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Original Research

A new injury severity scale for ocular complications following cosmetic filler injection

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Abstract

Background: Cosmetic filler injection can cause a variety of eye complications; however, there is currently no good way to evaluate injury severity and prognosis. By analyzing the injury manifestations of severe ocular complications following cosmetic filler injection and their prognosis, we propose a new injury severity scale. **Methods**: Twenty-two eyes of 22 patients experiencing ocular complications following cosmetic filler injection were followed for 6 months to observe injury characteristics, manifestations and prognosis. Best corrected visual acuity (BCVA), intraocular pressure (IOP), split lamp microscopy, fundus photography, optical coherence tomography (OCT), and fundus fluorescein angiography were examined at the onset and follow-up visits. **Results**: According to the immediate BCVA at the time of injury (with the presence or absence of brain infarction), a new injury severity scale was proposed, namely, Grades 1–4. Grade 1 (4 patients) and Grade 2 (2 patients) tended to have no atrophy of the globe. Grade 3 (12 patients) and Grade 4 (4 patients) were more likely to develop atrophy of the globe (4/12 patients and 2/4 patients, respectively) at the last follow-up. Grade 3 and Grade 4 were more likely to be complicated with ophthalmoplegia and ptosis (7/16 patients). **Conclusions**: The new injury severity scale we proposed can determine the prognosis of different ocular complications following cosmetic filler injection. Accordingly, we can inform injured patients regarding the possibility of phthisis bulbi and the extent of improvement of visual impairment, ophthalmoplegia, ptosis and stroke.

Keywords: injury severity scale; severe ocular complication; cosmetic filler injection; hyaluronic acid; autologous fat; ophthalmic artery occlusion; ocular ischemia syndrome

1. Introduction

Cosmetic filler injection, including mainly hyaluronic acid (HA) and autologous fat, has become an increasingly popular nonsurgical facial rejuvenating procedure. At the same time, severe ocular complications and even stroke following this treatment have also increased in frequency due to the rapidly expanding use, which can result in skin necrosis, vision loss, ophthalmoplegia, ptosis, atrophy of the globe and weakness of limbs. Early supratrochlear, supraorbital or dorsal nasal artery hyaluronidase injection or immediate intra-arterial thrombolysis (IAT) therapy reportedly may restore retinal circulation and reverse vision loss [1,2]. However, other studies have found that retrobulbar injections of hyaluronidase or IAT are unable to improve the visual outcome of patients exhibiting HA filler embolization [3,4]. If the BCVA is still hand motion or better than hand motion at the time of injury, visual impairment may improve to different degrees [5,6]. Therefore, physicians should be knowledgeable of their effective management. Limiting the volume per injection and avoiding penetration of the supratrochlear, supraorbital or dorsal nasal artery could represent a simple prophylactic strategy [7,8].

Sites that are at high risk for complications include the glabella, nasal region and forehead [9–11]. Patients experiencing severe ocular complications following cosmetic filler injection can be classified into four types according to their periocular manifestations, including ptosis, ophthalmoplegia, and enophthalmos [12]. However, such classification cannot reflect the severity of injury. Therefore, we propose a new injury severity scale aimed at predicting the possibility of phthisis bulbi and the extent of improvement of vision loss, ophthalmoplegia, ptosis and stroke.

2. Methods

2.1 Subjects

Twenty-two patients between 18 and 44 years of age who experienced severe ocular complications following cosmetic filler injection and came to the Department of Ophthalmology at Beijing Tsinghua Changgung Hospital were recruited from April 2017 to January 2020. All enrolled patients signed an informed consent form before the start of ocular examinations. The protocol was approved

by the Institutional Review Board for the Protection of Human Subjects of Beijing Tsinghua Changgung Hospital in compliance with the tenets of the Declaration of Helsinki.

2.2 Inclusion criteria

The inclusion criteria were as follows: (1) all patients experiencing ocular complications following cosmetic filler injection, including HA and autologous fat injection, with visual impairment to different degrees, with or without stroke; (2) main manifestations of ocular complications including visual impairment to different degrees, ptosis, ophthalmoplegia, ocular ischemia syndrome, and atrophy of the globe at the last follow-up (at the 6-month follow-up after injury); (3) all case studies started within 1 month of visual impairment of the affected eye being noticed by the patients.

