Update on Avoiding and Treating Blindness From Fillers: A Recent Review of the World Literature

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Abstract

Background: Sudden loss of vision secondary to filler treatments is a rare but catastrophic complication.

Objectives: The aim of this study was to update the published cases of blindness after filler injection that have occurred since we published our review of 98 cases in 2015, and to discuss prevention and management strategies.

Methods: A literature review was performed to identify all cases of visual complications caused by filler injection identified between January 2015 and September 2018.

Results: Forty-eight new published cases of partial or complete vision loss after filler injection were identified. The sites that were highest risk were the nasal region (56.3%), glabella (27.1%), forehead (18.8%), and nasolabial fold (14.6%). Hyaluronic acid filler was the cause of this complication in 81.3% of cases. Vision loss, pain, ophthalmoplegia, and ptosis were the most common reported symptoms. Skin changes were seen in 43.8% of cases and central nervous system complications were seen in 18.8% of cases. Ten cases (20.8%) experienced complete recovery of vision, whereas 8 cases (16.7%) reported only partial recovery. Management strategies varied greatly and there were no treatments that were shown to be consistently successful.

Conclusions: Although the risk of blindness from fillers is rare, practitioners who inject filler should have a thorough knowledge of this complication including prevention and management strategies.

Level of Evidence: 5

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The number of filler treatments performed globally has steadily increased, and in the United States the number of treatments annually has grown by >300% from 2000 to 2017.[1] As these procedures grow in popularity, we are also seeing an increase in related adverse events. A 10-year retrospective review (2007–2017) of the US Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) database reported 47 cases of blindness and 42 cases of vision impairment caused by filler injection.[2] This database encompasses mandatory reports of adverse events from manufacturers and

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voluntary reports from healthcare professionals and consumers. The records contain information about the outcome of the event and any interventions taken; however, there are limitations to the data as MAUDE is a passive surveillance database and can suffer from underreporting. In addition, some of the MAUDE data are incomplete, there are no strict criteria used to define clinical entities such as vision impairment, and in this database even consumers can file reports.[2] There may or may not be overlap between the cases reported in the MAUDE database and the cohort of published cases we report on herein. Nevertheless, it is likely that there are many other cases of visual complications from filler not captured in the MAUDE database or in our review of the world literature.

Three-dimensional filler treatments are performed by injecting filler into the subcutaneous preperiosteal space, which is the space through which the facial vasculature courses. Inadvertent canalization of the blood vessels that supply the facial tissues is especially concerning as many of these vessels anastomose with the ophthalmic artery and its branches which supply the retina. Animal studies suggest that the retina is only able to survive ~90 minutes without blood supply.[3] However, a more recent publication suggests time to retinal infarction in the case of complete central retinal artery occlusion may be shorter, of the order of 12 to 15 minutes.[4] Unless the block caused by the filler is promptly reversed, vision compromise may occur.

Our initial 2015 publication[5] on this devastating complication found 98 published cases of filler-related visual compromise in the world literature between 1906 and 2015. This follow-up paper describes a further 48 published cases from January 2015 through September 2018, bringing the total to 146 cases. Although the reported incidence is still small, the rate does appear to be increasing.

METHODS

The corresponding author (K.B.), with assistance from the College of Physicians and Surgeons of British Columbia librarian, conducted a Boolean search of the databases of the National Library of Medicine, Ovid MEDLINE, and Cochrane Library for the following string: (soft tissue augmentation OR filler OR injectable) AND (blindness OR ophthalmoplegia OR vision OR visual impairment OR retinal artery occlusion OR ophthalmic artery occlusion). The search was conducted in September 2018 and was limited to the English-language literature. In addition, the references cited in the identified articles were reviewed to identify any additional reports. The review was limited to injected fillers and associated ocular complications reported between January 2015 and September 2018.

RESULTS

A total of 48 new cases of filler-induced vision changes were identified between January 2015 and September 2018. Table 1 provides a description of the cases, the therapies employed, and the outcomes following therapy.

The most common locations of filler injection that caused vision changes were the nasal region (56.3%, n = 27), the glabella (27.1%, n = 13), the forehead (18.8%, n = 9), and the nasolabial fold (NLF) (14.6%, n = 7) (Figure 1). Of the 27 nasal injections, 12 were listed as nose, 7 nasal dorsum, 4 perinasal, 2 nasal bridge, 1 nasal tip, and 1 had injections in both the nasal tip and dorsum. Less common sites were the temple (2 cases), cheek (2 cases), chin (1 case), and upper eyelid (1 case). The exact anatomic location of injection was not listed in 1 case.

Hyaluronic acid (HA) was the filler that resulted in the greatest number of cases (81.3%, n = 39), followed by calcium hydroxylapatite (CaHa) (10.4%, n = 5). There was 1 case each (2.1%) from injections of autologous fat and polylactic acid (PLA). In 1 case the patient was told she had been injected with platelet-rich plasma (PRP), although the authors of that paper speculate that something else was injected in order to be viscous enough to occlude the arteries. The filler type was not reported (NR) in 1 case (Figure 2).

Geographically most cases were reported from Korea (n = 17), China (n = 8), Thailand (n = 6), the United States (n = 6), and Taiwan (n = 5). There was 1 case each out of Poland, Israel, Italy, Australia, Malaysia, and Japan (Figure 3).

Signs and Symptoms

On initial presentation, 26 cases (54.2%) were found to have complete vision loss, whereas the remaining cases had complete unilateral vision loss. In 27 cases (56.3%) pain was reported as 1 of the initial symptoms (described as periorbital, ocular, periocular, orbital, eye pain, or headache). In 21 cases (43.8%) associated skin changes, commonly described as erythematous to violaceous mottling or skin necrosis, were reported. Ophthalmoplegia (decreased extraocular movement) was reported in 26 cases (54.2%) and ptosis was seen in 25 cases (52.1%). Most commonly, the ophthalmoplegia and ptosis recovered completely. Nausea and/or vomiting were described as a presenting symptom in 8 cases (16.7%). Among the 48 cases, there were 9 cases (18.8%) of central nervous system (CNS) complications, including stroke-like features such as unilateral weakness or evidence of brain infarction on imaging. No deaths were reported. Ten cases (20.8%) reported complete recovery of vision, whereas 8 cases (16.7%) resulted in partial recovery of vision. Of the remaining cases, 25 (52%) had complete

