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Description of Impediments, Prevention and Administrations of Hyaluronic Acid Filler-A Review Article

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Abstract

Injection of cosmetic fillers such as Hyaluronic acid (HA), currently the most widespread and ordinarily performed procedure in cosmetic medicine worldwide and it have been studied quite safe. Though, impediments are slight, transitory and reversible. The vast majority of managements by HA are successful and the satisfaction rate of the patient is great. As escalating in its usage, the risk of impediments is also like to increase. All the relevant articles regained from PubMed and Google scholar under search words: "Hyaluronic acid complications", "dermal filler complications", "Injectable complications", "hyaluronic acid", and "Soft filler complications" were studied. Impediments are rare but can be hazardous. Some of the impediments can appear within a few hours or a few days. The most severe impediment of HA filler injection is Vascular occlusion. The early identification and appropriate treatment of serious impediment can restrain impediment and can even prevent the abnormality. Impediments may occur due to doctor injection technique. Paying attention to the technique used can avoid these impediments. The main focus of this article is to highlight the impediments caused by HA injections, and its stoppage and how to administer these impediments if they do appear.

Keywords: Hyaluronic acid; Dermal fillers; Impediments; administrations

Introduction

HA forms an integral portion of the natural extracellular matrix which is found in high amounts in several connective tissues including the skin, the vitreous humor of the eye and the synovial fluid [1]. Chemically, HA is a linear polysaccharide composed of recurring disaccharide units of glucuronic acid and N-acetylglucosamine [2]. The hyaluronic acid (HA) became one of the most widespread cosmetic procedures after it's authorized by the FDA in 2002. It is used for lip augmentation, scars treatment (including acne scars) [3], nasolabial, glabellar, marionette, neck [4] wrinkles or even in improving the demonstration of atopic dermatitis [5]. HA itself is a significant component of the connective tissue that reduces during the aging process. In its natural shape, the injectable HA lasts only 24-48 hours, thus the cosmetic product has to be stabilized through biochemical modifications [6]. New York, NY (March 20, 2019). The American Society of Plastic Surgeon (ASPS), the aesthetic society has just released its annual statistics for 2018. According to this statistic, total 810,240 Hyaluronic Acid procedures had been performed and It increased 12% from 2017-(increased 54% since 2013) [7]. There are numerous reports on the adverse events of this procedure in the literature, although the maximum of them are trivial and impermanent. However, some impediments can be overwhelming [8]. This article defines the impediments and how to handle them and offer suggestions to avoid serious adverse sequels.

Impediments

Hypersensitivity reaction

Antibody-mediated edema (angioedema): Dermal fillers are essentially foreign bodies, and some patients may develop hypersensitivity to injected products due to an immunoglobulin E (IgE)-mediated immune response (Type I hypersensitivity reaction). This may occur after initial or repeated exposure. IgE stimulates mast cells to degranulate, releasing proteases, heparin, histamine, cytokines, prostaglandins, leukotrienes, and platelet-activating factor, which result in the edema, erythema, pain, and itching characteristic of an allergic response. Angioedema occurs within hours of exposure. Reactions can be severe and can last for several weeks [9]. Edema may be confined to the injection sites but may also be more generalized. An acute idiopathic allergic response can also occur in which no allergen can be identified; the reaction may be localized, or there may be acute generalized facial edema.

Treatment of angioedema, whether of known cause or idiopathic, depends on the severity of the condition. In many cases, the swelling resolves spontaneously after a few hours or

days. If mast-cell mediated, the swelling is short-lived and responsive to antihistamines. For persistent edema or edema not responsive to antihistamines, oral prednisone is the mainstay of treatment. The patient should be strictly monitored to make sure the edema is not a result of an infectious etiology. Hastily progressing angioedema is treated as a medical emergency because of the risk of airway obstruction.

Non-antibody-mediated (delayed) edema: Delayed hypersensitivity reactions are characterized by induration, erythema, and edema, and are mediated by T lymphocytes rather than antibodies. They typically occur 1 day after injection but may be seen as late as several weeks after injection and may persist for many months [10,11]. Delayed hypersensitivity reactions are nonresponsive to antihistamines. The allergen should be removed. In the case of HA, this will involve treatment with hyaluronidase. Other fillers may require treatment with steroids until the filler resorbs, laser treatment, and/or extrusion [12]. Excision is a last resort. Symptoms should be controlled with the lowest possible dose of oral steroids (prednisone).

