

ORIGINAL RESEARCH REPORT

Adverse reactions to injectable soft tissue fillers: Memorable cases and their clinico-pathological overview

SOO-KEUN LEE¹, SO MIN KIM², SANG HYUN CHO², JEONG DEUK LEE²
& HEI SUNG KIM²

¹*Mein Skin Clinic, Seoul, Republic of Korea and* ²*Department of Dermatology, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea*

Abstract

Background: Filler injection is a minimally invasive procedure widely used for soft tissue augmentation. Although the safety profile is favorable, adverse events can occur, especially after illegal filler injection. **Objectives:** The authors present memorable cases of filler complications and review their clinico-pathological features and treatment strategies. **Patients and methods:** This is a retrospective, single-center case series. The authors identified eight patients with significant complications following filler injection. A medical record review was performed for clinical history, histopathological studies, and treatment. **Results:** Six female and two male subjects presented with significant filler complications. The time interval between filler injection and the development of a complication varied greatly among cases (immediately afterwards to 14 years following filler injection). Four of the patients received illegal filler injection where the injected material was either unknown (25%) or was told as paraffin (12.5%) or Vaseline® (12.5%). Hyaluronic acid fillers were used in two patients (25%) and the rest were injected with porcine atelocollagen (12.5%) and polyacrylamide hydrogel (12.5%). The complications were classified as an allergic reaction (25%), filler material migration (12.5%), injection necrosis + embolism (25%), and foreign body granuloma (37.5%), based on their clinico-pathological features and were treated accordingly. **Conclusion:** Adverse effects are not uncommon following filler injection. Physicians should be aware of the potential side effects, recognize their presentations, and understand how to manage them.

Key Words: *adverse reactions, memorable cases, soft tissue fillers*

Introduction

The use of soft tissue fillers for wrinkle treatment and soft tissue augmentation has increased dramatically in recent years. It is currently the second most common minimally invasive procedure performed among dermatologists next to botulinum toxin injections (1). The popularity of fillers is attributable to their ease of application, significant beneficial effects on appearance, and low rate of complication.

Although soft tissue fillers have a very favorable safety profile, adverse events can occur. Moreover, in East Asian countries, injection of illegal materials by unlicensed practitioners are widespread which often lead to serious complications (2).

Filler complications are divided largely into early and late events, and again into minor and major

complications (3). Minor complications of early onset such as bruising, swelling, and erythema are relatively common and may be considered as adverse sequelae rather than true complications. Delayed hypersensitivity reaction is a minor complication of late onset. Although rarely been reported, it can theoretically occur in implants with animal particles. More significant complications include overcorrection, surface irregularities, filler visibility, Tyndall effect, and granuloma formation. Complications of greater severity are visual impairment, skin necrosis, and anaphylaxis.

Currently, numerous agents are available for filler injection. Although some are less risky than others, all can induce adverse reactions (4–6). Biodegradable fillers such as collagen and hyaluronic acid (HA)

Soo-Keun Lee and So Min Kim contributed equally to this paper.

Correspondence: Hei Sung Kim, Department of Dermatology, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul 137-701, Republic of Korea. Tel: + 82-32-280-5105. Fax: + 82-32-506-9514. E-mail: hazelkimhoho@gmail.com

(Received 15 July 2014; accepted 16 September 2014)

ISSN 1476-4172 print/ISSN 1476-4180 online © 2014 Informa UK, Ltd.
DOI: 10.3109/14764172.2014.968584

are less likely to cause late complications as the filler products disappear spontaneously over a period of time. On the other hand, non-resorbable fillers often give rise to severe permanent reactions.

The goal of the present review is to highlight some of the more severe complications as well as those that have been less reported, identify filler materials and areas most prone to complications, and discuss the effective modes of treatment by sharing our experience.

Subjects and methods

This was a single-center study where data were collected retrospectively using electronic medical record entries and coding information. Written consent for photography release was obtained before images were taken. Telephone calls were placed to patients requesting additional information or photography when appropriate. The study was performed in accordance with the Declaration of Helsinki (1975) and approved by the institutional review board of Incheon St. Mary's Hospital, The Catholic University of Korea.