Table 1. Cases of Visual Complications in the World Literature

Case	Type of filler	Injection site	Symptoms	Signs	Management	Outcome (variable time for follow-up)	Country
1	Autologous fat	Forehead	RE vision loss, ocular pain, flashes of light	RE NLP, RAPD right eye	Within 20 minutes: ocular massage and ocular drops (0.5% timolol, brimonidine, and dorzolamide) and IV dexamethasone, IV mannitol, 40% glycerol PO, 500 mg acetazolamide PO, IV aprostadil, subsequent vinpocetine PO daily	RE vision recovery (slow improvement occurred over 90 min)	Poland[28]
2	CaHa	Nasal bridge	LE blurred vision, diplopia, periorbital pain, headache, vomiting	LE vision 20/63, ophthalmoplegia, exotropia, skin changes nose, glabella, and forehead	Systemic steroids, antibiotics, hyperbaric oxygen therapy	LE vision and skin recovery, motility improved	Taiwan[29]
3	CaHa	Nasal tip and nasal dorsum	LE decreased vision, headache nausea, vomiting	LE hand motion 30 cm, ophthalmoplegia, dilated pupil, RAPD, skin necrosis nasal dorsum, glabella, left forehead	Alprostadil, dextran, hyperbaric oxygen therapy	LE vision improved to 6/60	Taiwan[30]
4	CaHa	Both temples, both cheeks, forehead, chin	Right periobital pain, diplopia, nausea, vomiting	20/25 vision RE, ptosis, ophthalmoplegia, hematoma at injection area right temple	Oral steroids	Vision NR, ptosis resolved, RE abduction deficit marginally improved	United States[31]
5	CaHa	Nasal bridge (previous rhinoplasty)	RE blurred vision, periocular pain	RE vision 20/20 3 hours post, 20/32 2 months post, ophthalmoplegia, ptosis, RE exotropia, bruising on the nose bridge, and forehead	Aspirin, hot water compresses, aspiration of material injected; enoxaparin, acetylsalicylic acid, amoxicillin/clavulanate, prednisone, topical antibiotics, eyedrops, and ointment	RE vision 20/60 18 months post, visual field deterioration, ptosis, and ophthalmoplegia resolved	Israel[32]
6	CaHa	Glabella	LE decreased vision, diplopia, nausea, impaired consciousness	LE 20/200, ophthalmoplegia, dilated pupil without reflex, conjunctival injection, purpura glabella to left forehead, unable to sit by herself	Systemic steroids	LE 20/25, fixed dilated pupil, resolved ophthalmoplegia, consciousness improved after 2 days, necrosis and scarring of glabella	Japan[33]
7	HA	Nasal dorsum	RE vision loss, eye pain 2 days after admission, "cold" sensation	RE vision NLP, ptosis, ophthalmoplegia, conjunctival injection, subconjunctival hemorrhage, fixed pupil, proptosis, increased intraocular pressure, pustular lesions on forehead and nose, subsequent necrosis	1 week after, 1200 U HYAL injected into orbital apex diluted in 15 mL, 600 U HYAL into skin, ocular massage, IV fluids, IV steroids, antibiotics,	RE vision NLP, ptosis, ophthalmoplegia improved, skin improvement	United States[34]
8	HA	Mid-face (cheek)	RE vision loss, RE pain, right ear pain, headache, dizziness, and subjective left-sided face and arm weakness	No lid ptosis or proptosis, no facial change or arm weakness on her left side	Arrived for treatment within 20 minutes, 150 U HYAL into infraorbital foramen, 150 U into supraorbital notch, retrobulbar injection of 450 U of HYAL, 325 mg of aspirin	RE vision recovery	United States[6]
9	HA	Nose (27G cannula)	LE decreased vision, LE pain, nausea	LE light perception, ptosis, ophthalmoplegia, purple discoloration over left orbital area, forehead, nasal bridge, MRI acute infarction	6 hours later: 450 mL HYAL into nasal area, hyperbaric oxygen, low-level laser therapy, anterior chamber paracentesis, methylprednisolone, antiplatelet drugs, oral antibiotic given plus antiepileptic drug to prevent seizures, topical steroid and antibiotic eye drops	2 months later: LE vision light perception only; lid ptosis and ophthalmoplegia resolved, microphthalmia	Thailand[10]

Table 1. Continued

Case	Type of filler	Injection site	Symptoms	Signs	Management	Outcome (variable time for follow-up)	Country
10	HA	Nose (27G cannula)	RE vision loss, pain	RE vision NLP, ptosis, ophthalmoplegia, RAPD	450 mL HYAL nasal area, self-ocular massage (10 seconds for 3 cycles every hour for 24 hours), breathing into plastic bag, carbogen for 30 minutes every 2 hours, hyperbaric oxygen 5 hours after, oral acetazolamide, eye drop of dorzolamide + timolol, 325 mg PO aspirin daily	RE vision loss, recovery of ophthalmoplegia and ptosis	Thailand[10]
11	HA	Nose (25G cannula)	RE blurry vision, periorbital pain, HA	RE visual field defect, erythematous patch on nose and glabella area	15 min: 300 U HYAL to nose, nitroglycerin transdermal pad on chest; self ocular massage for 6 hours, rebreathing into a plastic bag; subsequent pulse electromagnetic frequency; hyperbaric oxygen 4 hours post	Recovery of visual field defect	Thailand[10]
12	HA	Nose (cannula)	RE vision loss, RE periorbital pain, HA, nausea, vomiting	RE vision NLP, pupil not reactive to light, ophthalmoplegia, ptosis, skin discoloration nasal tip and surrounding area	2 mL HYAL into nasal area, subsequent repeat nasal HYAL, next day 1000 U HYAL retrobulbar (which helped pain, EOM movement, ptosis), IV parecoxib, metoclopramide, acetazolamide, carbogen, timolol drops, and aspirin; subsequent hyperbaric oxygen	Vision NR, resolved ophthalmoplegia and ptosis	Thailand[10]
13	HA	Forehead (25G cannula)	LE decreased vision, headache	LE vision light perception only, ptosis, ophthalmoplegia, pupil dilated and slow reaction to light, purple discoloration along left supraorbital and supratrochlear arteries and upper eyelid, small subacute infarction left temporal lobe	Within 15 minutes: 9 mL intralesional HYAL and 8 mL retrobulbar HYAL (150 U/mL), nitroglycerin pad applied to chest, ocular massage, rebreathing in a plastic bag; IV antibiotic, systemic steroid and hyperbaric oxygen therapy; pulsed electromagnetic frequency applied	LE vision light perception only, ptosis partially improved, ophthalmoplegia almost fully improved	Thailand[10]
14	HA	Left temple (23G needle)	LE blurred vision (after second 0.1 mL deep on bone)	Blurred vision (visual exam NR) LE ptosis	7.5 mL HYAL (600 U/mL) injected over left forehead and temporal area; 2.5 mL HYAL (600 U/mL) then injected into and around supratrochlear notch; ocular massage for >4.5 hours and 90 minutes of hyperbaric oxygen performed	LE vision recovery; vision began to improve after injection into supratrochlear notch	Thailand[10]
15	HA	Glabella and nasal dorsum	RE vision loss inferior half of field, RE periorbital pain, HA	RE counting fingers, ophthalmoplegia, exotropia, erythematous skin discoloration over glabella, dorsum, and tip of the nose	HYAL 60 IU/mL subcutaneously over glabella and nasal dorsum 12 hours after start of symptoms	RE vision recovery, recovery of ophthalmoplegia and visual field defect, minimal skin scarring	Malaysia[35]
16	HA	Nasal tip	RE blurred vision, pain, dizziness	Decreased vision (visual exam NR), ptosis, ophthalmoplegia, chemosis and injection RE, erythematous patches on periocular and glabella region progression to necrosis	1500 U HYAL injected around injection site, methylprednisolone, nitroglycerin, alprostadil, prophylactic antibiotics, and daily dressing plus low-level laser therapy	No visual field defects, ophthalmoplegia, ptosis, skin all recovered	Korea[36]