Malar edema: Malar edema is a particularly serious impediment that has been frequently reported with all fillers when injected into the infraorbital hollow and tear troughs [13].

The phenomenon of malar edema can be described by an understanding of the anatomy of the lower eyelid. Injection of fillers may cause edema by either augmenting the impermeable blockade of the malar septum (impeding lymphatic drainage) or by direct pressure on the lymphatics when injection volumes are too hefty [13].

It is worth mentioning that malar edema is long-lasting and reacts poorly to management. The therapeutic approaches include head elevation, cold compresses, manual compression multiple times daily, lymphatic drainage, and methylprednisolone. In those patients treated with HA, hyaluronidase treatment should be given [13].

However, the best approach is to moderate its incidence by patient and filler selection; limiting filler volume, and by placing filler material deep into the malar septum at the instantaneous pre-periosteal level [13].

Pain: Pain is the most common side effect associated with Hyaluronic acid injection [14]. Pain can occur as a sequela of multiple needle punctures. If there is a striking radiation pain occurring along the vascular course, during the filler injections or after a few hours of the injection, it denotes a vascular complication and appropriate measures need to be taken. Pain can be minimized by slow introduction of a needle with the thinnest gauge possible. Use of long needles to reduce needle pricks, ice anesthesia, and warming up the filler to body temperature can minimize pain [15]. Pain is mild adverse effect and usually last less than one week.

Bruising/ecchymosis: Bruising is an understandable and common complication, though unwelcome by patients, of filler injections. Bruising is observed more frequently after injection into the dermal and immediate subdermal planes using fanning and threading techniques [16].

Bruising may be treated with cold compresses after the procedure, arnica, aloe vera, or vitamin K creams [17-19]. The risk of bruising may be reduced by injecting the filler slowly. If bruising appears, it can be reduced by pressing with a compress [20].

Different substances associated with anticoagulation including nonsteroidal anti-inflammatory drug medications, many vitamin/herbal supplements, and antiplatelet should be discontinued 7-10 days (not without consultation with the treating physician) prior to treatment to reduce the risk of bruising [19-21].

Injection site overcorrection and Tyndall effect: Overcorrection may appear as bumps, nodules, or irregularities, especially when too much of the material is injected. Hyaluronic acid products may be easily resolved using hyaluronidase. In the case of non-hyaluronic acid, a simple puncture with a wide bore needle and drainage of the excess product may suffice [21]. The Tyndall effect is caused by placing the HA fillers too superficially and it manifests as bluish discoloration, which can be treated by injecting 15-50 IU of hyaluronidase followed by massage [22].

Recommendations for hyaluronidase: <2.5 mm area: 10-20 U single injection

- 2.5 mm-1 cm: 2-4 injection points with 10-20 U per injection point
- Injections may be repeated if required [21]
- Old protocol: Repeated daily and continued for at least 4 days
- New protocol: Repeated hourly till resolution of the symptom

Redness of skin and telangiectasia: Instantaneously after injection, some skin redness is normal. If redness stays for more than a few days, a hypersensitivity reaction is likely. Treatments for rosacea may be effective, including oral tetracycline or isotretinoin. A medium-strength topical steroid is advocated for tenacious redness of the skin. Long-term use of high-potency steroids should be avoided, as they may cause atrophy and telangiectasias. Lasers can be effective for the management of telangiectasias and redness of the skin. Vitamin K cream is useful in accelerating the resolution of redness in addition to facial bruising [23]. Patients with rosacea have a higher risk of developing post-injection redness and should be warned of this prior to beginning the procedure.

Herpes activation: The risk of herpes activation following dermal filler injection due to direct damage to the axon caused by the needle, with subsequent tissue manipulation and inflammatory reaction 27 is estimated to be less than 1.45%. Since there are no defined guidelines, systemic antiviral prophylaxis can be performed in patients with a personal history of recurrent facial herpes (>3 episodes/year). Acyclovir 400mg three times per day for 10 days or valacyclovir 500mg twice per day for 7 days can be employed, starting 2 days before the procedure [24].