Patients who were treated for significant filler complications between March 2011 and February 2014 were identified and reviewed. The review included subjects' demographic data (gender and age), their symptoms and clinical presentation at the first visit, history (including time interval between the injection and the onset of symptoms, type of practitioner who performed the injection, injected filler material, and injection site), pathological reports, and treatment.

Results

Patients' characteristics

The clinical characteristics of patients with filler complications are summarized in Table I. Of the total eight patients, six (75%) were female and two (25%) male. Their average age was 48.6 years (range, 30–74). The complications were roughly classified into: an allergic reaction (25%), filler material migration (12.5%), embolism (25%), and foreign body granuloma (37.5%) based on their clinico-pathological features. The time interval between filler injection and the development of a complication varied greatly among cases (immediately afterwards to 14 years following filler injection). Four of the patients received illegal filler injection by non-medical practitioners (50%), where the injected material was either unknown (25%) or was told as paraffin (12.5%) or Vaseline® (12.5%). HA fillers were used in two patients (25%) and the rest were injected with porcine atelocollagen (12.5%) and polyacrylamide hydrogel (12.5%). Practitioners who gave injections

to the latter four patients included one plastic surgeon (12.5%), one dermatologist (12.5%), and two general physicians (25%). All cases were treated accordingly.

Representative cases of filler complication

Case 1 (Allergic reaction). A 48-year-old male came in with a 2 day history of linear erythema and swelling along both nasolabial folds (NLFs) (Figure 1). He had a history of Aquamid® (2.5% cross-linked polyacrylamide (PAAG)) injection to the NLFs where a touch-up was performed one week after the primary injection. The skin changes were said to have occurred two days after the touch-up. The clinical findings and history were highly suggestive of an allergic reaction and the patient was treated accordingly. After a week of oral steroids, the lesions resolved leaving post-inflammatory hyperpigmentation (PIH).

Case 2 (Filler material migration). A 74-year-old female presented with a swelling on the left upper eyelid. She had received filler injection to the forehead by an illegal practitioner 3 years ago and the lesion was said to have developed one month later. Clinical examination showed a yellowish, firm, and non-tender mass on the left upper eyelid. The ocular examination was otherwise normal. A skin biopsy from the lesion revealed diffuse granulomatous inflammation with numerous lipid vacuoles, epithelioid histiocytes, and multinucleated giant cells. From the clinical and histological findings, a diagnosis of filler migration was made and the patient was referred to a plastic surgeon for surgical intervention.

Cases 3 and 4 (Embolism). A 28-year-old female felt sharp pain following HA filler (Glytone®) injection to the nasal tip and dorsum (Figure 2). Thirty minutes after the injection, focal blanching as well as blue-purple discoloration of the nasal dorsum was observed, which was followed by the involvement of the glabella and left eye in 3 h. At the time of her visit to our hospital, she showed patchy necrosis of the nose and glabella and conjunctival infection, corneal edema, and hyphema of the left eye (Figure 3a). Following an immediate ophthalmologic evaluation, the patient received hyaluronidase injection, systemic steroids (IV and oral), oral aspirin, oral antibiotics, He-Ne laser, and dressing. At 4-week follow-up, the patient showed near-complete recovery with no visual loss and minimal scarring (Figure 3b).

A 42-year-old female presented with reticulated erythema involving the right NLF, right lower mandible, and the right side of the chin (Figure 4a). Hours into receiving HA filler (Perfecta®) injection to the NLFs, there were changes in the skin as well as pain in the right lower gums and teeth. Three days after the injection, the patient noticed slight depression of the gums between the lower lateral

Table I. Summary of the adverse events following soft tissue filler injection.