2.3 Ocular examinations

All enrolled subjects were subjected to a series of ocular examinations listed as follows: (1) best corrected visual acuity (BCVA) assessment, and the results were converted to the LogMAR scale; (2) intraocular pressure (IOP); (3) slit-lamp microscopy; (4) fundus photography; (5) fundus fluorescein angiography (FFA) (TRC-50 DX, Topcon company, Japan); (6) OCT (spectral-domain OCT, Heidelberg Engineering, Heidelberg, Germany); and (7) perimetry (Humphrey, Carl Zeiss company, Canada). These examinations were used to assist ophthalmologists in diagnosis and follow-up. All enrolled patients were followed up to 6 months after injury and underwent ocular examinations at each return visit. Because the doctors who treated the cases in the article were ophthalmologists, complete eye examinations were performed. According to our grading system, the crucial examination is BCVA. Other tests help the ophthalmologist diagnose and make a differential diagnosis.

3. Results

3.1 Demographic and injury characteristics of the involved eyes

Twenty-two patients, including 21 females and one male, were recruited for this study. Among them, no bilateral involvement was identified (0%). The most common injection site resulting in visual impairment was the forehead (9/22), followed by the nasal region (6/22) and the glabella (3/22). The most common filler material was HA (20/22), followed by autologous fat (2/22, case no. 7, 10). The subjective demographic and injury characteristics (including sex, age, involved eye, date, injection sites and filler materials) at the initial visit are listed in Table 1.

3.2 Subjective diagnosis, prognosis and pre/post-BCVA of the involved eyes

Four of the 22 patients had cases complicated with brain infarction, and they all exhibited immediate no light perception (immediate NLP) at the time of injury. Six of the 22 patients presented atrophy of the globe at the last follow-up, and moreover, they all presented immediate NLP at the time of injury. Sixteen of the 22 patients displayed immediate NLP at the time of injury, and this sign indicated a greater likelihood of being complicated with brain infarction (4/16 patients) with no possibility of improved visual acuity (16/16 patients). Five of the 22 patients had cases complicated with ophthalmic artery occlusion (OAO), and they all presented atrophy of the globe at the last follow-up. Eight of the 22 patients had cases that were complicated with ophthalmoplegia and ptosis, and these signs all improved to different degrees. Eleven of the 22 patient cases were complicated with central retinal artery occlusion (CRAO), and they all displayed immediate NLP with no improvement of visual acuity at the last follow-up. The subjective diagnosis, prognosis and pre/post-BCVA of the involved eyes are listed in Table 2.

Notably, one patient (case 9) did not lose her light perception at the time of injury, but she gradually exhibited NLP several minutes later. The injured eye of this patient was finally diagnosed with anterior ischemic optic neuropathy (AION) and choroidal artery occlusion (ChAO). After 1.5 months of further recovery, the BCVA of the injured eye improved to 20/1000. We called this sign delayed NLP (NLP that occurred not at the time of injury but within several minutes after the injury), which indicated the possibility of partial recovery of visual function at the last follow-up.

3.3 The new injury severity scale

Over the follow-up period, we found that the immediate manifestations at the time of injury can determine the prognosis of these patients. According to the immediate BCVA at the time of injury (with or without brain infarction), a new injury severity scale was proposed, comprising Grades 1, 2, 3 and 4. A higher score on this scale indicated a worse prognosis. According to whether there was final phthisis bulbi, Grade 3 was subdivided into 3A (no atrophy of the globe) and 3B (phthisis bulbi at the last follow-up); Grade 4 was subdivided into 4A (no atrophy of the globe) and 4B (phthisis bulbi at the last follow-up). Grade 1 (4 patients) and Grade 2 (2 patients) tended to have no atrophy of the globe. Grade 3 (12 patients) and Grade 4 (4 patients) were more likely to exhibit atrophy of the globe (4/12 patients and 2/4 patients, respectively) at the last follow-up. Grade 3 and Grade 4 were more likely to be complicated with ophthalmoplegia and ptosis (5/12 patients and 2/4 patients, respectively), but such signs could improve to different degrees. The new injury severity scale for the 22 involved eyes is listed in Table 3. Every grade's definition, mainly involving the artery, main diagnosis and main management of the new injury severity scale, is listed in Table 4.

Table 1. Demographic and injury characteristics of the 22 involved eyes.