Infections: Injectable fillers are also interconnected with infections, which can result from the breach of skin surface integrity. The infectious agents may be bacterial, viral or fungal. In order to reduce the risk of infection, the patients' history should be taken, including any history of current dental

procedures, any periodontal management planned within the next two weeks or any history of chronic sinusitis. The patient should not wear makeup either before or immediately after the procedure. Aseptic technique should be used, including proper skin sterilization with 2%-4% chlorhexidine or 70% isopropyl alcohol solution and avoiding contamination of the treatment area after cleansing the patient's skin. An injection approach should be used that reduces the number of skin piercings and uses the smallest gauge needle possible for injections. It is also important to avoid injecting into inflamed or infected skin, to avoid intraoral injections and to avoid injecting through previous layers of filler [25-27].

Post filler bacterial infection with *Mycobacterium abscessus* was reported in New York City in 2002 after a non-FDA approved HA filler was used (Hyacell) which was illegally imported from South America [28,29]. Reported three cases of Mycobacterium chelone infection after a dermal filler injection that was isolated from clinic tap water [30].

Formation of sterile abscess: Low-grade inflammation with negative bacterial culture may existent as a sterile abscess. In such cases, incision and drainage of the abscess and a choice of tetracycline have been found to be effective [31].

Angiogenesis: The tissue trauma caused, as a sequel of tissue expansion and/or by excessive molding and massage of the filler, can favor the appearance of new capillaries, arterioles, and venules. Neovessels may appear days or weeks after the procedure but should fade within 3-12 months without further management. Laser treatment has shown to be effective in these cases [32].

Hyperpigmentation of skin: "Hyperpigmentation is not an uncommon impediment in dermal filler procedures, particularly in subjects with Fitzpatrick skin types IV-VI, although post-injection hyperpigmentation can also be seen in other skin types [33,34].

For managing this problem, the first therapeutic approach should be with a bleaching agent such as topical hydroquinone (2%-8%) and Retin-A (tretinoin) combined with daily full-spectrum sunscreen application. In those cases of resistant post-inflammatory hyperpigmentation, chemical peels may also be used. If the treatment is not successful, the next steps include the treatment with intense pulsed light, a pulsed dye laser, or fractional laser [17].

Serious complications

Skin necrosis: Injection-induced necrosis is a rare but dreaded impediment associated with the use of soft tissue augmentation filler agents [35]. Necrosis can appear from interruption of the vascular supply to the area, potentially by compression or injury, but commonly from obstruction of the vessels through injection directly into an artery, causing an embolism that blocks blood supply [35,36]. In order to avoid severity, potentially irreversible impediments, all physicians should have a heightened awareness of the possibility of vascular compromise when using fillers, specifically, look for a regional blanch, and have an established treatment algorithm in place if a blanch is suspected or overtly occurs [37-42]. In these circumstances, patients often report symptoms of necrosis varying from extreme pain with geographic discoloration (such as a violaceous hue) to a dull persistent ache [43].

The risk of skin necrosis can be reduced by dissimilar strategies. All the injectors have to be familiar with the signs of skin necrosis and the appropriate therapy. For intravascular infarction, the panel recommended:

(a) To apply a warm gauze, tapping the area to facilitate vasodilatation and massage of the area

(b) To use topical nitroglycerin (1% or 2%) paste 2 or 3 times/ daily in the office and at home by the patient. Nitroglycerin sublingual tablets can be used

(c) Hyaluronidase injection (200-400 IU/ 1-2 mL) massage

(d) Although it was not absolutely proved, it was stated that acetylsalicylic acid (500 mg/8 h, 24-48 h) might be helpful

(e) If there are ocular symptoms (blurred vision, loss of vision, or ocular pain), the patient has to be urgently referred to the ophthalmologist

(f) Other strategies including systemic or topical steroids (prednisone 20-40 mg each day for 3-5 days), low molecular weight heparin, hyperbaric oxygen, sildenafil (1 per day for 3-5 days) have been proposed [21,41,44]

Retinal artery occlusion: The occlusion of the Central Retinal Artery (CRA), or some of its branches, is an uncommon but overwhelming visual impediment that can occur after an esthetic procedure with soft tissue fillers, such as autologous fat, hyaluronic acid, or collagen [45].