Sex/age	Injected filler material/injection site	History & clinical presentation	Histologic findings	Treatment/follow-up results	Classification of the adverse event
1 F/30	Therafill® (porcine atelocollagen)/NLFs	Slight swelling and erythema along both NLFs 3 weeks after filler injection		Systemic steroids/complete resolution	Allergic reaction
2 M/48	Aquamid® (2.5% cross-linked PAAG)/NLFs	Swelling and erythema along the lines of injection 2 days after touch-up (2nd Aquamid® injection)		Systemic steroids/resolution with PIH	Allergic reaction
3 F/74	Unknown/glabellar	A yellowish, firm, and non-tender mass on the left upper eyelid, which developed a month after receiving illegal filler injection	Inflammation with numerous empty round extracellular microcysts	Referred to a plastic surgeon for surgical intervention/follow-up loss	Filler material migration
4 F/28	Glytrone® (HA)/nasal tip and dorsum	Purplish discoloration of the nasal dorsum after 30 min, followed by patchy necrosis of the nose and glabellar. Conjunctival infection, corneal edema, and hyphema of the left eye 3 h after filler injection		Ophthalmologic evaluation, hyaluronidase injection + warm saline soaking + He-Ne laser + oral antibiotics and aspirin/full recovery with minimal scarring of the glabellar	Embolism + injection necrosis
5 F/42	Perfecta® (HA)/NLFs	Dusky erythema in reticular distribution along the right NLF. Pain and transient depression of the gums between the lower lateral incisor/canine and the first premolar/canine 3 days after filler injection		Topical bacitracin cream + aspirin/full recovery of the skin and gums at 1 week follow-up	Embolism
6 F/57	Paraffin/cheek & temple	Tender, multiple, subcutaneous masses on the right cheek and temple 1 year after filler injection	Diffuse fibrosis, numerous foreign body giant cells, microcysts, and a moderate degree of lymphohistiocytic infiltration	Oral antibiotics + intralesional injection of steroids/good improvement after 6 months of treatment	Foreign body granuloma + chronic inflammation
7 M/48	Vaseline/pemile shaft	Multiple, painful, oozing, red to yellow, ulcerative lesions 14 years after injection	Microcysts of various sizes present throughout the dermis. Lymphohistiocytic infiltration present at a moderate degree	Oral antibiotics + dressing/follow-up loss	Foreign body granuloma + chronic inflammation
8 F/62	Unknown/nose	Asymptomatic, diffuse, extremely lichenified plaque involving the nasal root and the upper half of the nasal dorsum for years. Filler injection by an illegal practitioner 40 years ago followed by injection of a "dissolving agent" by a non-medical personnel	Extreme fibrosis and epidermal thickening. Diffuse infiltration of lymphohistiocytes and foreign body giant cells	Surgical intervention by a plastic surgeon/reduction in lesion size	Foreign body granuloma

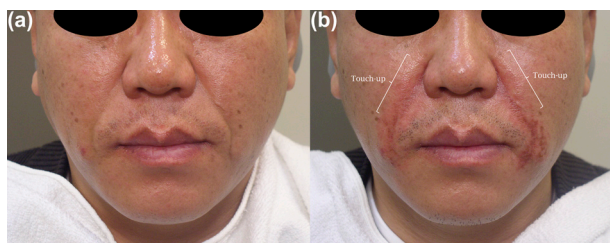


Figure 1. Allergic reaction. Photograph of patient 2 taken (a) just before touch-up to the nasolabial folds (NLFs), and (b) 2 days after touch-up.

incisor/canine and the first premolar/canine which was confirmed by a dentist (Figure 5a). A treatment of hyaluronidase injection, oral steroids, and aspirin was given and the patient showed good recovery in both the skin and gum after a week (Figures 4b and 5b).

Case 5 (Foreign body granuloma). A 57-year-old woman came in with multiple, tender, skin colored to red nodules on the right cheek and temple (Figure 6a). The pain and inflammation began a year after a filler injection by a non-medical practitioner to the face (mainly the cheeks and temple). The patient recalled the injected material as Paraffin®. A skin biopsy was performed which showed microcysts within the dermis together with diffuse lymphohistiocytic infiltration, foreign body giant cells, and fibrosis. Culture results for atypical mycobacteria were negative. With the findings, we made a final diagnosis of foreign body granuloma (with chronic inflammation). The patient improved greatly after receiving oral antibiotics, intralesional injection of steroids, and vascular laser therapy (V-beam Perfecta®, 595 nm, Candela Inc., MA, USA).

