

Pretreatment with systemic corticosteroid can mask early symptoms of hypersensitivity reaction to hyaluronidase following peribulbar block

Ashok Gupta,¹ Bruttendu Moharana,² Reeti Saini,¹ Arjun Gupta¹

¹Department of Ophthalmology, Drishti Eye Hospital, Panchkula, Haryana, India
²Department of Ophthalmology, All India Institute of Medical Science - Bhopal, Bhopal, Madhya Pradesh, India

Correspondence to
Dr Bruttendu Moharana;
dmoharana@gmail.com

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SUMMARY

Hyaluronidase is a hydrolytic enzyme that helps in breaking down hyaluronic acid, a component of the extracellular tissue matrix, thereby facilitating the dispersion of local anaesthetic drugs through tissue planes. It is a key component in peribulbar anaesthesia for ocular surgeries. Allergic response to hyaluronidase is relatively rare but a potentially vision-threatening complication. A preoperative intradermal hypersensitivity test is useful to detect such cases and avoid potential complications. Here we report a case of hypersensitivity reaction to hyaluronidase after peribulbar anaesthesia for cataract surgery where an intradermal hypersensitivity test was falsely negative, and presentation was delayed due to the use of preoperative systemic corticosteroids. However, correct, and timely diagnosis and treatment saved the eye from permanent vision loss.

BACKGROUND

Hyaluronidase is a bovine-derived hydrolytic enzyme that helps in breaking down hyaluronic acid, a component of the extracellular tissue matrix. This helps in a faster onset of action of local anaesthesia by facilitating its dispersion.¹ Allergic response to hyaluronidase has been reported earlier a few times. A preoperative intradermal hypersensitivity test is useful to detect such cases and avoid potential complications. Here we report a case of hypersensitivity reaction to hyaluronidase after peribulbar anaesthesia for cataract surgery where an intradermal hypersensitivity test was falsely negative, and presentation was delayed likely due to the use of preoperative systemic corticosteroids.

CASE REPORT

A 64-year-old male was presented for cataract surgery on the right eye. The corrected distance visual acuity (CDVA) was 20/60 on the right eye and NLP (no light perception) on the left eye, intraocular pressure (IOP) was 15 and 13 mm Hg on the right and left eye, respectively. The right eye had cataract (nuclear opalescence grade III) and the left eye was pseudophakic. The right eye fundus was normal. Optic atrophy was present in the left eye. There was a history of left phacoemulsification with intraocular lens (IOL) implantation under peribulbar anaesthesia (PBA) 3 years ago elsewhere. The previous clinical record showed the diagnosis of postoperative orbital cellulitis on the left eye which was managed with systemic antibiotics and antifungal drugs only. The patient was hypertensive

but non-diabetic. He had a history of chronic obstructive pulmonary disease (COPD).

We administered intravenous dexamethasone and etophylline + theophylline preoperatively to ease the symptoms of COPD. We routinely check for an allergic response to the components of PBA via intradermal injection which was negative for this patient. Skin preparation for cataract surgery was done with povidone-iodine solution (5%) on the right side. Peribulbar block containing 3.5 mL lignocaine 2%+epinephrine (1:200 000), 1.5 mL bupivacaine 0.5% and hyaluronidase 35 IU/mL (Hyaluronidase IP, Ovine, Hynidase, Shreya Life Sciences, Mumbai, India) was injected with a 26G needle at the junction of middle and lateral one-third of inferior orbital margin. He underwent uneventful phacoemulsification and IOL implantation on the right eye. On the postoperative day 1, CDVA was 20/20, IOP 16 mm Hg with unremarkable clinical findings. However, on postoperative day 2, the patient presented a blurring of vision, adnexal swelling, congestion and pain (figure 1A). On examination, the right eye's CDVA was 20/120, IOP was 46 mm Hg with epithelial oedema, lid swelling, conjunctival chemosis, moderate proptosis and restriction of extraocular movements (EOM) in all directions. The fundus examination showed media grade II due to corneal epithelial oedema, normal optic disc and macula. The patient was afebrile and without any systemic complaints. Intravenous mannitol (1 mg/kg, 20%) was administered immediately to lower IOP.