A literature review published in 2015 reported 98 cases of vision changes following filler injection. The injection sites identified with a higher risk of complications were the glabella (38.8%), nasal region (25.5%), nasolabial fold (13.3%), and forehead (12.2%). As regards, the filler type, autologous fat, was the most common causative material (47.9%) followed by hyaluronic acid (23.5%) [46].

The underlying mechanism of action leading to vision loss is retrograde flow [46,47]. If the tip of the needle pierces the wall of a distal branch of the ophthalmic artery, the force of injection can expand arterioles and cause retrograde flow [46,47]. Although this is the prevailing theory concerning the mechanism of occlusion, theories related to compression of vessels may also contribute [47].

The main indication is a blindness in the affected eye, usually painless, which can occur within seconds after injection. Other associated symptoms are a pain at the injection site and headache [45-48].

If visual loss has occurred, therapeutic measures should be instantaneously implemented, because maintained CRA occlusion for more than 60-90 min causes irreversible blindness [49]. The therapeutic procedures that have to be performed at the center where the procedure was made would be:

- Medical treatment [47]: One drop of topical timolol 0.5% and/or an acetazolamide 500 mg tablet (after excluding allergy to sulfonamides)
- To administer a sublingual pill (325 mg) of acetylsalicylic acid or one of nitroglycerin 0.6 mg
- To administer an intravenous infusion, 100 mL over 30 min, of mannitol 20%
- Digital massage [47]: It should start immediately while preparing the treatment and to continue once the drugs have been administered
- The patient should be placed in a supine position
- Ensure the patient's eyes are closed
- Apply firm pressure (enough to ensure that the eyeball is indented about 2-3 mm) on the eyeball through the closed eyelids
- Apply firm pressure for 5-15 s and quickly release
- Repeat this cycle for at least 5 min

If despite these measures the patient does not recover the vision in the first 15-20 min, the patient must be referred to an ophthalmology-specialized center for performing an anterior chamber paracentesis for decreasing intraocular pressure [47]. Because, up to now, fibrinolytic or hyaluronidase infiltrations have not demonstrated an unequivocal efficacy; their use is not widespread [47]. Due to the seriousness of the complication, prevention through a good understanding of facial vasculature anatomy and injection techniques is extremely important.

Biofilms: A biofilm is a group of bacteria surrounded by a protective and adhesive matrix, which was first realized on dental plaques [22,50]. Biofilms use the implanted filler as a surface on which to attach and defecate their own matrix. This matrix gives them the capability to survive, develop and resist antibiotic treatment up to a thousand times more effectively than planktonic bacteria. This defecated polymeric material entraps leukocytes and prevents phagocytosis [51,52].

These microorganisms develop DNA mutations and accomplish subsequent diversity [53-55]. These bacterial colonies become active when conditions are favorable, for instance after trauma and manipulation. They can cause a variety of clinical presentations including cellulitis, abscesses, nodules or granulomatous inflammation, which can manifest weeks, months or even years after dermal filler injections [51].

The current mechanisms for culture have not successfully identified the causative bacteria. Diagnosis can be confirmed using PCR of bacterial protein or fluorescence in situ hybridization [12]. Empiric antibiotics should be started while waiting for the PCR results; two or three antibiotic therapies would be appropriate, and macrolide and quinolone have been recommended, with clarithromycin 500 mg bid and ciprofloxacin 500 mg bid for 4-6 weeks. Hyaluronidase can help cleave and fragment the enclosing matrix, hence reducing the amount of biofilm and helping the antibiotics work [26].

Foreign-body granulomas: Foreign-body granulomas may form as the body's immune system reacts to a foreign body that cannot be broken down by the usual mechanisms.