Discussion

Volume enhancement has long been recognized as a key factor in restoring “youth.” Various soft tissue fillers have gained popularity among esthetic surgeons and dermatologists for their rapid and predictable results, relative ease of delivery, and favorable safety profiles. With a surge in demand, the pool of

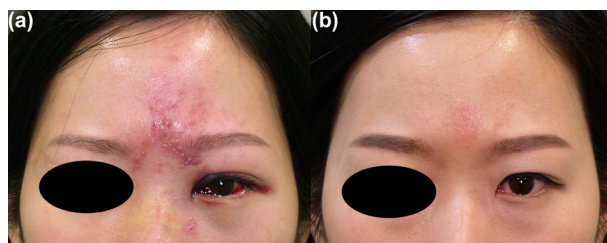


Figure 3. Injection necrosis and embolism. Photograph of patient 4 taken (a) at her time of arrival to our hospital, and (b) after 4 weeks.

providers has expanded from esthetic surgeons and dermatologists to include unlicensed practitioners with little or no formal training in medicine.

Even when administered by experienced hands, injectable fillers can cause various unintended reactions, ranging from minor and self-limited responses to severe complications requiring prompt treatment and close follow-up. Therefore, it is crucial that practitioners not only have a firm understanding on the potential complications of injectable fillers, but also know when to intervene and be confident in managing the entire spectrum of adverse events.

Both immediate- and delayed-type allergic (or hypersensitivity) reactions have been described with soft tissue fillers (3,4,7–14). Immediate hypersensitivity, with an onset within minutes of injection, is stimulated by IgE-mediated histamine release and manifests as urticaria, angioedema, and anaphylaxis. Delayed-type hypersensitivity, on the other hand, develops 48–72 h or later after injection and is mediated by macrophage/T cell interactions. Although delayed hypersensitivity reactions are exceedingly rare with non-animal-derived fillers, they have been reported in implants with animal particles (e.g., bovine or porcine atelocollagen) and also with polyacrylamide (PAAG) gel (4,12–14). The authors have experienced two patients with a delayed-type hypersensitivity reaction, where linear erythema and swelling appeared along the NLFs following filler injection. The onset of the event was 3 weeks after porcine atelocollagen (Therafill®) injection and 2 days after touch-up filler injection with PAAG (Aquamid®), respectively. Although we were not able to obtain skin biopsies from our patients, the timing,

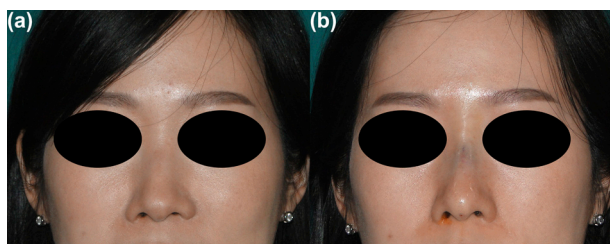


Figure 2. Injection necrosis and embolism. Photograph of patient 4 taken (a) before filler injection to the nasal tip and dorsum, and (b) immediately after filler injection.

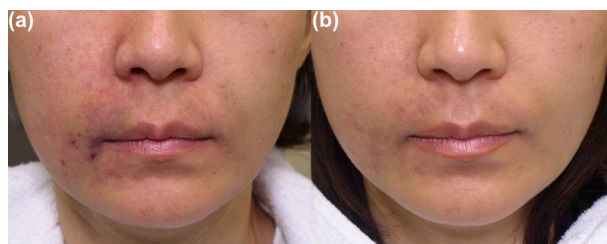


Figure 4. Injection necrosis and embolism. Photograph of patient 5 taken (a) hours after fillers injection to the NLFs, and (b) after 1 week.

