayed Complications
Injection site reactions	Infections
Erythema	Mycobacterial
Edema	Biofilm
Bruising	Nodules/abscesses
Infections	Foreign body granulomas
Hypersensitivity	Immune reactions
Asymmetry, lumps	Persistent discoloration
Dysesthesias, anesthesia, and paresthesia	Malar edema
Vascular occlusion and tissue necrosis	

**FIGURE 1.** Swelling and erythema of lower eyelids and upper malar areas following filler injection.



### Injection Site Complications

The most prevalent complications of soft tissue filler injection are the injection site adverse effects including bruising, edema, pain, erythema, and ecchymosis (Figure 1). These side effects are mostly transient and mild, lasting a few days.<sup>3</sup> Bruising is usually observed after injection of the filler material into the dermal layer when given by fanning or threading method. The occurrence of bruising can be reduced by slow injection of the filler material and, if occurred, cold compresses should be used.<sup>4</sup> Bruising typically disappears in a week's time. If the patient is on anticoagulant therapy, it should be discontinued at least 7–10 days before the procedure after consulting with the treating physician. The injection related pain and swelling can be minimized by application of ice prior to injection, the use of small gauge needle or blunt cannulas, and the combination of fillers with of local anesthetics, typically lidocaine. Cold compresses and NSAIDs can help in ameliorating the pain and swelling after the procedure. In severe cases, short course of oral steroids may be needed along with the NSAIDs. Mild erythema is also commonly seen after the injection but persistent erythema may require a short course application of moderate potency topical steroids. Vitamin K cream has been reported as beneficial in the management of purpura.<sup>5</sup>

### Dysesthesia, Anesthesia, and Paresthesia

An inadvertent trauma, direct injection into the nerve, or compression of the nerve by the filler material can cause nerve damage that may lead to dysesthesia, anesthesia, or pares-

**FIGURE 2.** Tyndall effect cause by hyaluronic acid injection into the tear troughs.



**FIGURE 3.** Hyaluronic acid injection of the nose leading to skin necrosis.



thesia, which may be transient or, rarely, permanent. The most commonly affected nerve during filler injections is the infra-orbital nerve, but rarely, Bell's palsy and marginal mandibular nerve damage has been reported.<sup>6,7</sup> A thorough knowledge of nerve anatomy is required before injection to prevent such adverse effects.

### Inappropriate Injection Technique-related Complications

A filler should be placed in the appropriate tissue layer. Inappropriate injection technique and too-high volumes can cause side effects like visible implants, palpable nodules, over-, or under-correction. Lumps and bumps at the site of injection are some of the most prevalent side effects seen with filler injections (Figure 2). They may be non-inflammatory, inflammatory, or infectious. Early onset lumps are usually due to suboptimal injection techniques like excess filler injection or too superficial placement of the injected material. Persistent non-inflammatory lumps are usually due to overcorrection and superficial injection and usually respond to massage, but in some cases, needle aspiration, drainage, and intralesional hyaluronidase injections may be required.<sup>8</sup>

Too superficial filler injection can lead to a bluish discoloration known as Raleigh scattering or Tyndall phenomenon, and sometimes due to hemosiderin deposition due to intradermal bleeding during the injection (Figure 3). It may persist for a long-time, if left untreated. Hyaluronidase injection is the preferred treatment option for this discoloration if a hyaluronic filler was used. Drainage of the filler is the recommended treatment of nodules caused by polymethyl methacrylate (PMMA) injections. A combination of intralesional neodymium-YAL laser and drainage seems to be even more effective.<sup>9</sup> Superficial injection of fillers containing calcium hydroxylapatite or poly-L-lactic acid can cause small, whitish nodules on the skin surface. Superficial silicone injections may lead to fibrosis and foreign body granulomas formation termed siliconomas presenting as nodules.<sup>10</sup>

**FIGURE 4.** Filler injection leading to long lasting swelling and induration of the left cheek and right lower eyelid.



**FIGURE 5.** Necrosis of the left upper cutaneous lip caused by a hyaluronic acid injection.



Facial overfilling with large volumes and/ or too frequent filler injections can cause non-esthetic results but also permanent structural defects in the treated areas.<sup>11</sup>

#### Allergic and Hypersensitivity Reactions

Fillers can lead to foreign body granulomas and hypersensitivity reactions, which manifest as induration, erythema, and nodular swelling at the injection site in a few days or even after years of injection. The diagnosis of granuloma is a histopathological one and a biopsy is required in suspected cases.