Although they can occur with all injectable dermal fillers, the incidence is very uncommon (from 0.01 to 1.0%) and usually appears after a latent period, which can be numerous months to years after injection [56,57] Diagnosis of granulomas is further problematical by the fact that clinicians are sometimes faced with patients with unknown or incomplete medical and cosmetic treatment history.

Granulomatous reactions to hyaluronic acid fillers can be cured with hyaluronidase with the dosing of 150 U/mL.

Once the infection has been ruled out or quiescent, granulomas may react to oral or intralesional steroids. If steroids are not enough, many patients will respond to the addition of 5-FU to the corticosteroids. In cases of repetitive failure of other therapies, surgical excision is the treatment of choice for foreign-body granuloma [17,19-21].

Conclusion

HA filler is very popular among dermal filler in the world. Complications associated with HA are rare to see. Some complications are mild and self-limiting and some rare complications can be devasting such as Skin necrosis and retinal artery occlusion. To avoid happening of these complications, the physician should be skillful to the injection site and volume of dose. The physician should disinfect the area of the injection site before injection. Early detection and appropriate medical care of serious complications can protect the patient from its dangerous result.

References

1. Stern R, Maibach HI (2008) Hyaluronan in skin: aspects of aging and its pharmacologic modulation. Clin Dermatol 26: 106-122.
2. Sudha PN, Rose MH (2014) Beneficial effects of hyaluronic acid. Adv Food Nutr Res 72: 137-176.
3. Lee JW, Kim BJ, Kim MN, Lee CK (2010) Treatment of acne scars using subdermal minimal surgery technology. Dermatol Surg 36: 1281-1287.
4. Han TY, Lee JW, Lee JH, Son SJ, Kim BJ, et al. (2011) Subdermal minimal surgery with hyaluronic acid as an effective treatment for neck wrinkles. Dermatol Surg 37: 1291-1296.
5. Frankel A, Sohn A, Patel RV, Lebwohl M (2011) Bilateral comparison study of pimecrolimus cream 1% and a ceramide-hyaluronic acid emollient foam in the treatment of patients with atopic dermatitis. J Drugs Dermatol 10: 666-672.
6. https://books.google.co.in/books?hl=en&lr=&id=N-mwH5P-CPAC&oi=fnd&pg=PR3&dq=Advanced+surgical+facial+rejuvenation:+Art+and+clinical+practice&ots=jOOcOeKX7n&sig=cWgldwVR20JTPuS52nHBTIKX-z8#v=onepage&q=Advanced%20surgical%20facial%20rejuvenation%3A%20Art%20and%20clinical%20practice&f=false
7. https://www.prnewswire.com/news-releases/new-data-from-the-aesthetic-society-delineates-the-top-5-procedures-performed-by-plastic-surgeons-in-the-us-and-the-rise-in-patient-demand-for-nonsurgical-options-300815321.html
8. Salati S, Al B (2017) Complications of dermal fillers -an experience from Middle-East J Pakistan Association. Dermatol 4: 12-18.

9. Van Dyke S, Hays GP, Caglia AE, Caglia M (2010) Severe acute local reactions to a hyaluronic acid-derived dermal filler. J Clin Aesthet Dermatol 3: 32-35.

10. Geisler D, Shumer S, Elson ML (2007) Delayed hypersensitivity reaction to Restylane®2007. Cosmetic Dermatol 20: 784-790.

11. Arron ST, Neuhaus IM (2007) Persistent delayed-type hypersensitivity reaction to injectable non-animal-stabilized hyaluronic acid. J Cosmet Dermatol 6: 167-171.

12. Cassuto D, Marangoni O, De Santis G, Christensen L (2009) Advanced laser techniques for filler-induced complications. Dermatol Surg 2: 1689-1695.

13. Funt DK (2011) Avoiding malar edema during midface/cheek augmentation with dermal fillers. J Clin Aesthet Dermatol 4: 32-36.

14. Lafaille P, Benedetto A (2010) Fillers: Contraindications, side effects and precautions. J Cutan Aesthet Surg 3: 16-19.

15. Vedamurthy M (2018) Beware what you inject: Complications of injectables-dermal fillers. J Cutan Aesthet Surg 11: 60-66.