Case no.	Gender	Age	Involved eye	Date	Injection sites	Filler materials
1	female	28	OS	17/04/2017	forehead	HA
2	female	27	OD	20/06/2017	-	HA
3	male	31	OD	25/07/2017	nasal	HA
4	female	42	OD	11/10/2017	glabellar	HA
5	female	38	OS	19/10/2017	forehead	HA
6	female	18	OS	26/10/2017	-	HA
7	female	21	OD	07/11/2017	forehead	autologous fat
8	female	30	OS	09/11/2017	-	HA
9	female	23	OS	12/11/2017	forehead	HA
10	female	36	OD	08/02/2018	glabellar	autologous fat
11	female	35	OS	13/02/2018	forehead	HA
12	female	37	OD	20/03/2018	-	HA
13	female	44	OS	16/10/2018	forehead	HA
14	female	21	OD	17/10/2018	nasal	HA
15	female	19	OD	04/12/2018	nasal	HA
16	female	30	OD	08/06/2019	nasal	HA
17	female	40	OS	08/06/2019	forehead	HA
18	female	31	OD	31/10/2019	nasal	HA
19	female	30	OS	20/11/2019	forehead	HA
20	female	35	OS	12/12/2019	forehead	HA
21	female	36	OS	19/12/2019	nasal	HA
22	female	44	OS	02/01/2020	glabellar	HA

HA, hyaluronic acid.

3.4 The relationship between injection site, filler material and the new injury severity scale

The most dangerous injection site resulting in more severe ocular complications (Grade 3 and Grade 4) was the glabella (3/3 patients). Autologous fat injection tends to result in a much worse prognosis (Grade 3 and Grade 4) than HA injection (2/2 patients).

4. Discussion

Severe ocular complications following cosmetic filler injection are rare, but as facial injections become increasingly popular, reports of the complications have increased [8]. How to predict the prognosis of these patients at the first time of injury is an urgent question that concerns both physicians and patients. The new injury severity scale (which does not involve subsequent special examinations such as FFA, OCT, fundus photography and perimetry) that we proposed in the text is helpful. According to the new scale, a higher grade indicates a worse prognosis. The first advantage of this new scale is that it provides the fastest severity assessment and prognosis analysis at the first time of injury. With this scale, we can inform patients about the possible prognosis even at the initial visit. Second, our new scale is easy to learn and promote at the grassroots level because it does not require subsequent special examinations.

The new scale is based on the anatomy of the central retinal artery (CRA), ophthalmic artery, internal carotid artery (ICA) and their branches (Fig. 1). The relationship of the three arteries is as follows: the CRA is the terminal branch of the ophthalmic artery, which is the first main branch of the ICA after it enters the intracranial space. The blood supply of the inner 5 layers of the retina is completely derived from the CRA, without any blood supply from collateral circulation. The blood supply of the forehead, glabella, and nasal region is also from distal branches of the ophthalmic artery, including the supraorbital artery, supratrochlear artery, and dorsal nasal artery (Figs. 1,2). It is assumed that if the injecting force is sufficiently high, the tiny droplet may retrograde into the ophthalmic artery and even the ICA. Following cessation of the injection, the filler may travel distally into and obstruct any branch(es) of the ophthalmic artery and ICA, including the CRA. Once the CRA or the ophthalmic artery is completely or severely diffusely obstructed, the inner 5 layers of the retina will lose their complete blood supply, and the eye that loses its blood supply will immediately lose LP. All patients classified into Grades 3 and 4 displayed immediate NLP because of complete or severely diffuse obstruction of the CRA or the ophthalmic artery. Branch ICA occlusion requires a higher injecting force and longer retrograde flow into the ophthalmic artery. Therefore, branch ICA occlusion indicates complete

Table 2. Subjective diagnosis, prognosis and pre-BCVA of 22 involved eyes.