Bovine collagen may lead to localized hypersensitivity reaction in a short time or a systemic hypersensitivity reaction manifesting as urticaria and fever, which may need a short term of oral corticosteroids. Reactions of foreign body granulomatous to fillers may happen after a long time, manifesting as indurated nodular swellings at the injection site, which may need intralesional corticosteroid injections. The hypersensitivity pathogenesis responses may be related to the presence of short amounts of protein contaminants in the fillers, which may lead to hypersensitivity reactions and granuloma formations.<sup>12</sup>

#### Vascular Adverse Effects

Filler-induced skin necrosis due to inadvertent intravascular injection of filler that causes impediment of the blood flow is a rare but serious adverse effect (Figures 4, 5). Recognition of intravascular injection at the earliest and quick, aggressive treatment is important to avoid irreversible damage. Vascular injections can be identified on the basis of occlusive symptoms, which present as immediate, severe pain and discoloration in cases of arterial occlusion and less severe, dull pain in cases of venous injection.<sup>13</sup> It is commonly noted over the glabellar region because of injection into the supratrochlear artery. Retinal embolism attributed to intravascular injection into the supratrochlear artery, supraorbital, angular, and dorsal nasal arteries

is also a rare side effect. In cases of retinal artery occlusion, acetazolamide, sublingual nitroglycerine, and intravenous infusion of mannitol should be given at the earliest to prevent permanent vision loss.<sup>14</sup> In cases associated with a hyaluronic acid filler, a hyaluronidase injection to dissolve the filler should be immediately performed as emergency procedure.<sup>15</sup> In case there is no improvement in the symptoms, anterior chamber paracentesis by an ophthalmologist should be performed to reduce the intraocular pressure.

Cerebral ischemic event because of retrograde flow of filler emboli in the internal carotid artery is another non-prevalent but life-threatening adverse effect.<sup>16</sup> This adverse effect can be avoided by aspirating the needle before injecting, keeping the needle moving while injecting, using a less dense filler, and injecting low volumes in two or three sessions rather than a high volume in a single session.<sup>17,18</sup> If any symptoms/signs of tissue necrosis appear, the injection must be stopped immediately, and an injection of hyaluronidase enzyme be performed to minimize the tissue necrosis. Other treatment options include warm compresses, massaging or tapping the area, and applying 2% nitroglycerin paste over the affected area to promote vasodilatation.<sup>7</sup> Topical oxygen therapy, systemic steroids, filler removal through puncture, low molecular weight heparin, sildenafil, and intravenous prostaglandin have been reported as beneficial in cases where hyaluronidase was ineffective.<sup>19</sup>

#### Malar Edema

This serious adverse effect occurs seen when fillers are injected into the infraorbital hollow and tear trough. Fillers can cause this type of edema by impeding the lymphatic drainage either due to direct pressure over the lymphatics or by augmenting the barrier of the malar septum. Malar edema is a challenging complication to manage as it usually is long-lasting and responds poorly to treatment modalities such as cold compresses, head elevation, lymphatic drainage, manual compression, and oral steroid therapy. This complication can be reduced by limiting the volume of filler material and by injecting slowly the filler material deep into the malar septum at the level of pre-periosteum.<sup>20</sup>

#### Infections

The risk of infections with filler injection may increase secondary to skin barrier damage. It is important to consider filler injections as a medical procedure when referring to the need of aseptic practices. The standard should be identical. A wide variety of bacterial, viral, and fungal infections have been observed with the use of fillers, mostly when hygienic measures were either missing or of low standard. Reactivation of herpes simplex virus infection is mostly seen after lip augmentation in patients with history of relapsing *herpes labialis*. It can be avoided by preventing the procedure in patients with active infection or by initiation of antiviral therapy at least 3 days before the procedure in patients with recurrent infection.