16. Gladstone HB, Cohen JL (2007) Adverse effects when injecting facial fillers. Semin Cutan Med Surg 26: 34-39.

17. Funt D, Pavicic T (2015) Dermal fillers in aesthetics: an overview of adverse events and treatment approaches. Clin Cosmet Investig Dermatol 6: 295-316.

18. Shah NS, Lazarus MC, Bugdodel R, Hsia SL, He J, et al. (2002) The effects of topical vitamin K on bruising after laser treatment. J Am Acad Dermatol 47: 241-244.

19. Fitzgerald R, Bertucci V, Sykes JM, Duplechain JK (2016) Adverse reactions to injectable fillers. Facial Plast Surg 32: 532-555.

20. De Boulle K, Heydenrych I (2015) Patient factors influencing dermal filler complications: prevention, assessment, and treatment. Clin Cosmet Investig Dermatol 8: 205-214.

21. Signorini M, Liew S, Sundaram H, De Boulle KL, Goodman GJ, et al. (2016) Global aesthetics consensus: avoidance and management of complications from hyaluronic acid fillers-evidence-and opinion-based review and consensus recommendations. Plast Reconstr Surg 137: 961.

22. DeLorenzi C (2013) Complications of injectable fillers, part I. Aesthet Surg J 33: 561-575.

23. Cohen JL, Bhatia AC (2009) The role of topical vitamin K oxide gel in the resolution of postprocedural purpura. J Drugs Dermatol 8: 1020-1024.

24. Gazzola R, Pasini L, Cavallini M (2012) Herpes virus outbreaks after dermal hyaluronic acid filler injections. Aesthet Surg J 32: 770-772.

25. Bailey SH, Cohen JL, Kenkel JM (2011) Etiology, prevention, and treatment of dermal filler complications. Aesthet Surg J 31: 110-121.

26. Ozturk CN, Li Y, Tung R, Parker L, Piliang MP, et al. (2013) Complications following injection of soft-tissue fillers. Aesthet Surg J 33: 862-877.

27. Cox SE, Adigun CG (2011) Complications of injectable fillers and neurotoxins. Dermatol Ther 24: 524-536.

28. Rousso J, Pitman M (2010) Enterococcus faecalis complicating dermal filler injection: A case of virulent facial abscesses. Dermatol Surg 36: 1638-1641.

29. Cohen JL (2008) Understanding, avoiding, and managing dermal filler complications. Dermatol Surg 1: 92-99.

30. Rodriguez JM, Xie YL, Winthrop KL, Schafer S, Sehdev P, et al. (2013) Mycobacterium chelonae facial infections following injection of dermal filler. Aesthet Surg J 33: 265-269.

31. Kadouch JA, Kadouch DJ, Fortuin S, van Rozelaar L, Karim RB, et al. (2013) Delayed-onset complications of facial soft tissue augmentation with permanent fillers in 85 patients. Dermatol Surg 39: 1474-1485.

32. Urdiales-Galvez F, Delgado NE, Figueiredo V, Lajo-Plaza JV, Mira M, et al. (2018) Treatment of soft tissue filler complications: Expert consensus recommendations. Aesthetic Plast Surg 42: 498-510.

33. Taylor SC, Burgess CM, Callender VD (2009) Safety of nonanimal stabilized hyaluronic acid dermal fillers in patients with skin of color: a randomized, evaluator-blinded comparative trial. Dermatol Surg 2: 1653-1660.

34. Heath CR, Taylor SC (2011) Fillers in the skin of color population. J Drugs Dermatol 10: 494-498.

35. Glaich AS, Cohen JL, Goldberg LH (2006) Injection necrosis of the glabella: protocol for prevention and treatment after use of dermal fillers. Dermatol Surg 32:276-281.

36. Hirsch RJ, Cohen JL, Carruthers JD (2007) Successful management of an unusual presentation of impending necrosis following a hyaluronic acid injection embolus and a proposed algorithm for management with hyaluronidase. Dermatol Surg 33: 357-360.