Case no.	Brain infarction	Phthisis bulbi	Pre-BCVA	1m-BCVA	Post-BCVA	Subjective diagnosis
1	Yes	Yes	immediate NLP	NLP	NLP	Stroke, CRAO, OIS
2	No	Yes	immediate NLP	NLP	NLP	OAO, ophthalmoplegia, ptosis
3	No	Yes	immediate NLP	NLP	NLP	OAO, ophthalmoplegia, ptosis
4	Yes	Yes	immediate NLP	NLP	NLP	Stroke, OAO, ophthalmoplegia, ptosis
5	No	No	immediate NLP	NLP	NLP	CRAO
6	No	Yes	immediate NLP	NLP	NLP	OAO, ophthalmoplegia, ptosis
7	No	No	immediate NLP	NLP	NLP	CRAO
8	No	No	immediate NLP	NLP	NLP	CRAO
9	No	No	delayed NLP	20/2000	20/1000	AION, ChAO
10	Yes	No	immediate NLP	NLP	NLP	Stroke, CRAO, ophthalmoplegia, ptosis
11	No	No	20/50	20/20	20/20	BRAO
12	No	No	20/20	20/20	20/20	BRAO
13	No	No	20/200	20/40	20/20	OIS, ophthalmoplegia, ptosis
14	Yes	No	immediate NLP	NLP	NLP	Stroke, CRAO
15	No	No	LP	20/160	20/160	AION
16	No	No	immediate-NLP	NLP	NLP	CRAO, enophthalmos
17	No	No	immediate-NLP	NLP	NLP	OIS, CRAO, ophthalmoplegia, ptosis
18	No	Yes	immediate-NLP	NLP	NLP	OAO, ophthalmoplegia, ptosis
19	No	No	immediate-NLP	NLP	NLP	CRAO
20	No	No	immediate-NLP	NLP	NLP	CRAO
21	No	No	20/25	20/25	20/25	BRAO
22	No	No	immediate-NLP	NLP	NLP	OIS, CRAO

Pre-BCVA means the worst BCVA before the first visit; 1m-BCVA means the BCVA at 1-month follow-up after injury; Post-BCVA means the BCVA at 6 months follow-up after injury; immediate NLP means NLP occurred at the time of injury; delayed NLP means NLP occurred not at the time of injury but within several minutes after the injury.

BCVA, best corrected visual acuity; LP, light perception; NLP, no light perception; CRAO, central retinal artery occlusion; OAO, ophthalmic artery occlusion; BRAO, branch retinal artery occlusion; ChAO, choroidal artery occlusion; OIS, ocular ischemic syndrome; AION, anterior ischaemic optic neuropathy.

or severely diffuse OAO or CRAO. This is the reason why all patients exhibiting stroke lost their LP immediately at the time of injury. Four of the 22 cases were complicated with brain infarction, and this rate is close to that in the literature, with a rate of 23.5% [9]. Vision loss in Grades 3 or 4 did not improve at the last follow-up. As reported in the literature, vision loss due to complete OAO or CRAO had no possibility of improvement [7,13,14].

Grade 2 displayed delayed NLP or LP at the time of injury. The mechanism is that the CRA and the ophthalmic artery were not completely obstructed. Ultimately, such patients in Grade 2 were possibly diagnosed with AION with ChAO and severe diffuse branch retinal artery occlusion (BRAO). Grade 1 displayed hand motion or better BCVA than hand motion at the time of injury. Ultimately, such patients in Grade 1 were possibly diagnosed with BRAO, ocular ischemic syndrome (OIS) with ChAO, and mild diffuse BRAO. The visual impairment in Grade 1 or 2 will improve to different degrees at the last follow-up [6]. Even some patients in Grade 1 can recover completely. Furthermore, Grade 1 or 2 tends to have no atrophy of the globe.

Notably, Grade 3 and Grade 4 patients were more likely to present atrophy of the globe at the last follow-up (4/12 and 2/4 patients, respectively). The possible mechanism is that tiny droplets refluxing into the ophthalmic artery may progress into the anterior ciliary artery (ACA) following cessation of the injection, resulting in severe diffuse anterior segment ischemic syndrome. Subsequently, the secretory function of the ciliary body decreases, leading to atrophy of the globe. As above, Grade 3 and Grade 4 were more likely to be complicated with ophthalmoplegia and ptosis, but such signs could improve to different degrees through subsequent treatment. Signs such as ophthalmoplegia and ptosis can be considered manifestations of OIS. Because the extraocular muscles and eyelids can obtain their blood supply from other nearby arteries, the improvement of ophthalmoplegia and ptosis is possible.

With regard to injection sites and materials, our results are consistent with the past literature. The most common injection site resulting in visual impairment was the forehead, followed by the nasal region and the glabella, which is the same finding as that in a previous report [1,5,9–11].

Table 3. The new injury severity scale for the 22 involved eyes.