**FIGURE 6.** Filler injection in the cheek leading to abscess formation.

Staphylococcal and streptococcal infections can lead to abscesses and cellulitis, which require a broad spectrum oral antibiotic therapy (Figure 6). *Mycobacterium chelonae* and *Mycobacterium abscesses* infection have also been shown after using contaminated fillers and usually documented as delayed onset infections.<sup>21,22</sup> Biofilm formation over the dermal fillers has also been demonstrated and can lead to a variety of side effects including cellulitis, nodules, abscesses, or granulomatous inflammation, which can present even years after dermal filler injections. Infections may also result from recent medical or dental procedures in the vicinity of dermal filler injection area. For instance, dental root infections or professional tooth cleaning can cause filler complications, such as infections that can mimic a dental infection.<sup>23</sup>

Empiric antibiotic therapy with two or three classes of antibiotics is recommended in cases of suspected biofilms while waiting for the PCR.<sup>24</sup> Another treatment option for the management of biofilm is low doses of triamcinolone with 5-fluorouracil injected into the lesion, which has been hypothesized to act by interacting with *AriR*, a regulatory gene that inhibits the formation of biofilm.<sup>6</sup> The risk of infection with filler injection can be minimized by using an aseptic injection, using the smallest gauge needle possible technique, reducing the number of piercings while injecting, and avoiding injecting into infected or inflamed skin, and avoiding injecting through previously injected filler.<sup>25</sup>

### Systemic Reactions

PMMA-induced hypercalcemia is a potentially deadly adverse event that has been reported with high volume injections even years after filler placement. Clinical symptoms resemble those of rheumatic disorders and include myalgia, arthralgia, and fatigue.<sup>26</sup>

### CONCLUSION

As esthetic procedures are increasingly being used by dermatologists and other esthetic providers, their reported adverse effects are also bound to increase. Henceforth, it is important that the treating provider is very familiar with the various complications and their management as some of the complications can be devastating. Proper patient selection, choosing the proper filler material, using appropriate injection technique, and having a good understanding of facial anatomy are crucial to minimizing complications.

### DISCLOSURES

The authors have no relevant conflicts to report.

