

Allergic reaction to hyaluronidase after retrobulbar anaesthesia: a case series and review

L. Delaere · T. Zeyen · B. Foets · J. Van Calster ·
I. Stalmans

Received: 27 January 2008 / Accepted: 11 July 2008
© Springer Science+Business Media B.V. 2008

Abstract *Background* The enzyme hyaluronidase (HA) is an adjunctive in retrobulbar anaesthesia (RA) that is used during ophthalmic surgery to improve the efficacy and speed of nerve blocks. Although uncommon, HA has been shown to be a potential cause of allergic responses. *Case reports* We describe three patients who experienced an allergic reaction to HA following ocular surgery in our department and provide an extensive overview of the literature on HA in RA. *Conclusions* Although rare and mostly benign, allergy to HA should be included in the differential diagnosis when chemosis, proptosis and restriction of eye movements occur after parabulbar or retrobulbar anaesthesia. The authors feel that the beneficial effect of HA in small volumes of RA warrants its use despite this potential complication.

Keywords Allergy · Hyaluronidase ·
Retrobulbar anaesthesia

Abbreviations

HA Hyaluronidase
RA Retrobulbar anaesthesia

Introduction

The enzyme hyaluronidase (HA) is an adjunctive agent in retrobulbar anaesthesia (RA) that is used during ophthalmic surgery to improve the efficacy and speed of nerve blocks [1, 2]. Hyaluronidase is a mucopolysaccharidase that breaks down hyaluronic acid, a key component of connective tissue, thereby facilitating the distribution of anaesthetic drugs (lidocaine and bupivacaine) [3]. Although uncommon, HA has been shown to be a potential cause of allergic responses.

Case reports

We describe three patients who experienced an allergic reaction to HA following ocular surgery in our department as well as one patient with a severe allergic reaction to topical postoperative medication, which may mimic the former. Several other cases of an allergic reaction after RA have been reported by different surgeons in our department, but these were not thoroughly documented and therefore are not described in this case series. In our institution, RA contains 2.5 cc³ lidocaine 2%, 2.5 cc³ bupivacaine 0.25% with 0.5% (1:200,000) adrenalin and 150 IU hyaluronidase (1 mg Hyason, Organon, the Netherlands). For glaucoma surgery, marcaine without adrenaline is used to prevent vasoconstriction around the optic nerve.

L. Delaere · T. Zeyen · B. Foets · J. Van Calster ·
I. Stalmans (✉)
Department of Ophthalmology, University Hospitals
Leuven, Campus St Raphaël, Kapucijnenvoer 33, 3000
Leuven, Belgium
e-mail: ingeborg.stalmans@uzleuven.be

Case 1

An 84-year-old woman with a history of uneventful trabeculectomy under RA on her left eye received a second RA for the same procedure on the right eye. The patient presented 1 day postoperatively with periorbital redness and oedema, proptosis, conjunctival chemosis and a restriction of ocular movements in all directions on the operated eye. The pupil was reactive to light. There was no purulent discharge from the eye. The patient was afebrile. The leucocyte count, erythrocyte sedimentation and C-reactive protein were normal, and the blood cultures were negative. A computed tomography (CT) scan showed proptosis of the right eye, increased density of the orbital fat and enlargement of all extraocular muscles. An air bubble was present in the orbit between the inferior and medial rectal muscle (Fig. 1). The picture was interpreted as a periorbital and orbital cellulitis of the right eye, the differential diagnosis being an infection or an aseptic inflammation. After treatment with intravenous amoxicillin and clavulanic acid (Augmentin 500 mg three times daily) for 24 h, there was no clinical improvement. Allergy to one of the components was suspected, and systemic steroids (Medrol 60 mg/day) were administered. One day later, all clinical parameters substantially improved.