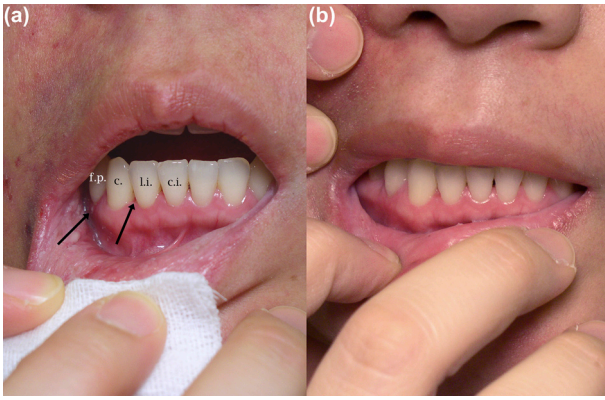


Figure 5. Injection necrosis and embolism. Photograph of patient 5 taken (a) 3 days after filler injection to the NLFs, and (b) after 1 week.

presentation, and persistence of the reactions were highly suggestive of delayed-type hypersensitivity. Although the patient with Therafill® injection had no specific recollection of prior porcine atelocollagen injection, she had a history of filler injection 2 years ago. The patient who received Aquamid® did not show any response after the initial injection, whereas a reaction occurred 2 days after touch-up, which was in turn given 1 week after the primary injection. In these cases, the hypersensitivity reaction may have been incited by any of the components of the filler agents injected, or by cross-reactivity with one of those components. Prevention consists of a careful history and physical examination. A skin testing may also minimize the risk of an adverse event. Our recommendations for treatment include hyaluronidase (if a HA product has been injected) and immunosuppressants including steroids.

Filler migration is another complication of soft tissue filler injection where semi-permanent (e.g., calcium hydroxyapatite (CaHa)) and permanent implants (e.g., PAAG) have a potential higher risk (3,4,15–19). It is less frequent with temporary fillers which are reabsorbed. Migration can occur up to several years after injection as shown in our patient.

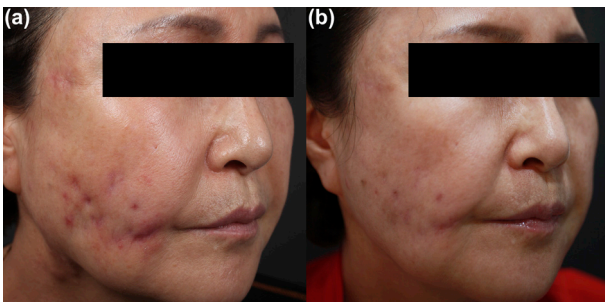


Figure 6. Foreign body granuloma with chronic inflammation. Photograph of patient 6 taken (a) before treatment (combination of oral antibiotics, intralesional injection, and vascular laser), and (b) after treatment.

The pathogenesis of filler migration has been explained by gravity, muscle movement, and post-operative massage of the injected material (15). The practitioner's skill is also important. To avoid complications, we recommend one to not inject filler materials in large volume and high concentration (20). The practitioner should also be cautious in treating areas of active muscle movement or thin skin such as the breast, and periorbital and nasal regions. In prior reports, filler migration from the forehead, glabellar, and nose to the eyelid had been most common (16–18). Since filler migration is mostly caused by permanent fillers, surgical excision is the recommended choice of treatment. Intralesional injection of steroids may be considered as an alternative.

The most severe and dreaded complication of fillers is tissue necrosis (1,6). It is caused by the interruption of a vascular supply from direct injury to the vessel, compression of the vessel, or obstruction of the vessel with a filler material (6). The nose, NLFs, and glabella have been the common injection sites for the complication (1,21–22). In terms of the filler material, both non-permanent (e.g., HA and collagen) and permanent (e.g., polymethylmethacrylate (PMMA) and CaHa) fillers have been the culprit of injection necrosis (1,5,21,22). Prevention and early recognition of the complication is absolutely crucial because treatment of subsequent skin necrosis is difficult. One should be extra careful in treating areas of terminal blood flow such as the nose tip and glabella (e.g., use a cannula, inject small amounts, etc.). Also, the practitioner should aspirate after inserting the needle to make sure that the filler material is not injected into the vessel. The key symptom of an intravascular injection is severe pain upon administration of the product. Other acute symptoms include blanching, duskiness, and ecchymosis. In case one encounters the symptoms, injection should be stopped immediately. A variety of treatments can be used including hyaluronidase (if an HA was injected), nitroglycerin paste, warm compresses, and topical and oral steroids (1,5–6,21–23).

