**CASE REPORT** 



# **Reversal of Post-filler Vision Loss and Skin Ischaemia with High-Dose Pulsed Hyaluronidase Injections**

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Abstract Nose filler injections are very popular in many Asian countries to improve nose shape and projection. However, due to the vascular supply of nose from the ophthalmic artery and its communication with branches of the facial artery in this region, there could be a possibility of ophthalmic complications in case of an accidental intraarterial injection of filler material. This may cause devastating complications of partial or complete vision loss with or without associated cutaneous ischaemic changes. We present a case report of a patient who developed features of vascular involvement after two ml of HA filler injection in the nasal dorsum, tip and columella. The patient initially developed tell-tale signs of impending skin necrosis in the nasal and forehead skin followed by ptosis, severe pain and progressive vision loss in the right eye until a point where the patient could only perceive light. The patient was managed with multiple doses of hyaluronidase in the involved skin and two doses of retrobulbar injection for vision loss. Significant recovery in the skin and ophthalmic components occurred within 20 days of filler injection. This case demonstrates that recovery of the ischaemic ophthalmic and cutaneous changes secondary to probable intra-arterial injection could be accomplished using

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combined retrobulbar and periorbital intracutaneous injections of high-dose pulsed hyaluronidase.

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**Keywords** Fillers · Vision loss · Blindness · Hyaluronidase · Ischaemia · Nose filler

#### Abbreviations

HDPH	High dose pulsed hyaluronidase
HA	Hyaluronic acid
ECA	External carotid artery
ICA	Internal carotid artery

#### Introduction

Accidental intra-arterial injection of fillers in the direct branches of the ophthalmic artery or arteries anastomosing with its branches has the potential of causing partial or complete vision loss [1, 2]. It is a rare complication, and detailed understanding of the vascular anatomy of the area to be injected is very important for avoiding this complication [3].

## **Case Report**

A forty-year-old woman received two ml of HA filler (brand not known) with 25 G cannula for nasal dorsum augmentation in a private clinic in Indonesia. She was earlier injected with one ml of HA filler in her nose about one month before and was not fully satisfied with the result. After about 10 min of filler injection, she started developing blanching of the nasal skin followed by upper eyelid ptosis, blurring of vision and deep pain in the right eye. For the first 30 min after the onset of signs and symptoms, local massage was performed. The injecting physician gave 30 units of hyaluronidase after about 30 min of onset of signs and symptoms, but there was no immediate improvement in the cutaneous or visual signs and symptoms.

The skin on the nose tip, nose bridge, columella, glabella, part of the forehead and bilaterally medial cheeks and nasolabial folds became dark purple/blue, and pain in the involved skin area continued to worsen. The pain in the eye also increased, and the loss of vision continued to worsen. After 1 h of nose filler injection, she only had a perception of light in the right eye. She was admitted to the hospital under a neurologist for observation. At the time of admission, the patient was conscious, fully alert and coherent. The patient continued to have worsening of cutaneous symptoms with discolouration and mottling of the demarcated ischaemic zone (Fig. 1) and continued pain in this area. She also started developing some pustules, indicative of regions of micro-necrosis, in the ischaemic zone. She also developed periorbital swelling, conjunctival congestion, chemosis, and her vision continued to be at the level of perception of light only. During her hospital stay, she received pain killers and IV fluids only.

As the consultants in the hospital had no experience in managing HA filler-related complications, on the third post-filler day, the case was referred to an aesthetic physician having experience of working with fillers and its complications. On clinical examination, the patient had periorbital oedema and right upper eyelid ptosis (Fig. 2). Due to limited facilities for diagnosis of the condition, only fundoscopy and VFI assessment could be performed on third post-filler injection day. It was found on fundoscopy that only 30 per cent sparing of the ophthalmic artery circulation was there, and her visual field index (VFI) was