INVESTIGATIONS

We fast-tracked all the investigations. A blood sample was sent for haematological workup. The report obtained later was non-significant for any infectious aetiology. When we re-examined the intradermal sensitivity site on the forearm, we noted induration and erythema of approximately 15 mm in diameter (figure 1B). We repeated the intradermal sensitivity test for all components of PBA. The drugs were freshly diluted with normal saline. The dilutions used for different drugs were 2% lignocaine (1 mL/100 mL), 0.5% bupivacaine (1 mL/100 mL) and hyaluronidase 750 IU/100 mL.² The site of injection of hyaluronidase showed wheal and flare within a minute time establishing type I allergic response (figure 1C). The sites injected with lignocaine and bupivacaine showed no reaction. MRI orbit was done urgently which showed diffuse oedema and thickening of periorbital soft tissue,



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Case report

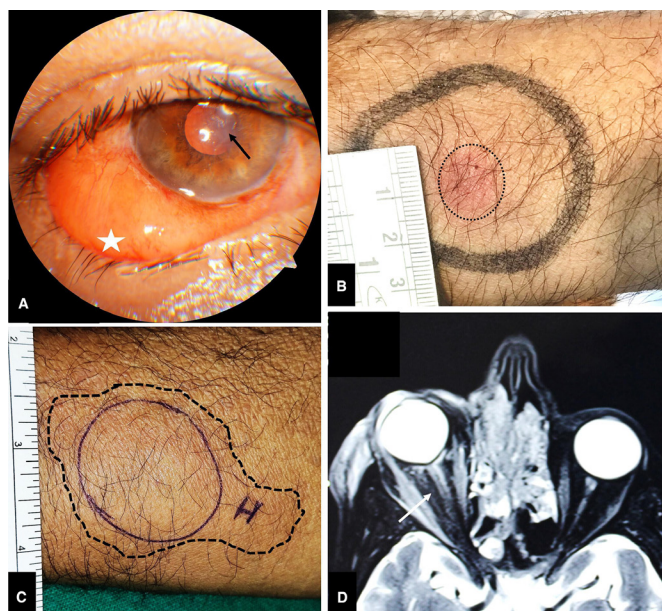


Figure 1 Clinical photograph of the patient 48 hours after cataract surgery with peribulbar anaesthesia showed conjunctival chemosis (white star) and corneal epithelial oedema (black arrow) (A). The site of the intradermal sensitivity test of the local anaesthetic drugs showed an induration of approximately 15 mm (black dashed circle) (B). The site of intradermal injection of hyaluronidase showed an induration of about 40×20 mm within minutes (dashed line) (C). The MRI orbit showed proptosis and orbital fat stranding (white arrow) suggestive of inflammation in orbital soft tissue (D).

intraconal and extraconal fat stranding, moderate proptosis on the right side (figure 1D).

DIFFERENTIAL DIAGNOSIS

Diagnosing hypersensitivity reaction to hyaluronidase correctly is of paramount importance. Apart from this condition, the differential diagnoses for postoperative pain, raised IOP, adnexal swelling, proptosis, ocular movement restriction includes retrobulbar haemorrhage (RBH) and infective orbital cellulitis.³ Orbital imaging (CT scan, MRI scan) aids in reaching the final diagnosis correctly.

RBH which usually occurs immediately after administration of retrobulbar injection and causes severe pain, tense proptosis, and subconjunctival haemorrhage was unlikely in our case. Sometimes contact allergy to topical eye drops mimics similar symptoms, but without any orbital signs.¹ The two most likely pathologies in our case were infective orbital cellulitis and hyaluronidase hypersensitivity. It is imperative to rule out possible infective aetiology as treatment with systemic steroids without proper antibiotic coverage may lead to cavernous sinus involvement.³ From the intradermal skin test, the diagnosis of hyaluronidase hypersensitivity was certain. This diagnosis was supported by the absence of constitutional symptoms and systemic and ocular risk factors for postoperative infection.

TREATMENT

The patient was treated with systemic corticosteroid (prednisolone 0.5 mg/kg), IOP lowering drugs (oral acetazolamide, brimonidine and timolol topical drugs) with antibiotic cover (amoxicillin+potassium clavulanate 625 mg three times per day and metronidazole 500 mg three times per day).

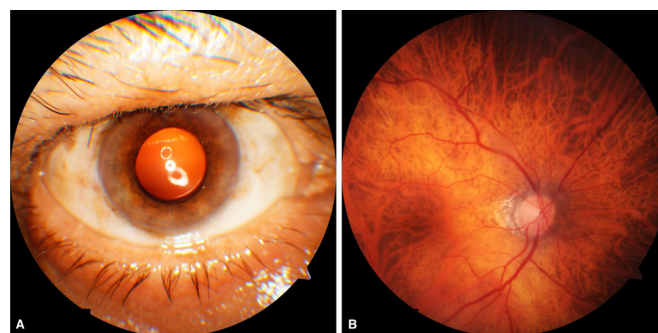


Figure 2 The conjunctival chemosis had completely resolved by the 10th day of treatment (A). The fundus photograph showed clear media with a normal optic disc (B).

OUTCOME AND FOLLOW-UP

By the third day after treatment, symptoms improved significantly. CDVA improved to 20/40 and IOP was reduced to 16 mm Hg. The oral prednisolone dose was tapered. Antibiotics were advised for 5 days. By the 10th day after treatment, conjunctival chemosis and proptosis subsided completely. The right eye's CDVA improved to 20/20 with IOP of 14 mm Hg and fundus was normal (figure 2A,B). Antiglaucoma drugs were withdrawn sequentially. The sequence of the event is highlighted in figure 3.