Table 1. Continued

Case	Type of filler	Injection site	Symptoms	Signs	Management	Outcome (variable time for follow-up)	Country
17	HA	Glabella and nasal dorsum (needle)	Vision loss	Type 1 (n = 2): no ptosis, no ophthalmoplegia Type 2 (n = 2): ptosis, no ophthalmoplegia; Type 3 (n = 2): no ptosis, ophthalmoplegia; Type IV (n = 3): ptosis, ophthalmoplegia (all 4 types showed vision loss)	NR	Type 1 (n = 2): no ptosis, ophthalmoplegia, enophthalmos; Type 2 (n = 2): ptosis improved, mild enophthalmos; Type 3 (n = 2): ophthalmoplegia improved, mild enophthalmos; Type 4 (n = 3): ophthalmoplegia, ptosis recovered (except 1 patient with strabismus), enophthalmos present, no improvement in vision	Korea[37]
18	HA	Glabella and nasal dorsum (needle)	Vision loss		NR		Korea[37]
19	HA	Glabella (needle)	Vision loss		NR		Korea[37]
20	HA	Glabella (needle)	Vision loss		NR		Korea[37]
21	HA	Glabella (needle)	Vision loss		NR		Korea[37]
22	HA	NLF (needle)	Vision loss		NR		Korea[37]
23	HA	NLF (needle)	Vision loss		NR		Korea[37]
24	HA	NLF (needle)	Vision loss		NR		Korea[37]
25	HA	Nasal dorsum (needle)	Vision loss		NR		Korea[37]
26	HA	Glabella, perinasal area, NLF	Vision loss, ocular pain	Vision NLP for 3 cases, 1 case hand motion, ophthalmoplegia (all 4 patients), skin necrosis (2 patients)	One patient had intra-arterial thrombolysis	Vision loss NLP all 4 patients, ophthalmoplegia improved in 3 of 4 cases, ocular misalignment	Korea[38]
27	HA	Glabella, perinasal area, NLF					Korea[38]
28	HA	Glabella, perinasal area, NLF				.	Korea[38]
29	HA	Glabella, perinasal area, NLF					Korea[38]
30	HA	Nose	LE decreased vision, orbital pain, HA, dizziness, nausea, vomiting	LE ptosis, ophthalmoplegia conjunctival injection, LE dilated pupil, color change forehead, nasal tip, medial side of orbit	HYAL (location not described), systemic steroid injections, antibiotics; skin lesion dressed with epidermal growth factor spray and antibacterial ointment	Vision NR, diplopia progressively resolved, skin improved with barely any scarring	Korea[39]
31	HA (29G needle)	Upper eyelid (superior sulcus)	RE blurred vision, pain, swelling and heaviness of RE	RE vision 20/400, slit lamp showed filler material in right anterior chamber	Temporal limb incision RE and irrigation and aspiration to remove filler (10 days post injection); gatifloxacin and rimexolone eye drops	RE vision 20/20; no residual filler in anterior chamber	Korea[40]
32	HA	Glabella	LE decreased vision	LE vision hand motion, ophthalmoplegia, ptosis, increased intraocular pressure, multiple cerebral infarctions, muscle weakness, dysarthria	NR	Vision NLP, ophthalmoplegia and weakness improved	Korea[41]
33	HA	Nose	LE vision loss after 1 hour	LE NLP, ptosis	Retrobulbar HYAL, 1500 U × 2 (300 U/mL solution) (32 hours later), partial RA recanalization	NLP	China[8]

Table 1. Continued

Case	Type of filler	Injection site	Symptoms	Signs	Management	Outcome (variable time for follow-up)	Country
34	HA	Nose	RE reduced vision	RE hand motion 5 cm, ptosis, ophthalmoplegia, visual field defect	Retrobulbar HYAL 1500 U × 1 (12 hourrs later), corticosteroids, no recanalization	20/60	China[8]
35	HA	Nose	LE vision loss	LE NLP, ptosis	Retrobulbar HYAL 3000 U × 2 (34 hours later), corticosteroids, partial recanalization	NLP	China[8]
36	HA	Forehead	LE reduced vision	LE 20/200, ptosis, ophthalmoplegia, visual field defect	Retrobulbar HYAL 1500 U × 2 (4 hours later), corticosteroids	NLP	China[8]
37	HA	Forehead (23G blunt cannula)	RE vision loss, ocular pain	RE NLP, ptosis, purple discoloration over nose, forehead	1500 U HYAL to forehead, nose, glabella, retrobulbar (>7 hours later), hyperbaric oxygen, aspirin, oral acetazolamide, IV dexamethasone	RE vision hand movements, skin improved	China[7]
38	HA	Nasal dorsum	RE pain, diplopia	20/20 initial then 20/200, ptosis, ophthalmoplegia, strabismus, exotropia, pupil dilation, visual field defect, erythematous to violaceous discoloration nasal dorsum and glabella	Topical timolol, tobramycin-dexamethasone ophthalmic eye drops, ocular massage, IV prostaglandin E1, periocular injection of anisodamine, IV dextran, IV ozagrel, oxygen therapy, IM methylcobalamin, dexamethasone, topical antibacterial	Vision improved to 20/16, ocular position normalized, skin healed normally	China[42]
39	HA	NR	RE vision loss, pain	RE NLP	HYAL subcutaneous, hyperbaric oxygen, oral acetazolamide, IV injections Ginkgo biloba extract, cobamamide, dexamethasone	NLP	China[43]
40	HA	Forehead	RE vision loss	RE NLP, pupil fixed, dilated, nonreactive, mottled erythema around injection site	HYAL injection (no details), ocular massage, hyperbaric oxygen therapy	RE vision loss, skin improved (decreased erythema)	China[44]
41	HA	Nose	RE vision loss, left upper limb weakness 9 hours later	RE vision loss, weakness left elbow, left hand and wrist	NR	RE vision loss, persistent upper-limb weakness	Taiwan[45]
42	HA	Nose	RE vision loss, ocular pain, nausea, dizziness	RE ptosis, no light reflex, ecchymosis over nasal and glabellar area, left upper-limb weakness, brain infarcts on MRI	NR	NR	Taiwan[46]
43	HA	Glabella and nasal dorsum (needle)	RE vision loss	RE vision loss	IATT was performed using 1000 U HYAL and 60,000 U urokinase into the trunk of the right ophthalmic artery	RE vision loss	Taiwan[47]
44	HA	Brow	RE decreased vision, flashing sensation	Vision NR initial, subsequent MRI ophthalmic review normal	HYAL brow and forehead (375 IU/mL) then 300 U (0.8 mL) HYAL twice in area of supratrochlear and supraorbital notches (relief after second injection)	Vision recovery	Australia[9]
45	HA (patient told this by injector)	Forehead, nose	Vision NR, pain	LE ptosis, eyelid edema, subconjunctival hemorrhage, necrosis skin forehead, glabella, nasal skin, no loss of visual function	Oral antibiotic therapy and topical warm packs; subsequent IV antibiotics, IV methylprednisolone plus daily application of collagenase-antibiotic ointment	Vision recovery, LE ptosis recovered, 1 month after, some skin scarring	Italy[48]
46	NR	Nose	LE decreased vision	LE vision finger counting, best corrected 20/200	NR	20/100	United States[49]