Case no.	Grade 1	Grade 2	Grade 3		Grade 4	
			Grade 3A	Grade 3B	Grade 4A	Grade 4B
1						√
2				√		
3				√		
4						√
5			√			
6				√		
7			√			
8			√			
9		√				
10					√	
11	√					
12	√					
13	√					
14					√	
15		√				
16			√			
17			√			
18				√		
19			√			
20			√			
21	√					
22			√			

Grade 1 indicates hand motion or better BCVA than hand motion at the time of injury; Grade 2 indicates LP at the time of injury or delayed NLP; Grade 3 indicated immediate NLP at the time of injury; Grade 3A indicates immediate NLP at the time of injury but no atrophy of the globe at the last follow-up; Grade 3B indicates immediate NLP at the time of injury and atrophy of the globe at the last follow-up; Grade 4 indicated immediate NLP complicated with stroke at the time of injury; Grade 4A indicates immediate NLP complicated with stroke at the time of injury but no atrophy of the globe at the last follow-up; Grade 4B indicates immediate NLP complicated with stroke at the time of injury and atrophy of the globe at the last follow-up.

BCVA, best corrected visual acuity; LP, light perception; NLP, no light perception.

The most common filler material was HA and, second, autologous fat. However, the prognosis with autologous fat injection was much worse than that with HA injection [15–18], as in our study, 2 patients experienced severe vision loss following autologous fat injection (case nos. 7, 10). Case no. 7 was categorized into Grade 3A and ultimately showed permanent loss of LP. Case no. 10 was classified as Grade 4A; this patient not only lost her LP but also underwent stroke, ophthalmoplegia and ptosis. We hypothesize that this may be due to the larger size of autologous fat particles than HA molecules. The size of autologous fat particles varies widely, ranging from 0.02 mm to 1.4 mm [19], while the molecular size of HA varies in a small range, from 0.35 mm to 0.90 mm [20]. Therefore, autologous fat particles can obstruct the main trunk and all branches of the ophthalmic artery (approximately 1.3 mm in diameter of the trunk), leading to much worse and more diverse prognosis [21,22]. In contrast, HA molecules usually obstruct the distal branches of the ophthalmic artery [23].

To date, ocular complications following cosmetic filler augmentation cannot be prevented completely, but measures should be taken to minimize the possibility. According to the literature, reducing the injection pressure, verification of no blood reflux into the syringe before injection, using a blunt needle and use of duplex ultrasound are definitely effective preventive methods [14,19,20,24]. Once such complications occur, vasodilators, anterior chamber paracentesis, ocular massage, anticoagulation or thrombolysis should be given as soon as possible [25]. Physicians should be aware of these severe ocular complications and be knowledgeable regarding effective management.

Table 4. The new injury severity scale.

	Definition	Mainly involved artery	Main diagnosis	Main management
Grade 1	hand motion or better BCVA than hand motion at the time of injury	BRA, ACA, SPCA, LPCA	BRAO, OIS with/without ChAO, mild diffuse BRAO, AION	vasodilator
Grade 2	LP at the time of injury or delayed NLP	BRA, SPCA, LPCA, ACA	severe diffuse BRAO, AION with ChAO, OIS with ChAO	vasodilator, anterior chamber paracentesis, ocular massage, anticoagulation, thrombolysis, glucocorticoids
Grade 3	immediate NLP at the time of injury	CRA, OA, SPCA, LPCA, ACA	severe diffuse CRAO or OAO	
Grade 3A	no atrophy of the globe at the 6 months follow-up after injury	CRA, OA, SPCA, LPCA	severe diffuse CRAO or OAO	
Grade 3B	atrophy of the globe at the 6 months follow-up after injury	ACA, CRA, OA, SPCA, LPCA	severe OIS complicated with severe diffuse CRAO or OAO	same as Grade 3A above, vitrectomy combined with silicone oil tamponade*
Grade 4	immediate NLP complicated with stroke at the time of injury	ICA, CRA, OA, ACA, SPCA, LPCA	cerebral infarction, severe diffuse CRAO or OAO	life support therapy, multidisciplinary consultation, vasodilator, anterior chamber paracentesis, ocular massage, anticoagulation, thrombolysis, glucocorticoids
Grade 4A	no atrophy of the globe at the 6 months follow-up after injury	ICA, CRA, OA, SPCA, LPCA	cerebral infarction, severe diffuse CRAO or OAO	
Grade 4B	atrophy of the globe at the 6 months follow-up after injury	ICA, ACA, CRA, OA, SPCA, LPCA	cerebral infarction, severe OIS complicated with severe diffuse CRAO or OAO	same as Grade 4A above, vitrectomy combined with silicone oil tamponade*

*Vitrectomy combined with silicone oil tamponade is one of the methods to treat ocular atrophy and maintain appearance.
BCVA, best corrected visual acuity; BRA, branch retinal artery; SPCA, short posterior ciliary artery; LPCA, long posterior ciliary artery; ACA, anterior ciliary artery; OA, ophthalmic artery; ICA, internal carotid artery; LP, light perception; NLP, no light perception; CRAO, central retinal artery occlusion; OAO, ophthalmic artery occlusion; BRAO, branch retinal artery occlusion, ChAO, choroidal artery occlusion; OIS, ocular ischemic syndrome; AION, anterior ischaemic optic neuropathy.