Fig. 2 Post-filler vision loss, Day 3—periorbital swelling with the inability to open right eye and complaining of near-total vision loss with perception of light only. The right eye is showing conjunctival congestion and chemosis. Ischaemic changes in skin seen in the picture

found to be only 19%. It was immediately decided to start with a high dose of pulsed hyaluronidase protocol. So, about 40 h after the filler injection in the nose, the first dose of 1500 units of hyaluronidase (Mesologica, 1500 Units/ vial) was injected in the ischaemic zone spread over the nose bridge, columella, nose tip, glabella, forehead and bilaterally on medial parts of cheeks and nasolabial folds. No immediate change was seen in the skin condition. There was also no immediate improvement in vision loss. Six hours after the first hyaluronidase injection, it was decided to inject another high dose of hyaluronidase and a second dose of 1500 units of hyaluronidase was injected in the same area. The patient was also recommended to take oral aspirin (80 mg per day) and antibiotics (Cefixime 200 mg twice a day).



Fig. 1 Post-filler vision loss, Day 2—the swelling in right periorbital area with the inability to open right eye. Skin shows purple, blue discolouration with some pustules





Fig. 3 Post-filler vision loss, Day 4—after two doses of 1500 units of intracutaneous hyaluronidase. Ischaemic changes in the skin in the form of discolouration and multiple small areas of skin necrosis. Inability to open the right eye with conjunctival congestion and chemosis

On the fourth post-filler day, the patient still had extensive discolouration of the skin of the nose and adjoining areas, including multiple small areas of skin necrosis (Fig. 3). As vision had not improved with subcutaneous injection of two doses of high-dose hyaluronidase injection alone, it was decided to give a retrobulbar injection of hyaluronidase also. The first dose of 900 units of hyaluronidase was injected, 600 units by superior and 300 units by inferior retrobulbar injection technique, more than 72 h after the filler injection. As the same time, the third dose of 1500 unit of hyaluronidase was injected in the ischaemic skin zone.

On the fifth post-filler day, there was some improvement in the discolouration of the skin and reduction in affected skin area at the periphery of the involved skin (Fig. 4). The fourth dose of 1500 units hyaluronidase was given in the affected skin area. At the same time, the second dose of 900 units of hyaluronidase was given in the retrobulbar area by the same superior and inferior approach. Four hours after the second dose of retrobulbar hyaluronidase injection, the patient reported significant relief from diffuse blunt pain in the right eye. Her vision also improved from the perception of light to seeing hand movements.

On the sixth post-filler injection day, another fundoscopy was performed, and it was found that there was no vascular obstruction after two doses of retrobulbar hyaluronidase and vessels were found to be of normal size. There was, however, some oedema over the optic nerve head and sclera around the macula (Fig. 5). The fifth dose of 1500 units of hyaluronidase was given in the ischaemic skin zone.

On the seventh post-filler injection day, the patient could do some movement of the right upper eyelid. Her vision



Fig. 4 Post-filler vision loss, Day 5—after three doses each of 1500 units of intracutaneous hyaluronidase and one dose of 900 units of retrobulbar hyaluronidase. Ischaemic changes in the skin are resolving, improvement in discolouration, ischaemic area getting well demarcated, Periorbital swelling improving

also improved, swelling in the eyelids and conjunctiva started decreasing (Fig. 6).

On the eighth post-filler injection day, she could move her right upper eyelid partially so that her 50% palpebral aperture could be seen now. Her vision also improved significantly, and she could see the shape of large objects with her right eye. The affected skin started showing a return to normal skin colour at most places (Fig. 7) and continued to improve with signs of healing as seen on the ninth (Fig. 8) and eleventh days (Fig. 9).

On day 12, she could move her right upper eyelid to a large extent so that her 90% right palpebral aperture could be seen now. A large part of the affected skin was showing signs of recovery and healing, leaving only some small areas of skin necrosis and scarring (Fig. 10). On the 13th post-filler injection day, fundoscopy was performed again, and some oedema in the optic nerve head was still present. The skin continues to show improvement as seen on the fourteenth day (Fig. 11).

On the 21st post-filler day, normal movement of the eyelids was noticed, and there was nearly 70% recovery of the vision in the right eye by this time. The visual field index of the right eye was found to be 66% (Fig. 12a, b). The cutaneous component of the complication was also recovering very well with small areas of skin necrosis along with healing changes and scars at multiple areas (Fig. 13).