Table 1. Continued

Case	Type of filler	Injection site	Symptoms	Signs	Management	Outcome (variable time for follow-up)	Country
47	Patient told injection was PRP, but not viscous so likely something else	Forehead	RE vision loss, RE pain, syncope	RE vision loss, ptosis, left-sided hemiparesis, forehead necrosis	Antibiotic ointment for skin and pulsed dye laser to the scar	RE vision loss, residual weakness of left upper and lower extremity	United States[50]
48	Polylactic acid	Forehead	RE vision decreased, RE pain, dizziness, left upper and lower extremity weakness and loss of consciousness	RE counting fingers progressed to NLP, RE RAPD, skin necrosis right forehead, neurologic exam unremarkable	IV methylprednisolone and 60 mg prednisone	RE vision loss, skin lesions improved	United States[51]

CaHa, calcium hydroxylapatite; HYAL, hyaluronidase; IV, intravenous; LE, left eye; NLP, no light perception; NR, not reported; PO, per os (by mouth); PRP, platelet-rich plasma; RAPD, relative afferent pupillary defect; RE, right eye; U, units. • Note that only English-language articles were included in this review. There was 1 paper in which the abstract was available in English that reported 18 cases out of a single institution between 2014 and 2016. This paper was not included in the analysis. For 6 patients the injection site was the forehead, 8 patients were injected in the nose, and the other 4 patients were injected in both sites. The injected material was autologous fat and HA. Only 3 patients showed improvement of vision, the rest remained with no light perception.[52] • There was another case of blindness reported in the Netherlands of blindness after HA injection into the nasal dorsum. Only the abstract was available in English and so it was not included in this review.[53] • There was 1 case reported from the US FDA MAUDE database where compensation was given to the plaintiff after HA filler injected into the temple caused permanent blindness; however, given the limited details and uncertainty as to whether this had been published previously and in what year the case occurred, it was not included.[2]

vision loss, 1 had worsened vision, vision remained the same in 2 cases, and the outcome was not reported in 2 cases. Treatments were employed in all cases where there was vision recovery, and are discussed in more detail below. It is important to note that in only 1 of the 10 cases of complete vision recovery was there documentation of no light perception prior to intervention. In the other 9 cases that described full recovery of vision there was either no reported initial objective visual exam, the vision was reduced and documented as counting fingers or with visual acuities ranging from 20/400 to 20/63, or a visual field defect was described.

Treatments included ocular massage, intraocular pressure–lowering agents, intravenous (IV) steroids, subcutaneous and retrobulbar hyaluronidase (RBH), and IV thrombolytic therapies. Given the lack of consistent reporting on treatment, and the wide variety of treatments, it is hard to draw conclusions regarding efficacy. In 13 of 48 cases (27%) the treatments used were not reported. Commonly reported treatments include the use of hyaluronidase in 51% (20/39 cases where HA filler was used), systemic steroids in 35.4% (17/48 total cases), and hyperbaric oxygen in 20.8% (10/48). In 1 case of complete and 2 cases of partial vision recovery, RBH was used;[6–8] however, only 1 case of complete recovery was attributed directly to the RBH.[6] One case that improved from no light perception to hand movement received multiple treatments, including RBH, instituted 7 hours after injection.[7] Another case had RBH injected 12 hours after filler treatment; this patient's vision improved from hand motion at 5 cm to 20/60, but the authors commented that the treatment likely made no contribution to this partial recovery of vision, because it coincided with the resolution of corneal edema and the gradual absorption of retinal hemorrhage.[8] In 2 cases of complete vision recovery hyaluronidase was injected in the region of the supraorbital or supratrochlear notch and it was reported to immediately bring resolution to the visual disturbance.[9,10]

DISCUSSION

Background

With the increased use of soft tissue fillers, it is important to be aware of potential devastating ocular complications. To minimize the risk of intravascular injection, injectors should have a thorough knowledge of vascular anatomy and a complete understanding of risk factors and safe injection techniques. Further, they should be able to recognize the symptoms and signs of vascular compromise and be able to implement a treatment protocol immediately should this complication occur. The potential for vision loss, skin necrosis, and CNS complications such as stroke should be included on consent forms. Although this complication is very rare, informed consent requires that the practitioner review this potential life-altering condition with the patient.

A clear understanding of vascular anatomy can minimize the risks of complications. The ophthalmic artery begins behind the eye, branching into vessels including the supraorbital, supratrochlear, and dorsal nasal arteries (Figure 4). When high-risk sites such as the glabella, nose,

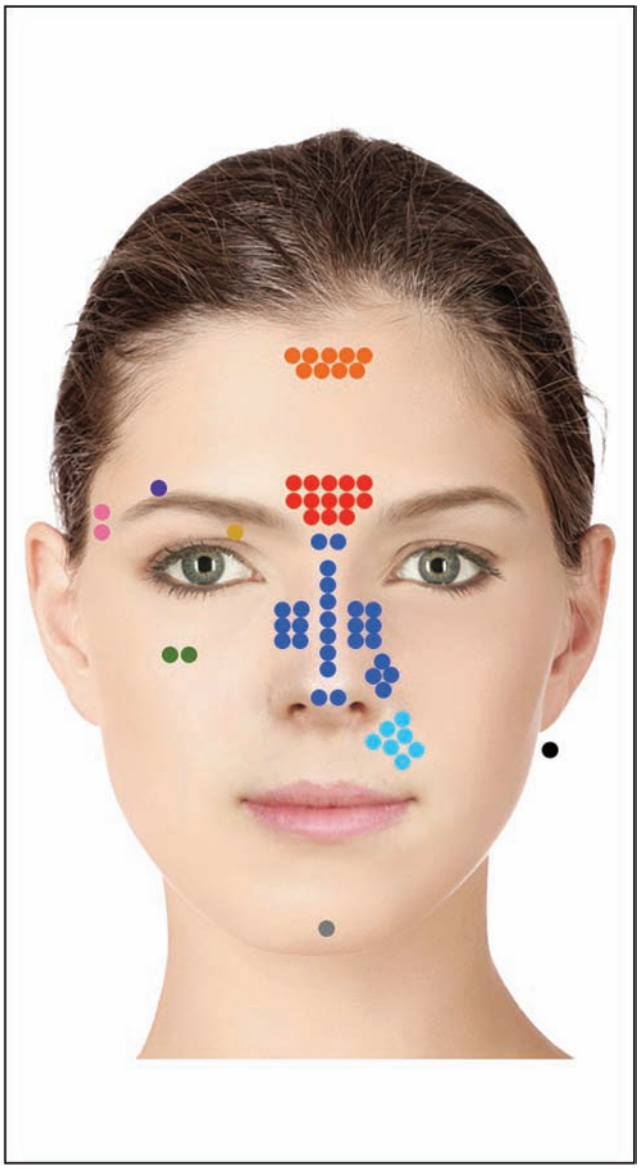

Figure 1. Location of filler injection resulting in visual complication. The single black dot represents a case where the anatomic location of injection was not specified.

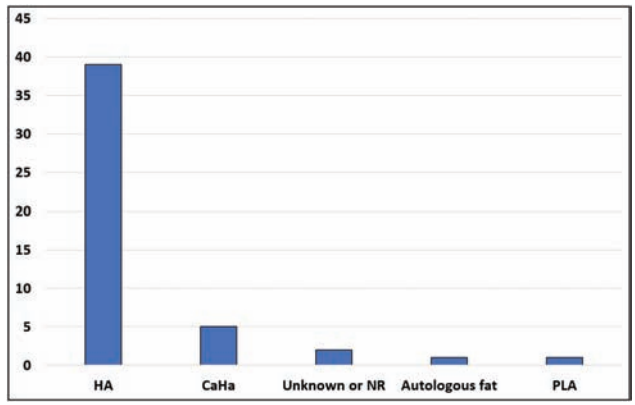

Figure 2. Number of cases of visual complications from each filler type.