Fig. 1 Computed tomography scan of the orbit. Proptosis of the right eye, increased density of the orbital fat and enlargement of all extraocular muscles

Case 2

A 74-year-old woman who had been previously exposed to HA in a RA during a trabeculectomy of the left eye 1 year earlier underwent the same intervention on the right eye. The patient presented with symptoms of orbital inflammation 1 day after the intervention, which gradually worsened. At the onset of the symptoms, she was thought to be allergic to the postoperative eyedrops tobramycin and dexamethasone (Tobradex) and, consequently, these were replaced by preservative-free ofloxacin (Trafloxal edo) and dexamethasone (Dexamethasonemonofree). The next day she showed severely swollen eyelids (Fig. 2), extensive chemosis, and restricted eye movements. She had no fever. The best corrected visual acuity decreased from 6/10 the first day postoperatively to 25/100 the second day. Treatment with a high dose of intravenous amoxicillin and clavulanic acid (Augmentin) 1000 mg twice daily (bid) and methylprednisolone (Medrol) 64 mg once daily (qd) was started. Twelve hours later, the swelling had diminished, and the visual acuity had recovered to 6/10.

Case 3

Case 3 was a 48-year-old male, and dates from 1988. At this time, RA contained Thiomucase (50 IU/ml HA; Exel Farma, Belgium). The patient's past ophthalmologic history included an extracapsular-lens extraction

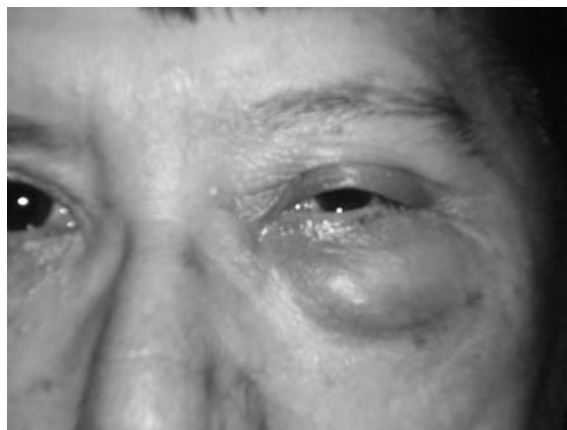


Fig. 2 Periorbital swelling 12 h after treatment with Medrol was started



Fig. 3 Swollen eyelids on the operated eye

under general anaesthesia on the left eye, followed by a removal of the opacified posterior capsule under RA. He received a second RA for an extracapsular lens extraction on the right eye. The following day, he complained of itching on the neck and in the throat. The eyelids of the right eye were manifestly swollen and red. No enlarged adenopathies were found upon palpation of the neck region. The next day, the oedema had extended to the cheek. An antihistamine (Fenistil retard) was given orally. Because swallowing difficulties arose, the patient received an injection of corticosteroids. The following day, the swelling had decreased. At this stage the causative allergen was still unknown, and the postoperative eyedrops containing prednisolone (Predmycine P) were replaced by dexamethasone and chloramphenicol (DeIcol). An intradermal allergy test, however, revealed a reactivity to HA.

Case 4 (differential diagnosis: allergic reaction to topical medication)

A 48-year-old woman underwent a vitrectomy under general anaesthesia because of retinal detachment in the right eye. Two days after the operation, she had pain around the right eye. There was manifest oedema, erythema of the eyelids and chemosis (Fig. 3). The eye motility was only slightly restricted and painful. Antibiotics (6 g) administered intravenously were started together with Medrol (64 mg qd). A CT scan showed a preseptal cellulitis (Fig. 4). One day later, the symptoms had subsided.



Fig. 4 Computed tomography orbital

Discussion

An allergic reaction to HA is a rare but recognized complication of RA. The true incidence is estimated to be around $1/2000$ [4–6], but it is hard to determine the actual incidence because mild allergic reactions to HA may have been mistaken for allergic reactions to topical postoperative medications. Moreover, the condition presumably often remains unrecognized because of the spontaneous recovery of the patient.

Table 1 presents a review of previously described cases of postoperative allergic reactions to parabulbar or retrobulbar anaesthesia. Kempeneers et al. [4] was the first author to describe this phenomenon in five patients and to prove the immunoallergic aetiology of the reaction to HA.