Vascular embolism is another rare, but serious complication of filler injection (1,24–27). Visual impairment resulting from the obstruction of the ophthalmic vasculature has been reported following filler injection to the glabella, nose, and forehead (1,24–27). If an ophthalmic involvement is suspected, prompt consultation with an ophthalmologist is recommended. We have experienced two interesting cases of injection necrosis + emboli. In our first patient, HA filler (Glytone®) injection to the nose (nasal tip and dorsum) led to necrosis of the nasal dorsum and glabella. Ocular symptoms (conjunctival infection, corneal edema, and hyphema) from filler emboli were also present. Interestingly, unlike prior cases, our patient did not experience any visual loss. We postulate that his vision was spared because the emboli moved from the ophthalmic artery into the

lacrimal artery instead of the central retinal artery. However, as a consequence of lacrimal artery occlusion, hemolacria (bloody tears) was observed in our patient. Our second patient received HA filler (Perfecta®) injection to both NLFs. In addition to the reticulated erythema of the right NLF, right lower mandible, and the right side of the chin, there was pain and depression in the gums between the lower lateral incisor/canine and the first premolar/canine. Filler emboli in this particular case have most likely entered the inferior alveolar artery which supplies the dental branches. We believe this is the first report of filler embolism causing gingival depression. Overall, the prevention and treatment strategies for filler emboli are similar to those of injection necrosis.

Granuloma is a delayed complication, the majority of which results from injections of semi-permanent and permanent fillers (2–4,6). Though they usually appear within the first 6 months of injection, delayed granulomas have been reported years after the injection (2,28–32). The hypothesized causes of foreign body granuloma include iatrogenic factors such as agent impurities, large injected volumes, and repeated injections (2). Naturally, the risk of granuloma is much higher following injection of an illegal material. All three of our patients with foreign body granulomas happened to receive injections by non-medical practitioners. Recently, biofilm (accumulation of microorganisms within a self-developed matrix) has also been added as a possible cause of granuloma formation (1,6,33). Because their growth rate is slow, biofilms are usually not identifiable by culture. They may present as sterile abscesses or cause a chronic inflammatory response (34,35). In the event of granuloma formation, judicious intralesional steroid injections coupled with massage are the main stays of treatment (2,3,36,37). Prolonged antibiotics and hyaluronidase can also be beneficial by reducing the biofilm mass (1,6,34,35,38). In severe cases of foreign body reaction and where conservative measures are not effective, surgery may be the best option (2,3,31,39).

Volume restoration has become an important focus for a better facial and body contour. Soft tissue fillers are a popular choice for volume restoration with their minimal downtime and rapid results. However, the injectables are not without risk; the risk is substantially higher with illegal substances. With this in mind, we stress the importance of public education regarding the potentially disastrous consequences of unregulated filler injection. It is extremely important that both patients and physicians understand the possible filler complications including those which are urgent as well as the ones less common and under-recognized. Allergic reaction, filler migration, vascular compromise, and filler granulomas are possible filler complications that must be identified and treated properly to prevent potentially permanent disfigurement.