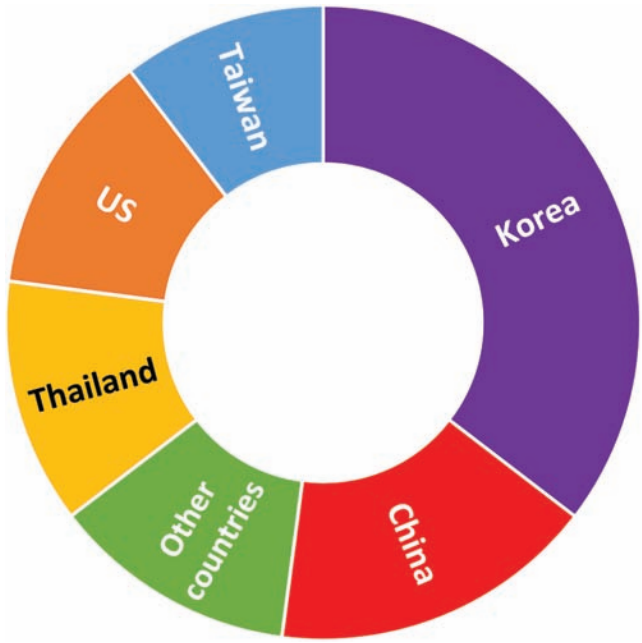

Figure 3. Geographic distribution of cases of visual complications from filler.

and forehead are injected, there is a risk of intra-arterial injection of filler. However, there are many anastomoses between different arteries of the face and branches of the ophthalmic artery system, putting virtually any anatomic location of injection at risk for ocular complications.[5] It should also be stated that expert mastery of vascular anatomy is not failsafe as vascular anatomy is highly variable and vascular events may still occur in the hands of experienced and expert injectors.[11]

Vascular complications can occur when injecting with a needle or a cannula. Detailed documentation of the needle or cannula type used was only reported in 16 of 48 cases (33.3%). A needle was used in 10 cases and cannula in 6 cases, with the cannula size ranging from 27G to 23G. Cannulas have been shown to cause vascular complications in other studies, and in 1 survey 17% of injectors who noted vascular complications were injecting fillers with cannulas, most commonly 25G, but also 23G.[11]

The mechanism of action of blindness after filler injection has been hypothesized to involve intra-arterial injection of filler followed by subsequent retrograde embolization into the ophthalmic artery system (Figure 4).[12] When enough filler is delivered into a vessel and pushed retrogradely with injection pressures greater than the sum of the systolic arterial pressure and the frictional forces due to viscous flow, embolization to the ophthalmic artery can

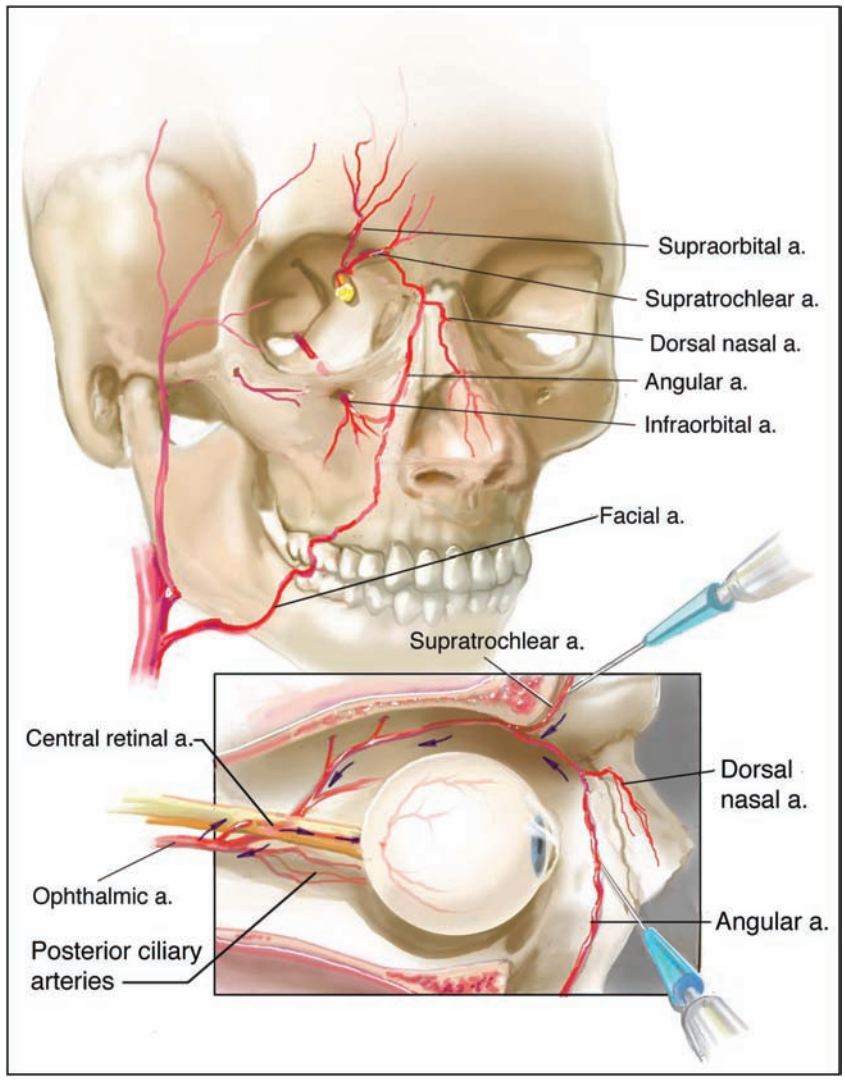

Figure 4. Vascular anatomy of the face. A selection of facial vessels are highlighted here. This is one depiction of the blood vessels of the face and there is individual anatomic variability. Inset demonstrates the mechanism of action of filler-induced blindness. In this diagram, filler is shown being injected directly into the supratrochlear artery or into the angular artery, which anastomoses with the supratrochlear artery. From here filler can travel retrogradely, as shown by the arrows, into the ophthalmic artery and its branches, blocking blood supply to the retina and causing visual complications.

occur.[13] In a recent cadaver head perfusion model, injection pressures above the systolic arterial pressure were needed to transfer filler into the ophthalmic artery (166.7 mm Hg).[12] Furthermore, it does not take a large volume to occlude the vessel. In 1 study the average volume of filler necessary to fill the supratrochlear artery from the glabella to the bifurcation of the ophthalmic and central retinal arteries was 0.085 mL (range, 0.04–0.12 mL).[14] Filler can be dispersed to multiple vessels with enough pressure and travel retrogradely to the orbit or to the internal carotid artery and cerebral circulation, causing CNS complications, and/or distally to the smaller branches supplying the skin. This is consistent with the clinical finding in this report of skin and CNS complications occurring in 43.8% and 18.8%, respectively, of the cases of visual compromise after filler injection.