Most of the patients with an allergic reaction to HA reported to date had one previous uneventful RA containing HA, implying that sensitization had taken place [7, 8]. The most common prior exposure to HA was a RA for the same treatment on the contralateral eye. However, as a reaction at first administration is also possible, different mechanisms for hypersensitivity reactions have been suggested [4]. The onset of the allergic response is also reportedly variable: immediate (intraoperative), early (within a few hours), intermediate (within a few days) or late (within weeks) [8]. These findings suggest that both type I and type IV hypersensitivity are likely to contribute to this

response [4, 9, 10]. Periorbital oedema within minutes of administration of the drug usually represents a type I immediate immunoglobulin (Ig)E-mediated response to HA. These patients had no known prior exposure to HA [9, 10]. In most cases, however, as in our case series, the onset of symptoms was delayed for over 24 h. This delayed onset is suggestive of a type IV delayed hypersensitivity, which is not an antibody-mediated response, but a T-cell-mediated allergic reaction [4].

The most common symptoms include periorbital oedema and erythema, conjunctival chemosis, itch or pain, proptosis and extraocular muscle motility restriction (ranging from mild restriction to total ophthalmoplegia). In all cases, the cornea and the anterior chamber are clear, and the fundus is normal. There is the occasional loss of vision because of compression of the optic nerve or elevation of intraocular pressure due to increased venous pressure [4, 11]. Patients with non-immediate reactions are generally not febrile and are in a good systemic condition, while those with an immediate reaction without previous RA and, thus, type I hypersensitivity, do show general symptoms (see Table 1). Quincke's oedema (as in our third patient) is a rare presentation characterized by itching in the area of the neck and throat and swallowing difficulties. Generalized anaphylactic reactions to HA have not been seen after RA but are described resulting from other routes of administration [12, 13].

For the diagnosis, blood analysis, including a white blood cell count, may be useful to make the differential diagnosis with an infection. Computed tomography scan imaging can be used for differential diagnoses of orbital inflammation. A CT scan in a patient with an allergic reaction shows proptosis and swelling of the periorbital soft tissue, including infiltration and haziness of the orbital fat and enlargement of the extra-ocular muscles. Skin allergy testing is the most specific way to make the diagnosis of a HA hypersensitivity reaction [4]. Intradermal and skin prick testing are common methods used for determining the drug responsible for the allergic reaction [8, 11]. The negative prick test of our second patient excludes an immediate IgE-mediated hypersensitivity, which is consistent with the late onset of clinical features. Confirmation of a delayed cell-mediated immunoallergic reaction can be made by lymphocytic transformation tests [4]. An intradermal

skin test can be done when the skin prick test results are unclear. Patch and scratch tests remain negative in this case [9, 11].

Allergy to HA should be included in the differential diagnosis when angio-oedema, proptosis and restriction of eye movements occur after parabolbar or retrobulbar anaesthesia. When these typical symptoms occur, it is important to exclude other more dangerous causes, which require immediate therapy. When early intraoperative proptosis and pain occurs, a retrobulbar haemorrhage must be suspected. Later postoperative proptosis, erythema and pain may represent orbital cellulitis. Previous HA exposure, the absence of fever and infectious parameters (normal white cell count) and negative tissue cultures suggest the likelihood of an allergic reaction rather than an infection. A poor response to antibiotics, a quick response to steroids and, in particular, positive skin allergy tests confirm this diagnosis. Although general sensitization has taken place, HA allergy should also be considered in individuals with no known prior exposure when early (perioperative) periorbital swelling occurs.

Another differential diagnosis is contact allergy to topical eyedrops. Our fourth case is just such an example. The most important difference between this and HA allergy is the absence of orbital involvement in a reaction to topical medication, clinically shown as normal eye movements. Patch tests are the skin tests of choice to confirm contact dermatitis.

Broad spectrum antibiotics are most commonly started at the onset of symptoms to cover for a possible infective focus. Treatment with steroids results in resolution of the signs and symptoms within a few days. Significant clinical improvement can also be seen with systemic antihistamines, thereby avoiding the side effects of high doses of corticoids; however, recovery takes somewhat longer with antihistamines than with steroids. Without treatment, the reaction will eventually disappear spontaneously, but the symptoms are likely to worsen over the first days and recovery takes longer. Especially in the presence of compromised optic nerve function, the administration of systemic steroids should be considered at an early stage because this may prevent permanent functional loss.