Declaration of interest: The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

References

- Ozturk CN, Li Y, Tung R, Parker L, Piliang MP, Zins JE. Complications following injection of soft-tissue fillers. *Aesthet Surg J*. 2013;33:862–877.
- Park TH, Seo SW, Kim JK, Chang CH. Clinical outcome in a series of 173 cases of foreign body granuloma: improved outcomes with a novel surgical technique. *Facial Plast Reconstr Aesthet Surg*. 2012;1:29–34.
- Gladstone HB, Cohen JL. Adverse effects when injecting facial fillers. *Semin Cutan Med Surg*. 2007;26:34–39.
- Requena L, Requena C, Christensen L, Zimmermann US, Kutzner H, Cerroni L. Adverse reactions to injectable soft tissue fillers. *J Am Acad Dermatol*. 2011;64:1–34.
- Park TH, Seo SW, Kim JK, Chang CH. Clinical experience with hyaluronic acid filler complications. *J Plast Reconstr Aesthet Surg*. 2011;64:892–896.
- Daines SM, Williams EF. Complications associated with injectable soft-tissue fillers: a 5-year retrospective review. *JAMA Facial Plast Surg*. 2013;15:226–231.
- Lupton JR, Alster TS. Cutaneous hypersensitivity reaction to injectable hyaluronic acid gel. *Dermatol Surg*. 2000;26:135–137.
- Arron ST, Neuhaus IM. Persistent delayed-type hypersensitivity reaction to injectable non-animal-stabilized hyaluronic acid. *J Cosmet Dermatol*. 2007;6:167–171.
- Andre P. Evaluation of the safety of a non-animal stabilized hyaluronic acid (NASHA-Q medical, Sweden) in European countries: a retrospective study from 1997 to 2001. *J Eur Acad Dermatol Venerol*. 2004;18:422–425.
- Lowe NJ, Maxwell CA, Lowe P, Duick MG, Shah K. Hyaluronic acid skin fillers: adverse reactions and skin testing. *J Am Acad Dermatol*. 2001;45:930–933.
- Andre P, Lowe NJ, Parc A, Clerici TH, Zimmermann U. Adverse reactions to dermal fillers: a review of European experiences. *J Cosmet Laser Ther*. 2005;7:171–176.
- Siegle RJ, McCoy JP, Schade W, Swanson NA. Intradermal implantation of bovine collagen. Humoral immune responses associated with clinical reactions. *Arch Dermatol*. 1984;120:183–187.
- Stegman S, Chu S, Armstrong R. Adverse reactions to bovine collagen implant: clinical and histological features. *J Dermatol Surg Oncol*. 1988;14:39–48.
- Chrastil-La Towsky B, Wesley NO, MacGregor JL, Kaminer MS, Arndt KA. Delayed inflammatory reaction to bio-alcamid polyacrylamide gel used for soft-tissue augmentation. *Arch Dermatol*. 2009;145:1309–1312.
- Cheng NX, Xu SL, Deng H, Ding XB, Zhang XM, Wu DH, et al. Migration of implants: a problem with injectable polyacrylamide gel in aesthetic plastic surgery. *Aesthetic Plast Surg*. 2006;30:215–225.
- Sa HK, Woo KI, Suh YL, Kim YD. Periorbital lipogranuloma: a previously unknown complication of autologous fat injections for facial augmentation. *Br J Ophthalmol*. 2011;95:1259–1263.
- Malik S, Mehta P, Adesanya O, Ahluwalia HS. Migrated peiocular filler masquerading as arteriovenous malformation: a diagnostic and therapeutic dilemma. *Ophthal Plast Reconstr Surg*. 2013;29:18–20.
- Lee MJ, Sung MS, Kim NJ, Choung HK, Khwarg SI. Eyelid mass secondary to injection of calcium hydroxylapatite facial filler. *Ophthal Plast Reconstr Surg*. 2008;24:421–423.
- Gundeslioglu AO, Hakverdi S, Erdem O, Ozen EC, Inan I, Emilk D. Axillary lipogranuloma mimicking carcinoma metastasis after silicon breast implant rupture: a case report. *J Plast Reconstr Aesthet Surg*. 2013;66:72–75.