Clinical Features

This update shows that HA filler causes 81.3% of cases of visual complications compared to 2.1% due to autologous fat. This is in contrast to our last paper[5] where autologous fat was the leading cause (47.9%) of complications. The increase in cases involving HA filler is likely caused by the growing popularity of HA as a filling agent in recent years because of its reversibility and favourable safety profile. According to ASPS data, HA fillers made up 77.7% of the soft-tissue filler market in the United States in 2017.[1]

This update showed 10 cases (20.8%) with complete recovery of vision and 8 cases (16.7%) with partial recovery of vision. Previously[5] there were only 2 cases out of 98 (2%) with complete vision recovery. This improvement

in outcome from this complication could reflect the fact that more cases were reported with HA filler, which has been shown to offer better outcomes than autologous fat.[5] It is also possible that general preparedness, education, and early intervention may be responsible for the improved outcomes. This remains to be substantiated by a larger dataset.

Thirty-eight cases (79.2%) were reported in Asia. There are limited data to evaluate why the great majority of cases were found in this region. This preponderance could represent a reporting bias: many of the large case series have come from Asia. Further, "diamond-shaped reflation" to increase the anterior projection of the central face has become culturally desirable in Asia.[15] This area includes the glabella, nose, medial cheek, and NLF, sites that are high-risk anatomic locations for injections.

This update showed that the nose has surpassed the glabella as the most common location for this complication at 56.3% of cases followed by the glabella (27.1%), forehead (18.8%), and NLF (14.6%) (Figure 1). In our previous publication, the highest-risk location was the glabella (38.8%), nasal region (25.5%), NLF (13.3%), and forehead (12.2%).[5]

Visual compromise most commonly occurred immediately after injection. Ocular pain or headache occurred in the majority of cases (56.3%). Nausea and vomiting secondary to increased intraocular pressure occurred in 8.2% of cases. Obstruction of the blood supply to the extraocular muscles or innervating nerves caused ophthalmoplegia in 54.2% of cases. Reduced blood supply to the levator palpebrae superioris muscle or its innervating nerves caused ptosis in 52.1% of cases. Although vision recovery was less common due to the permanence of retinal damage, ophthalmoplegia and ptosis more commonly recovered, likely because the nerves and muscle regenerate after vascular compromise. Skin changes, including necrosis and subsequent scarring, were seen in 43.8% of cases. Central nervous system complications, including stroke-like features, were seen in 18.8% of cases.

Prevention

Because there is an absence of documented, validated, effective treatments for blindness arising from filler injections, the most rational strategy for avoiding blindness from fillers is prevention. Although evidence is lacking, numerous strategies have been proposed to avoid adverse events such as vision loss. The following are the key prevention strategies:

1) Be familiar with the anatomy, location, and depth of facial vessels and the common variations. Injectors should understand the optimal depth and plane of injections at different sites. The safest plane to be injecting is likely deep and directly on bone or very superficially in the dermis. The subcutaneous plane, although frequently injected to achieve cosmetic improvement, is the highest-risk location as the vasculature most commonly courses through this region.
2) Inject slowly and with minimal pressure.
3) Consider using a cannula. Some authors recommend a cannula in the belief it is less likely to pierce blood vessels. However, there are cases of vascular compromise from cannulas of various sizes. A consensus paper on this topic recommended that for those who use cannulas, a 25G or larger is preferred as a 27G or smaller cannula has a greater potential to penetrate arterial walls.[16]
4) Inject small increments at a time to prevent a bolus of filler traveling retrogradely.
5) Move the needle tip while injecting to avoid depositing a large amount of filler in one location.
6) Aspirate before injection. This recommendation is controversial because it may not be possible to retrieve flashback into a syringe through fine needles when thick gels are involved. Additionally, the small size and collapsibility of facial vessels restrict the efficacy of aspiration.[17]
7) Exercise extreme caution when injecting a patient who has undergone a previous surgical procedure in the area.
8) Consider mixing the filler with epinephrine to promote vasoconstriction because it is more difficult to cannulate a vasoconstricted artery.
9) Consider using targeted digital pressure to occlude major periorbital vessels and prevent inadvertent retrograde travel of filler.[18] A cadaveric study[19] showed that compressing the superior nasal corners with the fingers during cosmetic filler injections reduced the risk of filler traveling into the orbit. This technique may be particularly beneficial when injecting high-risk areas such as the nose.

Treatment

Prior to instituting a treatment strategy, it is important to document the vision changes and confirm the diagnosis, providing this assessment does not significantly delay treatment. Whenever possible, immediate evaluation by an ophthalmologist is best. Some of the cases reported were criticized for not having recorded any objective measurements as there is the possibility that vascular visual spastic events may mimic vascular embolic events (such as classic or retinal migraine).[20] Near vision should be checked (33 cm) with a visual acuity chart, with 1 eye being checked at a time. If this chart is unavailable, getting the patient to read a magazine or count fingers will suffice. The swinging flashlight test can be performed to screen for normal pupillary reaction. Extraocular movements and ptosis should be evaluated and fundoscopy should

also be considered. The patient should be asked about any pain, visual changes, weakness in the extremities, or other symptoms such as nausea, headache, and dizziness. A strength exam of the extremities should be performed. Skin findings, including any blanching, erythema, duskiness, or reticulate changes, should be documented and capillary refill tested in the affected area.

Many injectors do not have experience with treating ocular complications although they may be aware of the reported issues. When possible, practitioners injecting cosmetic fillers should have an established working relationship with their ophthalmologic colleagues who have been previously briefed about this rare but potentially devastating emergency and who understand the importance of timely help. In addition, those who are injecting HA filler should have a sufficient and routinely updated supply of hyaluronidase immediately available in case this should be required. These 2 steps allow the patient to be seen and treated without the potential delay that can easily occur in a busy emergency department. If there is any concern about CNS involvement the stroke team or a neurologist should be involved.

Currently there is no evidence-based, accepted standard of care for treating visual compromise caused by filler. Treatments that have been employed vary widely and successful strategies are rare. Treatment should be instituted urgently before the damage secondary to retinal ischemia is irreversible.[3,4] If an HA filler was used, hyaluronidase should be injected into the skin at the site of injection and along the path of anastomosing arteries. Physicians could also consider injecting hyaluronidase into the area of the supraorbital or supratrochlear notch in an attempt to cannulate the arteries and push the hyaluronidase retrogradely. Cannulating these arteries is likely to prove very challenging; however, there have been 2 reported cases of immediate recovery of vision with this technique.[9,10] The application of hyaluronidase via a retrobulbar or peribulbar injection has been described[21,22] as a method of getting hyaluronidase closer to the area of blockage. It is controversial whether this technique is successful at salvaging vision loss and what sort of practitioners should be attempting this technique. There have been several anecdotal successes with RBH in this context.[23] In this update 3 cases experienced partial or complete vision recovery after treatment with RBH although only 1 case[6] directly attributed success to the RBH. However, RBH did not improve vision in other reports.[8,24] Controversy over the efficacy of RBH continues; we have at this stage more hypothesis than evidence. Other treatments that can be instituted in the office include topical timolol,[25,26] rebreathing into a paper bag,[16,26] ocular massage,[16,25,26] and oral aspirin.[16,25,26] Treatments that may be considered by an ophthalmologist or appropriate specialist include intravenous acetazolamide,[16,25,26] mannitol,[25,26] prostaglandins,[26] anterior chamber paracentesis,[16,25,26] sublingual glyceryl trinitrate,[16] hyperbaric oxygen,[25,26] or direct intravascular or IV injection of hyaluronidase with urokinase.[16,27] Heparin, systemic steroids, and antibiotics could also be considered.[25,26]