After three months, the patient was found to have been fully recovered from the visual loss, and there was minimal skin deformity in the form of very small areas of scarring at multiple places (Fig. 14).

#### Discussion

In the last decade, filler injections have become a very popular choice for treatment of various types of facial treatments due to their less invasive nature and minimal downtime compared to surgical cosmetic procedures. The increasing use of fillers all over the world has also brought attention to relatively rare but potentially life-altering complications which have been reported in recent years. The teaching of facial anatomy has created much awareness regarding avoidance of the complications [4] related to fillers. At the same time, increasing use of fillers globally has led to more vascular complications being reported now. The severe complications of fillers are with accidental intra-arterial injection leading to complications in the form of skin necrosis, vision loss and cerebral vascular accident [5].

Use of HDPH successfully in the case of cutaneous complications has proven beyond a doubt that high doses of hyaluronidase can restore microcirculation in the areas Fig. 5 Post-filler vision loss, Day 6—fundus examination, after four doses each of 1500 units of Intracutaneous Hyaluronidase and two doses each of 900 units of retrobulbar hyaluronidase showing good retinal circulation with some oedema over optic nerve head and macular region





**Fig. 6** Post-filler vision loss, Day 7—after five doses each of 1500 units of intracutaneous hyaluronidase and two doses each of 900 units of retrobulbar hyaluronidase. Ischaemic changes in the skin started resolving in the form of improvement in discolouration. Periorbital swelling, along with conjunctival congestion and chemosis improving



Fig. 8 Post-filler vision loss, Day 9—further healing in the ischaemic zone with scabs over superficial skin necrosis areas. Patient able to open eye partially





Fig. 7 Post-filler vision loss, Day 8—healing started in the ischaemic zone. Islands of healed skin visible, scabs started appearing in the areas of superficial skin necrosis

affected by HA filler emboli [6–8], and the same principle has a theoretical potential to help in restoring retinal microcirculation after it gets clogged with HA emboli.

Fig. 9 Post-filler vision loss, Day 11—more healing in the ischaemic zone with scabs started falling off. Patient able to open the right eye more than before

During the cutaneous involvement caused by intra-arterial filler injection, the Livedo pattern usually shows the boundary of ischaemic skin from the surrounding healthy

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**Fig. 10** Post-filler vision loss, Day 12—healing in the ischaemic area nearly complete with only a few scabs and scars. The patient could move her right upper eyelid with about 90% right palpebral aperture seen now



Fig. 11 Post-filler vision loss, Day 14—more healing in the ischaemic area with some scarring. Patient able to open right eye almost fully

skin due to the involvement of microcirculation. In a study, the average particle size of HA filler (Restylane) was found to be 189  $\mu$ m [9]. The cross-linked HA fillers have particle sizes that match arteriole sizes in the subdermal plexus (100–400  $\mu$ m) [10], as well as in the retinal arteriolar diameter (141.6 6 ± 18.6  $\mu$ m) [11]. In the retina also, the microcirculation clogging with HA particles leads to perfusion failure and vision loss.

The commercial preparations of the injectable form of hyaluronidase are classified according to their origin. Although those of bovine origin (i.e. Wydase<sup>®</sup>, Wyeth Ayerst Pharmaceuticals) are no longer available due to their high immunogenicity, the ovine variant (i.e. Vitrase<sup>®</sup>, ISTA Pharmaceuticals) is currently available. The human recombinant hyaluronidase (i.e. Hylenex<sup>®</sup>, Halozyme Therapeutics), derived from hamsters' ovary cells is another variant [12].