Although other surgeons in our ophthalmology department have also observed cases of allergic reactive to HA, this condition was more frequently

Table 1 Review of previously described cases of postoperative allergic reactions to hyaluronidase

Study	Age (years)/ gender	Previous RA ^a	Time to onset of symptoms	Special symptoms	DVA	Treatment ^a	Time to recovery after treatment ^a	Skin allergy testing	
								Patch test	Skin tests HA/ other
Leibovitch et al. [11]	75/F	Yes	12 h		/	po AB + CS		–	+/-
	87/F	Yes	24 h		/	po AB + CS		–	+/-
	70/M	No	24 h		/	po AB, later CS	3 days	–	+/-
	85/F	Yes	48 h		/	po AB	2 days	–	+/-
	75/F	Yes	72 h		/	iv AB + antihistamines	5 days	–	+/-
Musa et al. [9]	50/F	Yes	36 h	IOP rise 55 mmHg	yes	Iv CS po mannitol + acetazolamide	2 days	–	+/-
	71/M	No	Immediate	Generalized rash	NA	Stop surgery iv CS, antihistamines	6 h	–	
Quhill et al. [5]	70/F	Yes	5 days		Yes	iv AB 24 h*, later high dose systemic CS	1 day; fully: 4 weeks		+/NA
Eberhart et al. [6]	NA	Unknown	1 day		/(1*)				+/-
	NA	Unknown	1 day		/(1*)				
	NA	Yes	1 day		/(1*)				
Youssef et al. [7]	72/F	Yes	1 day		6/9	po antihistamines iv AB, later im chlorpheniramine maleate	1 day		+/NA
Nicholson et al. [26]	41/F	No	5 min peroperative	Swelling contralateral	No	iv chlorpheniramine + CS	20 min		NA
Ahluwalie et al. [8]	77/F	Yes	28 h	After 4 h: nausea, vomiting After 1 day: left RAPD	HM	iv AB later chlorpheniramine + AB			+/-
Varma et al. [27]	79/F	Yes	2 days		Yes	iv AB	24 h; fully: 1 weeks		
Kirby et al. [10]	67/F	Yes (2*)	Few min peroperative	Hypertension, sweating, nausea, incontinence		Supportive therapy	Few hours	–	+/-
Minning et al. [28]	7/F	Yes	30 min postoperative	IOP rise	NA	Antihistamines	NA		+

Table 1 continued

Study	Age (years)/ gender	Previous RA ^a	Time to onset of symptoms	Special symptoms	DVA	Treatment ^a	Time to recovery after treatment ^a	Skin allergy testing	
								Patch test	Skin tests HA/ other
Kempeneers et al. [4]	73/F	Yes	12 h	34 mmHg	LP	iv AB acetazolamide, timolol, later lateral canthotomy high dose iv CS	24 h; IVA: 3 weeks (3*)		+/-
	62/F		Few weeks			High dose CS + AB	48 h; fully: 4 weeks		+/-
	57/M	Yes (2*)	"Postoperative"			iv CS			
		Yes (2*)	Few hours	Hemifacial swelling		Immediate high dose iv CS + AB	24 h; fully: 1 week		+/-
Taylor et al. [29]	63/M	Yes	1 day			iv AB + CS	48 h; fully: 5 days		+/-
	54/F	Yes	2 days			None	8 weeks		+/-
	54/F	NA	Immediate peroperative	Oedema extending to the contralateral eye		Antihistamines	'Rapidly'		+
	Present study								
Patient 1	84/F	Yes	1 day	Nausea, vomiting	No	iv AB, later + CS	2 days		NA
Patient 2	74/F	Yes	1 day	Nausea, vomiting	Yes	Collyria without preservatives iv AB + CS	2 days		-
Patient 3	31/M	Yes	1 day	Itch neck and throat. Swallowing difficulties		iv shot CS. Topical CS + AB instead of CS	1 day	-	+/-

F, Female; M, male; DVA, decrease in visual acuity; IVA, increase in visual acuity; po, per oral; iv, intravenous; AB, antibiotics; CS, corticosteroids; IOP, intraocular pressure; NA, not available; im, intramuscular; RAPD, relative afferent pupil defect; HM, hand movements; LP, light perception; ID, intradermal testing; HA, hyaluronidase; other, the other components of RA (xylocaine, marcaine, adrenaline)

^a 1*. Spontaneous recovery, small amount of hyaluronidase used: 0.25 cc³ 150 U/cc³; 2*, with the same symptoms but less pronounced; 3*, the disc remained somewhat pale and a concentric constriction of the field of vision was documented

reported by the glaucoma surgeons than within the other subdisciplines. The authors propose the following hypothetical explanation. The glaucoma surgeons in our department are the only ones to use RA without adrenaline (to avoid vasoconstriction around the optic nerve). Adrenaline may attenuate the symptoms of an allergic reaction. Therefore, an allergic reaction to HA may have been masked or mistaken for an allergic reaction to topical drugs in patients that received RA containing adrenaline. Of note, one should realize that adrenaline itself could also cause an allergic reaction.