Limitations

The primary limitation is that this is a retrospective review of case reports. Case reports are inherently limited, because the quality of the conclusions we can extract is limited by the data that are reported. Inconsistent details were included in each case report and in many cases details were sparse. One particular challenge is identifying the specific anatomic sites that cause blindness as in some cases more than 1 injection location was listed. As such, all locations where injections were performed at the time of visual compromise were documented and for the sake of completeness we have included them all herein. So, for example, in one case the temples, cheeks, forehead, and chin were all injected and the authors did not specify or know which site caused the visual compromise. For the purposes of Figure 1 each location was listed as a potential location for visual compromise; however, it is unlikely that the chin injection was the cause of blindness as it is less high risk than the other injection sites. Although we have tried to identify and review all the cases of visual complications from filler that have been published in the English world literature, this may likely underrepresent the true number of cases due to unreported cases or those documented in the non-English literature.

CONCLUSIONS

There were 48 cases of blindness following filler treatment reported in the world literature between January 2015 and September 2018. During the same time period approximately 9.5 million cosmetic filler procedures were performed in the United States alone.[1] Although visual complications are inevitably underreported in the literature as reflected by the higher numbers seen in the US FDA's MAUDE database,[2] the risk of blindness remains extremely low. Nevertheless, 48 newly published cases in nearly 4 years is an increase over 98 cases published from 1906 to 2015, bringing the total number of cases to 146 in 113 years. This increase in incidence could be the result of the growing number of filler treatments being performed (including an increase in nonexpert injectors) as well as an increase in reporting.

For the years 2015 to 2018, the majority (81.3%) of published cases of vision compromise caused by filler were from HA filler; and the highest-risk injection location was the nose (56.3% of cases). Our previous report of 98 cases of

visual compromise caused by filler between 1906 and 2015 showed that autologous fat was the most common cause. The increased reports of complications from HA fillers could reflect the rise in popularity of this filler type in recent years.

With the increasing global popularity of filler injections, it is important that injectors are aware of the risks of blindness from filler and are prepared to do everything they can to mitigate that risk. Our goal with this paper was to collate the reports in the medical literature, highlight some of the clinical features, and report the treatment strategies that have been employed in order to stimulate discussion. Further research with animal or human cadaveric models to evaluate treatments and other novel approaches would help to expand our understanding of this complication. Currently, the visual prognosis is most often grave and the majority of cases have proved irreversible. No universal consensus exists with regards to the best treatment strategies; however, injectors should be aware of management strategies, be prepared to implement them urgently, and/or elicit the assistance of colleagues who can help manage this complication. We must continue to learn from the experience of others, share our knowledge, and communicate openly to build consensus in order to reduce the risk of this devastating complication and improve outcomes.

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REFERENCES

1. American Society of Plastic Surgeons. 2017 Plastic Surgery Statistics Report. https://plasticsurgery.org/documents/News/Statistics/2017/cosmetic-procedure-trends-2017.pdf. Accessed December 1, 2018.
2. Rayess HM, Svider PF, Hanba C, et al. A Cross-sectional analysis of adverse events and litigation for injectable fillers. *JAMA Facial Plast Surg.* 2018;20(3):207-214.
3. Hayreh SS, Podhajsky PA, Zimmerman B. Nonarteritic anterior ischemic optic neuropathy: time of onset of visual loss. *Am J Ophthalmol.* 1997;124(5):641-647.
4. Tobalem S, Schutz JS, Chronopoulos A. Central retinal artery occlusion - rethinking retinal survival time. *BMC Ophthalmol.* 2018;18(1):101.
5. Beleznay K, Carruthers JD, Humphrey S, Jones D. Avoiding and treating blindness from fillers: a review of the world literature. *Dermatol Surg.* 2015;41(10):1097-1117.
6. Chestnut C. Restoration of visual loss with retrobulbar hyaluronidase injection after hyaluronic acid filler. *Dermatol Surg.* 2018;44(3):435-437.
7. Hu XZ, Hu JY, Wu PS, Yu SB, Kikkawa DO, Lu W. Posterior ciliary artery occlusion caused by hyaluronic acid injections into the forehead: a case report. *Medicine (Baltimore).* 2016;95(11):e3124.
8. Zhu GZ, Sun ZS, Liao WX, et al. Efficacy of retrobulbar hyaluronidase injection for vision loss resulting from hyaluronic acid filler embolization. *Aesthet Surg J.* 2017;38(1):12-22.
9. Goodman GJ, Clague MD. A rethink on hyaluronidase injection, intraarterial injection, and blindness: is there another option for treatment of retinal artery embolism caused by intraarterial injection of hyaluronic acid? *Dermatol Surg.* 2016;42(4):547-549.
10. Thanasarnaksorn W, Cotofana S, Rudolph C, Kraisak P, Chanasumon N, Suwanchinda A. Severe vision loss caused by cosmetic filler augmentation: case series with review of cause and therapy. *J Cosmet Dermatol.* 2018;17(5):712-718.
11. Goodman GJ, Roberts S, Callan P. Experience and management of intravascular injection with facial fillers: results of a multinational survey of experienced injectors. *Aesthetic Plast Surg.* 2016;40(4):549-555.
12. Cho KH, Dalla Pozza E, Toth G, Bassiri Gharb B, Zins JE. Pathophysiology study of filler-induced blindness. *Aesthet Surg J.* 2019;39(1):96-106.
13. Lazzeri D, Spinelli G, Zhang YX, Nardi M, Lazzeri S. Panophthalmoplegia and vision loss after cosmetic nasal dorsum injection. *J Clin Neurosci.* 2014;21(5):890.
14. Khan TT, Colon-Acevedo B, Mettu P, DeLorenzi C, Woodward JA. An anatomical analysis of the supratrochlear artery: considerations in facial filler injections and preventing vision loss. *Aesthet Surg J.* 2017;37(2):203-208.
15. Bae JM, Lee DW. Three-dimensional remodeling of young Asian women's faces using 20-mg/ml smooth, highly cohesive, viscous hyaluronic acid fillers: a retrospective study of 320 patients. *Dermatol Surg.* 2013;39(9):1370-1375.
16. Humzah MD, Ataullah S, Chiang C, Malhotra R, Goldberg R. The treatment of hyaluronic acid aesthetic interventional induced visual loss (AIIVL): a consensus on practical guidance. *J Cosmet Dermatol.* 2019;18(1):71-76.
17. Carey W, Weinkle S. Retraction of the plunger on a syringe of hyaluronic acid before injection: are we safe? *Dermatol Surg.* 2015;41(Suppl 1):S340-S346.
18. Rodriguez LM, Martin SJ, Lask G. Targeted digital pressure to potentially minimize intravascular retrograde filler injections. *Dermatol Surg.* 2017;43(2):309-312.
19. Tansatit T, Moon HJ, Apinuntrum P, Phetudom T. Verification of embolic channel causing blindness following filler injection. *Aesthetic Plast Surg.* 2015;39(1):154-161.
20. Fagien S. Commentary on a rethink on hyaluronidase injection, intra-arterial injection and blindness. *Dermatol Surg.* 2016;42(4):549-552.
21. Carruthers JD, Fagien S, Rohrich RJ, Weinkle S, Carruthers A. Blindness caused by cosmetic filler