5. Conclusions

Severe ocular complications resulted from cosmetic facial fillers are often catastrophic, and the severity of the injury and possible prognosis are of common concern to both physicians and patients. The new injury severity scale we proposed can well predict the patient's damaged blood vessels, the likelihood of phthisis bulbi, and the degree of future recovery. In this way, it may help ophthalmologists to make a clear diagnosis earlier and give timely treatment measures, and at the same time, it can also inform patients of possible unfavorable prognosis earlier, and reduce subsequent legal disputes.

Several representative cases are as follows:

Case No. 1

A 28-year-old Asian woman was referred to our hospital from a nearby beauty salon for decreased visual acuity in her left eye on April 17, 2017. In China, beauty salons or clinics are also registered and operated by professional plastic surgeons. There are no non-medical practitioners operating for these patients. The patient complained of nausea and dizziness during the injection of HA for augmentation foreheadplasty half an hour before admission to our hospital.

On physical examination, there was a dark area and an injection site visible on the left forehead (Fig. 3A). Examination of the left eye showed no light perception or pupil dilation with a diameter of 4 mm, and a relative afferent pupillary defect was detected. IOP (NCT) was 12.0 mmHg OD and 10.0 mmHg OS. The optic disc and the entire retina of the left eye were pale and swollen, and there was a cherry-red spot suggestive of CRAO. Furthermore, we could see the narrowed retinal artery with an internal embolus on the fundus photograph (Fig. 3B). Ocular anterior and posterior segments were not abnormal in the right eye.

The injured eye was diagnosed with CRAO, and emergency medical care was performed. Hyaluronidase was injected into the retrobulbar region and dark frontal area (total 1500 U). Anterior chamber paracentesis was managed. At the same time, the patient received prompt intra-arterial thrombolytic therapy by the injection of urokinase (200,000 units), but the vision loss did not improve. Digital subtraction angiography (DSA) showed that the left ocular artery developed well but that most of its branches did not de-