### REFERENCES

- Wollina U, Goldman A. hyaluronic acid dermal fillers: safety and efficacy for the treatment of wrinkles, aging skin, body sculpting and medical conditions. *Clin Med Rev*. 2011;3:107–121.
- Rohrich RJ, Nguyen AT, Kenkel JM. Lexicon for soft tissue implants. *Dermatol Surg*. 2009; 35(Suppl 2):1605–1611
- Bergeret-Galley C, Latouche X, Illouz YG. The value of a new filler material in corrective and cosmetic surgery: Derma Live and Derma Deep. *Aesthetic Plast Surg*. 2001;25:249–55.
- Gladstone HB, Cohen JL. Adverse effects when injecting facial fillers. *Semin Cutan Med Surg*. 2007; 26(1):34–39
- Cohen JL, Bhatia AC. The role of topical vitamin K oxide gel in the resolution of postprocedural purpura. *J Drugs Dermatol*. 2009; 8(11):1020–1024
- Fitzgerald R, Bertucci V, Sykes JM, Duplechain JK. Adverse reactions to injectable fillers. *Facial Plast Surg*. 2016;32(5):532–555
- Signorini M, Liew S, Sundaram H, De Bouille KL, Goodman GJ, Monheit G et al. Global aesthetics consensus group. Global aesthetics consensus: avoidance and management of complications from hyaluronic acid fillers—evidence- and opinion-based review and consensus recommendations. *Plast Reconstr Surg*. 2016; 137(6):961e–971e
- Lafaille P, Benedetto A. Fillers: contraindications, side effects and precautions. *J Cutaneous Aesthet Surg* 2010; 3:16–9.
- Goldman A, Wollina U. Polymethylmethacrylate-induced nodules of the lips: clinical presentation and management by intralesional neodymium:YAG laser therapy. *Dermatol Ther*. 2019;32(1):e12755.
- Wollina U, Goldman A, Naoum C. Side effects in aesthetic medicine. Spectrum, management and avoidance. *Hautarzt*. 2013;64(3):155–62.
- Ginat DT, Schatz CJ. Imaging features of midface injectable fillers and associated complications. *Am J Neuroradiol*. 2013;34(8):1488–95.
- Cohen JL. Understanding, avoiding, and managing dermal filler complications. *Dermatol Surg*. 2008;34:S92–9.
- Bigatà X, Ribera M, Bielsa I, Ferrándiz C. Adverse granulomatous reaction after cosmetic dermal silicone injection. *Dermatol Surg*. 2001;27:198–200.
- Sclafani AP, Fagien S. Treatment of injectable soft tissue filler complications. *Dermatol Surg*. 2009; 35:1672–1680.
- Philipp-Dormston WG, Bergfeld D, Sommer BM, Sattler G, Cotozana S, Snozzi P, Wollina U, Hoffmann KPJ, Salavastru C, Fritz K. Consensus statement on prevention and management of adverse effects following rejuvenation procedures with hyaluronic acid-based fillers. *J Eur Acad Dermatol Venereol*. 2017;31(7):1088–1095.
- Loh KT, Chua JJ, Lee HM, Lim JT, Chuah G, Yim B, Puah BK. Prevention and management of vision loss relating to facial filler injections. *Singap Med J*. 2016; 57(8):438–443.
- Funt D, Pavicic T. Dermal fillers in aesthetics: an overview of adverse events and treatment approaches. *Clin Cosmet Invest Dermatol*. 2013;6:295–316.
- McClellan DE, Goldstein JC. Blindness secondary to injections in the nose, mouth, and face: cause and prevention. *Ear Nose Throat J*. 1995;74:182–8.
- Lemperle G, Rullan PP, Gauthier-Hazan N. Avoiding and treating dermal filler complications. *Plast Reconstr Surg*. 2006;118:S92–107.
- Funt DK. Avoiding malar edema during midface/cheek augmentation with dermal fillers. *J Clin Aesthet Dermatol*. 2011; 4(12):32–36
- Daines SM, Williams EF. Complications associated with injectable soft-tissue fillers: a 5-year retrospective review. *JAMA Facial Plast Surg*. 2013;15: 226–31.
- Rodriguez JM, Xie YL, Winthrop KL, Schafer S, Sehdev P, Solomon J et al. *Mycobacterium chelonae* facial infections following injection of dermal filler. *Aesthet Surg J*. 2013; 33: 265–9.
- Ramzi AA, Kassim M, George JV, Amin A. Dental Procedures: Is it a Risk Factor for Injectable Dermal Fillers? *J Maxillofac Oral Surg*. 2015;14(Suppl 1):158–60.
- Cassuto D, Sundaram H. A problem-oriented approach to nodular complications from hyaluronic acid and calcium hydroxylapatite fillers: classification and recommendations for treatment. *Plast Reconstr Surg*. 2013; 132: 48S–58S.
- Bailey SH, Cohen JL, Kenkel JM. Etiology, prevention, and treatment of dermal filler complications. *Aesthet Surg J*. 2011; 31:110–21.
- Goldman A, Staub H, Wollina U. Hypercalcemia due to polymethylmethacrylate injections? (Literature review and case reports). *Georgian Med News*. 2018;(282):17–20.

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