injection: a review of cause and therapy. *Plast Reconstr Surg.* 2014;134(6):1197-1201.
22. Carruthers J, Fagien S, Dolman P. Retro or peribulbar injection techniques to reverse visual loss after filler injections. *Dermatol Surg.* 2015;41(Suppl 1):S354-S357.
23. DeLorenzi C. Commentary on: efficacy of retrobulbar hyaluronidase injection for vision loss resulting from hyaluronic acid filler embolization. *Aesthet Surg J.* 2017;38(1):23-27.
24. Hwang CJ, Mustak H, Gupta AA, Ramos RM, Goldberg RA, Duckwiler GR. Role of retrobulbar hyaluronidase in filler-associated blindness: evaluation of fundus perfusion and electroretinogram readings in an animal model. *Ophthalmic Plast Reconstr Surg.* 2019;35(1):33-37.
25. de Lacerda D. Prevention and management of iatrogenic blindness associated with aesthetical filler injections. *Dermatol Ther.* 2018;31(6):e12722.
26. Walker L, King M. Visual loss secondary to cosmetic filler injection aesthetic complications. *J Clin Aesthet Dermatol.* 2018;11(5):E53-E55.
27. Chiang C, Zhou S, Chen C, Ho DS, Zhang H, Liu K. intravenous hyaluronidase with urokinase as treatment for rabbit retinal artery hyaluronic acid embolism. *Plast Reconstr Surg.* 2016;138(6):1221-1229.
28. Szantyr A, Orski M, Marchewka I, Szuta M, Orska M, Zapała J. Ocular complications following autologous fat injections into facial area: case report of a recovery from visual loss after ophthalmic artery occlusion and a review of the literature. *Aesthetic Plast Surg.* 2017;41(3):580-584.
29. Sung WI, Tsai S, Chen LJ. Ocular complications following cosmetic filler injection. *JAMA Ophthalmol.* 2018;136(5):e180716.
30. Chou CC, Chen HH, Tsai YY, Li YL, Lin HJ. Choroid vascular occlusion and ischemic optic neuropathy after facial calcium hydroxyapatite injection—a case report. *BMC Surg.* 2015;15:21.
31. Dagi Glass LR, Choi CJ, Lee NG. Orbital complication following calcium hydroxylapatite filler injection. *Ophthalmic Plast Reconstr Surg.* 2017;33(3S Suppl 1):S16-S17.
32. Cohen E, Yatziv Y, Leibovitch I, et al. A case report of ophthalmic artery emboli secondary to calcium hydroxylapatite filler injection for nose augmentation—long-term outcome. *BMC Ophthalmol.* 2016;16:98.
33. Marumo Y, Hiraoka M, Hashimoto M, Ohguro H. Visual impairment by multiple vascular embolization with hydroxyapatite particles. *Orbit.* 2018;37(3):165-170.
34. Ramesh S, Fiaschetti D, Goldberg RA. Orbital and ocular ischemic syndrome with blindness after facial filler injection. *Ophthalmic Plast Reconstr Surg.* 2018;34(4):e10 8-e110.
35. Sharudin SN, Ismail MF, Mohamad NF, Vasudevan SK. Complete recovery of filler-induced visual loss following subcutaneous hyaluronidase injection. *Neuro-Ophthalmol.* 2018. doi: 10.1080/01658107.2018.1482358.
36. Bae IH, Kim MS, Choi H, Na CH, Shin BS. Ischemic oculomotor nerve palsy due to hyaluronic acid filler injection. *J Cosmet Dermatol.* 2018;17(6):1016-1018.
37. Myung Y, Yim S, Jeong JH, et al. The classification and prognosis of periocular complications related to blindness following cosmetic filler injection. *Plast Reconstr Surg.* 2017;140(1):61-64.
38. Kim A, Kim SH, Kim HJ, Yang HK, Hwang JM, Kim JS. Ophthalmoplegia as a complication of cosmetic facial filler injection. *Acta Ophthalmol.* 2016;94(5):e377-e379.
39. Lee JI, Kang SJ, Sun H. Skin necrosis with oculomotor nerve palsy due to a hyaluronic acid filler injection. *Arch Plast Surg.* 2017;44(4):340-343.
40. Kim DY, Eom JS, Kim JY. Temporary blindness after an anterior chamber cosmetic filler injection. *Aesthetic Plast Surg.* 2015;39(3):428-430.
41. Lee WS, Yoon WT, Choi YJ, Park SP. Multiple cerebral infarctions with neurological symptoms and ophthalmic artery occlusion after filler injection. *J Korean Ophthalmol.* 2015;56(2):285-290.
42. Chen W, Wu L, Jian Xl, et al. Retinal branch artery embolization following hyaluronic acid injection: a case report. *Aesthet Surg J.* 2016;36(7):NP219-NP224.
43. Shi H, Liang LL, Cui ZH. Ophthalmic artery occlusion after cosmetic facial filler injections. *JAMA Ophthalmol.* 2018;136(6):e180764.
44. Hao JL, Pant OP, Lu CW. Central retinal artery occlusion following hyaluronic acid fillers injection. *Am J Med Sci.* 2018;356(2):e25.
45. Li KT, Huang YH, Chen CH, Chou LW. Delayed-onset cerebral infarction after cosmetic facial injection using hyaluronic acid. *J Formos Med Assoc.* 2016;115(7):587-588.
46. Lin YC, Chen WC, Liao WC, Hsia TC. Central retinal artery occlusion and brain infarctions after nasal filler injection. *QJM.* 2015;108(9):731-732.
47. Chen YC, Wu HM, Chen SJ, et al. Intra-arterial thrombolytic therapy is not a therapeutic option for filler-related central retinal artery occlusion. *Facial Plast Surg.* 2018;34(3):325-329.
48. Salval A, Ciancio F, Margara A, Bonomi S. Impending facial skin necrosis and ocular involvement after dermal filler injection: a case report. *Aesthetic Plast Surg.* 2017;41(5):1198-1201.
49. Shahlaee A, Sridhar J, Rahimy E, Shieh WS, Ho AC. Paracentral acute middle maculopathy associated with postviral Purtscher-like retinopathy. *Retin Cases Brief Rep.* 2019;13(1):50-53.
50. Prado G, Rodríguez-Feliz J. Ocular pain and impending blindness during facial cosmetic injections: is your office prepared? *Aesthetic Plast Surg.* 2017;41(1):199-203.
51. Ragam A, Agemy SA, Dave SB, Khorsandi AS, Banik R. Ipsilateral ophthalmic and cerebral infarctions after cosmetic polylactic acid injection into the forehead. *J Neuroophthalmol.* 2017;37(1):77-80.
52. Hu XZ, Chen SQ, Zhang Q, Wu PS, Lu W. Clinical analysis of visual loss caused by facial cosmetic fillers injection. *Zhonghua Yan Ke Za Zhi.* 2017;53(8):594-598.
53. Schelke LW, Fick M, van Rijn LJ, Decates T, Velthuis PJ, Niessen F. [Unilateral blindness following a non-surgical rhinoplasty with filler]. *Ned Tijdschr Geneeskd.* 2017;161:D1246.