It is pertinent that hyaluronidase is delivered to the place where the obstruction is thought to be present. If the filler travels to a distant location from the site of injection, it seems reasonable to inject the area where ischaemic changes are manifesting [13]. The end arterial circulation of the affected skin is available for direct treatment with hyaluronidase by flooding the affected area and unplugging the end arteries. The central retinal artery, being the end artery in case of vision loss, is not accessible to the direct treatment due to its deep location. Retrobulbar injection provides a suitable route to deliver hyaluronidase in this deep location [3]. This can be performed by the injecting physician, in an emergency, using a 25G, 1.5-inch-long needle from the inferotemporal quadrant of the orbit [3]. Detailed knowledge of retrobulbar injection is essential for performing this procedure and the assistance of an ophthalmologist colleague, if available, can be of great help.

However, there has not been much evidence of the use of hyaluronidase in reversing visual changes, in case of accidental embolization of ophthalmic circulation. To date, a very limited number of cases of reversal of vision loss, caused by HA fillers, have been reported. In one such report, authors could reverse subjective vision loss during filler injection by injecting widely in the subcutaneous plane in the brow and forehead area. Besides, two doses of 300 IU of hyaluronidase were given in the area around the supraorbital and supratrochlear notch [14].

In another case of post-filler temporary vision loss, the patient had subjective total vision loss with eye pain along with headache, dizziness and subjective weakness of one side of the body. She was injected with two doses of 150 IU in the supraorbital and infraorbital foramen region intracutaneously and seeing no response, was injected with three doses of 150 IU hyaluronidase in retrobulbar area, successively in a few minutes. The patient showed complete recovery immediately [15].

Recently, another case has been reported with visual loss in the lower half of the right eye and ophthalmoplegia after filler injection. The patient was treated with a single dose of 60 IU of intracutaneous injection in the nasal skin after 12 h of filler injection. There was a complete recovery of vision and ophthalmoplegia at three months [16].

In our case, all the changes in skin were documented regularly to show the progression of cutaneous ischaemic signs and the role of HDPH in improving the skin ischaemia. Once the skin ischaemia was corrected with HDPH, there was spontaneous healing of the skin involved over the next two weeks. The change in the visual loss was also documented with supporting ophthalmic examination, vision chart and fundoscopy. In this case, not only was

#### a Central 24-2 Threshold Test



Fig. 12 a Post-filler vision loss, Day 21—visual field index of the right eye is 66% with progressive improvement in the vision. b Post-filler vision loss, Day 21—normal visual field index of the left eye

there a reversal of vision loss, but the extensive skin ischaemia also recovered with minimal skin necrosis followed by minimal scarring. The residual scarring was very little compared to what would have happened if hyaluronidase was not injected in the affected area. The fundoscopy, in this case, has also established the role of hyaluronidase in re-establishing the circulation in retinal circulation as its role has not been established previously in improving circulation [17].

The proposed mechanism of recovery in this case due to retrobulbar injection of large doses of hyaluronidase could be that it leads to HA emboli being dissolved due to its enzymatic action [18]. The immediate improvement in pain in the eye after the second retrobulbar injection in both cases also points to this direction. The large bolus dose of hyaluronidase could dissolve a large amount of HA filler, thus reducing the pressure in the eye and hence reducing pain caused by the pressure effect of filler.

### Conclusion

It is crucial for injectors to be aware of the management of the potentially disastrous and life-altering complications of vision loss with or without skin ischaemia, after accidental intravascular injection from cosmetic filler procedures. We have reported a case of near complete recovery of postfiller vision loss and cutaneous ischaemia with only minimal skin scarring. Use of high doses of hyaluronidase could help in managing post-filler vision loss and impending skin necrosis, thus promising successful visual and cutaneous outcomes in the future.



Fig. 12 continued



Fig. 13 Post-filler vision loss, Day 21—normal movement of the right upper eyelid with nearly 70% recovery of the vision in the right eye. The ischaemic skin zone has recovered very well without any skin necrosis and showing some scars at multiple areas



Fig. 14 Post-filler vision loss, three months—full recovery of vision in the right eye with complete healing of cutaneous component with minimal scarring

#### **Compliance with Ethical Standards**

**Conflict of interest** The authors declare that they have no conflicts of interest to disclose.

Human and Animal Rights This article does not contain any studies with human participants or animals performed by any of the authors.

**Informed Consent** Informed consent of the patient was taken for this case report.

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