20. Breiting V, Aasted A, Jorgensen A, Opitz P, Rosetzsky A. A study on patients treated with polyacrylamide hydrogel injection for facial corrections. *Aesthetic Plast Surg.* 2004;28:45–53.
21. Park KY, Son IP, Li K, Seo SJ, Hong CK. Reticulate erythema after nasolabial fold injection with hyaluronic acid: the importance of immediate attention. *Dermatol Surg.* 2011;37:1697–1699.
22. Grunebaum LD, Bogdan Allemann I, Dayan S, Mandy S, Baumann L. The risk of alar necrosis associated with dermal filler injection. *Dermatol Surg.* 2009;35:1635–1640.
23. Kleydman K, Cohen JL, Marmur E. Nitroglycerin: a review of its use in the treatment of vascular occlusion after soft tissue augmentation. *Dermatol Surg.* 2012;38:1889–1897.
24. Kwon DY, Park MH, Koh SB, Dhong ES, Baek SH, Ryu HJ, Park KW. Multiple arterial embolism after illicit intranasal injection of collagenous material. *Dermatol Surg.* 2010;36:1196–1199.
25. Kim YJ, Kim SS, Song WK, Lee SY, Yoon JS. Ocular ischemia with hypotony after injection of hyaluronic acid gel. *Ophthal Plast Reconstr Surg.* 2011;27:152–155.
26. Sung MS, Kim HG, Woo KI, Kim YD. Ocular ischemia and ischemic oculomotor nerve palsy after vascular embolization of injectable calcium hydroxylapatite filler. *Ophthal Plast Reconstr Surg.* 2010;26:289–291.
27. Peter S, Mennel S. Retinal branch artery occlusion following injection of hyaluronic acid (Restylane). *Clin Experiment Ophthalmol.* 2006;34:363–364.
28. Di Benedetto G, Pierangeli M, Scalise A, Bertani A. Paraffin oil injection in the body: an obsolete and destructive procedure. *Ann Plast Surg.* 2002;49:391–396.
29. Legaspi-Vicerra ME, Field LM. Paraffin granulomata, “Witch’s Chin” and nasal deformities. *J Clin Aesthet Dermatol.* 2010;3:54–58.
30. Ellis LZ, Cohen JL, High W. Granulomatous reaction to silicone injection. *J Clin Aesthet Dermatol.* 2012;5:44–47.
31. Sinrachtanant C, Tantiniorn W, Warnnissorn M, Assanasen P. Sclerosing lipogranuloma of the nose: a new treatment using adipose tissue transplantation. *Facial Plast Surg.* 2003;19:363–367.
32. Vargas-Machuca I, Gonzalez-Guerra E, Angulo J, del Carmen Farina M, Martin L, Requena L. Facial granulomas secondary to Dermalive microimplants: reports of a case with histopathologic differential diagnosis among the granulomas secondary to different injectable permanent filler materials. *Am J Dermatopathol.* 2006;28:173–177.
33. Rohrich RJ, Monheit G, Nguyen AT, Brown SA, Fagien S. Soft-tissue filler complications: the important role of biofilms. *Plast Reconstr Surg.* 2010;125:1250–1256.
34. Dayan SH, Arkins JP, Brindise R. Soft tissue fillers and biofilms. *Facial Plast Surg.* 2011;27:23–28.
35. Bjarnsholt T, Tolker-Nielsen T, Givskov M, Janssen M, Christensen LH. Detection of bacteria by fluorescence in situ hybridization in culture-negative soft tissue filler lesions. *Dermatol Surg.* 2009;35:1620–1624.
36. Vazquez-Martinez OT, Ocampo-Candiani J, Mendez-Olvera N, Sanchez Negron FA. Paraffinomas of the facial area: treatment with systemic and intralesional steroids. *J Drugs Dermatol.* 2005;5:186–189.
37. Lowe NJ, Maxwell CA, Patnaik R. Adverse reactions to dermal fillers: Review. *Dermatol Surg.* 2005;31:1616–1625.
38. Nyhlen A, Ljungberg B, Nilsson-Ehle I, Odenholt I. Bacterial effect of combination of antibiotic and neoplastic agents against *Staphylococcus aureus* and *Escherichia coli*. *Chemotherapy* 2002;48:71–77.
39. Wolfram D, Tzankov A, Hildegunde PK. Surgery for foreign body reactions due to injectable fillers. *Dermatology.* 2006;213:300–304.