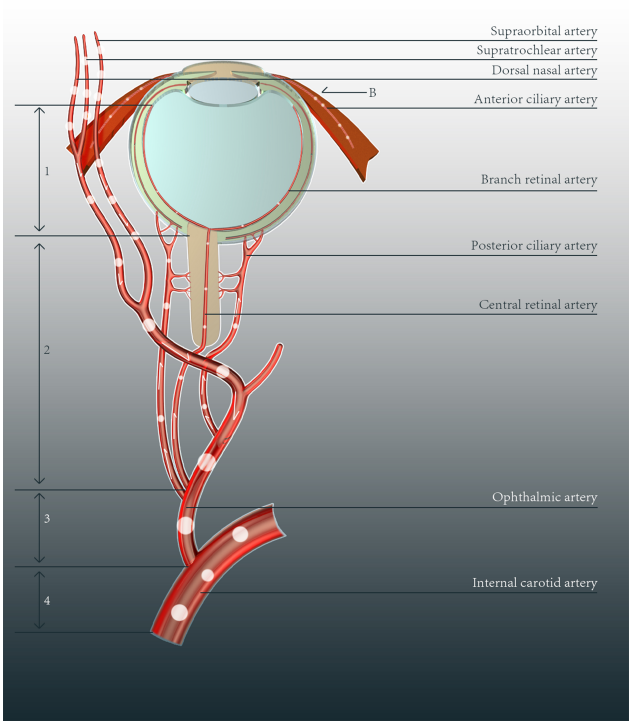

Fig. 1. Schematic diagram of the new injury severity scale for ocular complications following cosmetic filler injection based on the anatomy of the central retinal artery (CRA), ophthalmic artery, ICA and their branches. (1) When a small amount of filler particles retrogrades into the beginning of CRA or ciliary artery and eventually block their distal branches, the new injury severity scale is usually Grade 1, and the final diagnosis is usually BRAO, OIS with ChAO, mild diffuse BRAO. (2) When a large amount of filler particles retrogrades into the beginning of CRA but do not completely block its main trunk, the new injury severity scale is usually Grade 2, and the final diagnosis is usually AION with ChAO and severe diffuse BRAO. (3) When a large amount of filler particles retrogrades into the beginning of the ophthalmic artery but do not reach the ICA, the new injury severity scale is usually Grade 3, and the final diagnosis is usually severe diffuse CRAO or OAO with or without severe OIS. (4) When filler particles retrograde into the ICA, the new injury severity scale is usually Grade 4, and the final diagnosis is usually cerebral infarction or severe diffuse CRAO or OAO with or without severe OIS. (B) B means Grades 3B or 4B. When a large amount of filler particles eventually blocks the ACA, the patient usually exhibits atrophy of the globe at the 6-month follow-up after injury.

velop, which indicated that most branches of the ocular artery were occluded (Fig. 3C). The patient also received oral aspirin (100 mg/day, 1 week), intravenous dexamethasone (1000 mg/day, 3 days), subcutaneous low molecular weight heparin (4100 units/12 hours, 3 days) and local eye drops, including levofloxacin and prednisolone acetate (four times a day).

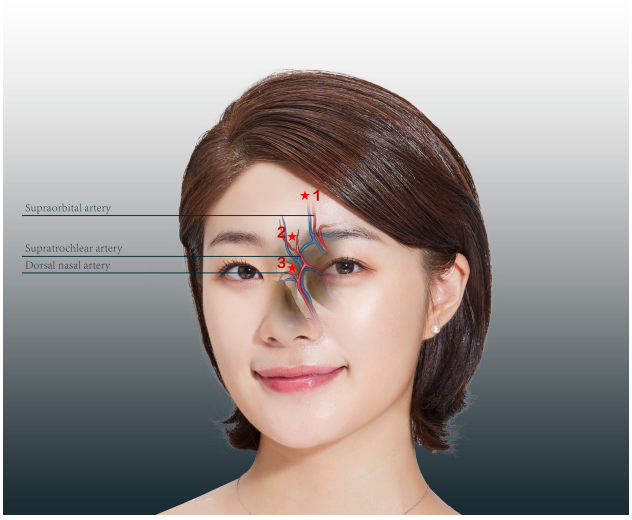

Fig. 2. The graph showing facial danger zones (red five-pointed star) related to the specific artery. 1, 2, and 3 indicate the forehead, glabella, and nasal region related to the supraorbital artery, supratrochlear artery, and dorsal nasal artery, respectively.

Six days after the incident, the patient complained of right upper limb weakness, with the muscle strength decreasing to Grade 4 from Grade 5. Prompt brain computed tomography showed minor hemorrhage accompanied by infarction lesions in the left frontal and parietal lobes.

Seven days later, the BCVA was 20/20 OD, and NLP OS remained. IOP (NCT) was 13.0 mmHg OD and 5.0 mmHg OS. Examination of the right anterior and posterior segments showed no obvious abnormalities. The anterior segment of the left eye showed corneal edema and pupillary dilation with a diameter of 8 mm and partial posterior synechia. The fundus examination revealed a swollen optic disc, minor hemorrhage in the macular region and a paler retina than before (Fig. 3D).

Two weeks after the patient underwent rehabilitation training, the muscle strength of the right limb increased to Grade 5 from Grade 4. However, the visual acuity of the left eye was still NLP, and the globe turned atrophic. The injury was eventually diagnosed as left brain infarction, phthisis bulbi, CRAO and amaurosis of the left eye.

Case No. 4

A 42-year-old female complained of sudden visual loss in her right eye following HA facial filler injection into the glabellar region on September 19, 2017. Visual loss was accompanied by weakness of the left arm while she was receiving cosmetic augmentation at a beauty salon 24 days prior. A review of her systems revealed no history of previous ocular or systemic disease. The patient had been admitted elsewhere for 20 days and was given oral steroids and aspirin.