37. Grunebaum LD, Bogdan Allemann I, Dayan S, Mandy S, Baumann L (2009) The risk of alar necrosis associated with dermal filler injection. Dermatol Surg 2: 1635-1640.

38. Kwon SG, Hong JW, Roh TS, Kim YS, Rah DK, et al. (2013) Ischemic oculomotor nerve palsy and skin necrosis caused by vascular embolization after hyaluronic acid filler injection: A case report. Ann Plast Surg 71: 333-334.

39. Peter S, Mennel S (2006) Retinal branch artery occlusion following injection of hyaluronic acid (Restylane). Clin Exp Ophthalmol 34: 363-364.

40. Kim YJ, Kim SS, Song WK, Lee SY, Yoon JS (2011) Ocular ischemia with hypotony after injection of hyaluronic acid gel. Ophthalmic Plast Reconstr Surg 27: 152-155.

41. Schanz S, Schippert W, Ulmer A, Rassner G, Fierlbeck G (2002) Arterial embolization caused by injection of hyaluronic acid (Restylane). Br J Dermatol 146: 928-929.

42. Coleman SR (2002) Avoidance of arterial occlusion from injection of soft tissue fillers. Aesthet Surg J 22: 555-557.

43. Sclafani AP, Fagien S (2009) Treatment of injectable soft tissue filler complications. Dermatol Surg 2: 1672-1680.

44. Beer K, Downie J, Beer J (2012) A treatment protocol for vascular occlusion from particulate soft tissue augmentation. J Clin Aesthet Dermatol 5: 44-47.

45. Park SW, Woo SJ, Park KH, Huh JW, Jung C, et al. (2012) Iatrogenic retinal artery occlusion caused by cosmetic facial filler injections. Am J Ophthalmol 154: 653-662.

46. Beleznay K, Carruthers JD, Humphrey S, Jones D (2015) Avoiding and treating blindness from fillers: A Review of the world literature. Dermatol Surg 41: 1097-1117.

47. Loh KT, Chua JJ, Lee HM, Lim JT, Chuah G, et al. (2016) Prevention and management of vision loss relating to facial filler injections. Singapore Med J 57: 438-443.

48. Carruthers JD, Fagien S, Rohrich RJ, Weinkle S, Carruthers A (2014) Blindness caused by cosmetic filler injection: A review of cause and therapy. Plast Reconstr Surg 134: 1197-1201.

49. Hayreh SS, Zimmerman MB (2005) Central retinal artery occlusion: visual outcome. Am J Ophthalmol 140: 376-391.

50. Kunjur J, Witherow H (2013) Long-term complications associated with permanent dermal fillers. Br J Oral Maxillofac Surg 51: 858-862.

51. Cassuto D, Sundaram H (2013) A problem-oriented approach to nodular complications from hyaluronic acid and calcium hydroxylapatite fillers: classification and recommendations for treatment. Plast Reconstr Surg 132: 48s-58s.

52. Marusza W, Mlynarczyk G, Olszanski R, Netsvyetayeva I, Obrowski M, et al. (2012) Probable biofilm formation in the cheek as a complication of soft tissue filler resulting from improper endodontic treatment of tooth 16. Int J Nanomedicine 7: 1441-1447.

53. Narins RS, Coleman WP, Glogau RG (2009) Recommendations and treatment options for nodules and other filler complications. Dermatol Surg 35: 1667-1671.

54. Funt D, Pavicic T (2013) Dermal fillers in aesthetics: an overview of adverse events and treatment approaches. Clin Cosmet Investig Dermatol 6: 295-316.

55. Constantine RS, Constantine FC, Rohrich RJ (2014) The ever-changing role of biofilms in plastic surgery. Plast Reconstr Surg 133: 865e-872e.

56. Lemperle G, Gauthier-Hazan N, Wolters M, Eisemann-Klein M, Zimmermann U, et al. (2009) Foreign body granulomas after all injectable dermal fillers: part 1. Possible causes. Plast Reconstr Surg 123: 1842-1863.

57. Lemperle G, Gauthier-Hazan N (2009) Foreign body granulomas after all injectable dermal fillers: part 2. Treatment options. Plast Reconstr Surg 123: 1864-1873.