DISCUSSION

Hyaluronidase is a mucopolysaccharidase that degrades glycosaminoglycans found in the intercellular matrix. The addition of this drug facilitates the spread of local anaesthetic agents used in ophthalmological surgeries.¹ This helps in hastening the onset of action of anaesthetic drugs, use of a lesser volume of drugs, low incidence of IOP rise, less surgical site distortion and myotoxicity.⁴ Animal-derived hyaluronidase (bovine and ovine) preparations can be associated with allergic reactions and toxicities. There have been few reports describing the allergic

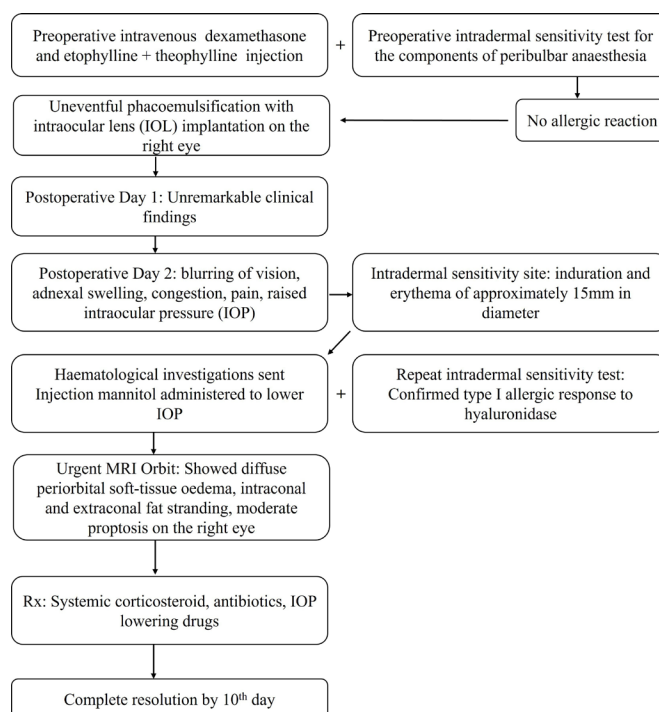


Figure 3 The sequence of symptoms, diagnosis and management.

reaction to hyaluronidase after retrobulbar or peribulbar anaesthesia.^{1–3 5–10} The incidence rate ranges from 1 in 2000 to 6 in 100 000.^{5–8} Ninety-eight cases of adverse events associated with the use of animal-derived hyaluronidase in ophthalmology settings had been reported to The United States Food and Drug Administration (US-FDA) between January 1998 and August 2011.⁴

Being an uncommon occurrence, hyaluronidase hypersensitivity can be misdiagnosed easily. There have been reports of misdiagnosis as infective orbital cellulitis where clinical improvement did not occur with antibiotic treatment alone.^{1 6 10} In our case, the patient had previously been misdiagnosed elsewhere as 'infective orbital cellulitis' in the contralateral eye (left eye). He received treatment with systemic antibiotics and antifungal drugs without any systemic steroids. The eye ultimately developed optic atrophy.

While operating on the other eye (right eye), we duly checked for sensitivity to hyaluronidase. But the administration of preoperative systemic corticosteroid confounded the fact that the patient was allergic to hyaluronidase by giving a false negative intradermal sensitivity test. To the best of our knowledge, there has been no report on masking of hyaluronidase allergy due to systemic corticosteroid. Irreversible optic nerve damage and the relative afferent pupillary defect can occur as early as 24 hours.³ We were able to diagnose the case correctly and timely. Early

treatment with systemic corticosteroid and IOP lowering drugs saved the eye from permanent vision loss.

Diagnosis of hyaluronidase hypersensitivity needs a high index of suspicion. Ophthalmologists should be extra cautious if the patient is receiving systemic corticosteroid for any comorbidity as it may mask the intradermal sensitivity test and early symptoms of the allergic reaction. Early exclusion of infective cause and timely treatment with systemic steroid and IOP management can prevent permanent damage to the optic nerve and loss of vision.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

Patient's perspective

I was afraid of the outcome when problems similar to the previous surgery happened. I am happy that timely action by the doctors saved my vision.

Learning points

- Keep a high index of suspicion for hyaluronidase hypersensitivity if pain, adnexal swelling, proptosis, ocular movement restriction occurs after injection of local anaesthesia.
- Rule out infective aetiology, treat early with systemic steroids and watch out for raised intraocular pressure (IOP).
- Allergic reactions can be masked by systemic corticosteroids. Be watchful of patients' comorbidities and their treatments.

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