At presentation, her BCVA was NLP in the right eye and 20/20 vision in the left eye. IOP (NCT) was 11.0 mmHg OD and 10.8 mmHg OS. A slit-lamp examination of the

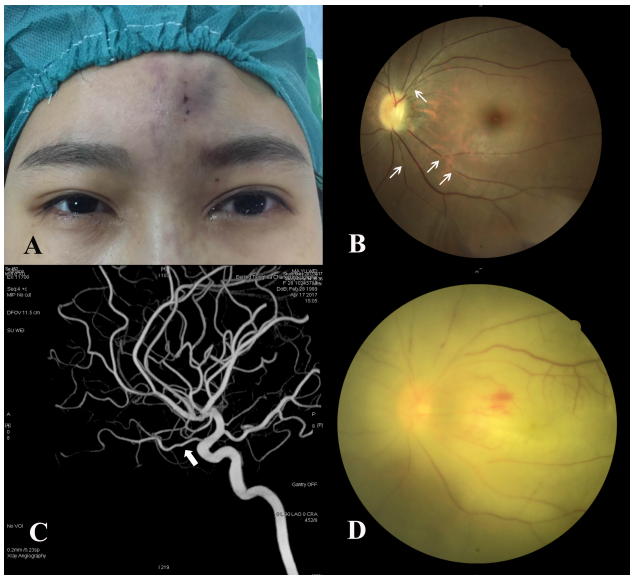

Fig. 3. Typical clinical and imaging features of a patient with hyaluronic acid-induced central retinal artery occlusion (CRAO). (A) Photography of the external aspect of the eyes of case no. 1 showed a dark area and an injection site visible on the left forehead, taken at approximately the 6th hour after HA injection. (B) Fundus photography of the injured eye of case no. 1 showing a pale and swollen optic disc and retina, cherry-red spot, narrowed retinal artery with internal embolus (white arrow), taken on the same day as Fig. 3A. (C) Digital subtraction angiography (DSA) of case no. 1 showing that the left ocular artery developed well (white arrow) but that most of its branches did not develop, which indicated that most branches of the left ocular artery were occluded, taken on the same day as Fig. 3A. (D) Fundus photography of the injured eye of case no. 1 showing a swollen optic disc, minor hemorrhage in the macular region and a paler retina than before, taken on the 7th day after HA injection. HA, hyaluronic acid.

right eye revealed swollen upper eyelids (covered with a piece of gauze) and external strabismus (Fig. 4A). The conjunctiva was injected, and stromal edema and Descemet's membrane striae were evident in the cornea. The ocular anterior chamber of the injured eye revealed hyphema with a height of 4 mm. The pupil, iris, lens, and fundus could not be seen (Fig. 4B). The left eye was normal.

The injured eye was diagnosed with cerebral artery occlusion, OAO, anterior segment ischemia, hyphema and amaurosis. We recommended vitrectomy and silicone oil tamponade for the injured globe to prevent its atrophy, but the patient refused.

Abbreviations

ACA, anterior ciliary artery; AION, anterior ischemic optic neuropathy; BCVA, best corrected visual acuity; BRAO, branch retinal artery occlusion; ChAO, choroidal

Fig. 4. Typical clinical features of a patient with severe anterior segment ischemia (ASI) caused by hyaluronic acid. (A) Photography of the external aspect of the eyes of case no. 4 showing swollen upper eyelids covered with a piece of gauze and external strabismus of the right eye, taken on the 24th day after HA injection. (B) Anterior segment photography of the injured eye of case no. 4 showing severe mixed conjunctival hyperemia, corneal stromal edema and Descemet's membrane striae and hyphema with a height of 4 mm, taken on the same day as Fig. 4A. Because of corneal stromal edema, the pupil, iris, lens, and fundus cannot be seen. HA, hyaluronic acid.

artery occlusion; CRA, central retinal artery; CRAO, central retinal artery occlusion; DSA, Digital subtraction angiography; FFA, fundus fluorescein angiography; HA, hyaluronic acid; IAT, intra-arterial thrombolysis; ICA, internal carotid artery; IOP, intraocular pressure; LP, light perception; NCT, noncontact tonometer; NLP, no light perception; OAO, ophthalmic artery occlusion; OCT, optical coherence tomography; OIS, ocular ischemic syndrome; RAPD, relative afferent pupillary defect.

Author contributions

SS, XD, MC and YH conceived, planned the study and wrote the manuscript. SS, LL, XD, WS, GZ, QW, LW, YJ, AC, YY, MC, YH acquired the data. SS, LL, XD, WS, GZ, QW, LW, YJ, AC, YY, MC, YH analyzed the data and participated in the discussion and provided the comments. All authors have read and approved the manuscript.

Ethics approval and consent to participate

The Institutional Review Board of Beijing Tsinghua Changgung Hospital approved the study protocol, and each participant provided written informed consent.

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Conflict of interest

The authors declare no conflict of interest.

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