In view of this mostly benign, yet uncomfortable and sporadically sight-threatening complication of RA with HA, one may wish to (re)consider the utility of adding HA to RA. Conflicting results have been reported on the advantage of HA addition to local anaesthetics. Although there are some reports of HA as an adjunctive in RA for ophthalmic surgery improving the efficacy and speed of nerve blocks [14–20], other authors do not report any beneficial effect of adjunctive HA [21–23]. Interestingly, Schulenburg et al. [24] concluded that HA reduces the volumes needed for local anaesthesia. In addition, careful review of the literature revealed that HA has added value in terms of efficacy and speed of the anaesthesia and avoids a significant increase in intra-ocular pressure when small volumes (5–8 ml) are used [14–20]. No beneficial effect of HA has been observed to date when larger volumes are used (8–10 ml) [21–23]. Of note, these larger volumes induced a marked rise in intra-ocular pressure, which is unfavourable for the optic nerve, particularly in glaucoma patients. Moreover, peroperative hypertony also increases the risk of complications during any intra-ocular surgery.

When all of these considerations are taken into account, the authors suggest that the use of HA indeed retains its added value despite the potential allergic reaction and that small volumes of RA are mandatory.

Conclusion

In summary, although rare and mostly benign, an allergic reaction to retrobulbar HA can occur. Therefore, HA in RA should be used with vigilance for the symptoms of this condition to allow rapid treatment and avoidance of permanent visual loss in

severe cases. However, the authors do suggest that the beneficial effect of HA in small volumes of RA warrants its use despite this potential complication.

Acknowledgements The authors thank Prof. Dr. Jan Ceuppens for his clinical expertise and Prof. Dr. Ilse Mombaerts for critically reading the manuscript.

References

- Rowley SA, Hale JE, Finlay RD (2000) Sub-Tenon's local anaesthesia: the effect of hyaluronidase. *Br J Ophthalmol* 84:435–436
- Alwitry A, Chaudhary S, Gopee K, Butler TK, Holden R (2002) Effect of hyaluronidase on ocular motility in sub-Tenon's anesthesia: randomized controlled trial. *J Cataract Refract Surg* 28:1420–1423
- Afify AM, Stern M, Guntenhöner M, Stern R (1993) Purification and characterization of human serum hyaluronidase. *Arch Biochem Biophys* 305:434–441. doi: [10.1006/abbi.1993.1443](https://doi.org/10.1006/abbi.1993.1443)
- Kempeneers R, Dralands L, Ceuppens J (1992) Hyaluronidase induced orbital pseudotumor as a complication of retrobulbar anesthesia. *Bull Soc Belge Ophtalmol* 243: 159–166
- Quhill F, Bowling B, Packard RB (2004) Hyaluronidase allergy after peribulbar anesthesia with orbital inflammation. *J Cataract Refract Surg* 30:916–917. doi: [10.1016/j.jcrs.2003.08.024](https://doi.org/10.1016/j.jcrs.2003.08.024)
- Eberhart AH, Weiler CR, Erie JC (2004) Angioedema related to the use of hyaluronidase in cataract surgery. *Am J Ophthalmol* 138:142–143. doi: [10.1016/j.ajo.2004.02.035](https://doi.org/10.1016/j.ajo.2004.02.035)
- Youssef Z, Pennefather PM, Watts MT (2005) Orbital cellulitis vs allergic reaction to hyaluronidase as the cause of periorbital oedema. *Eye* 19(6):691–692 (author reply 692). doi: [10.1038/sj.eye.6701553](https://doi.org/10.1038/sj.eye.6701553)
- Ahluwalia HS, Lukaris A, Lane CM (2003) Delayed allergic reaction to hyaluronidase: a rare sequel to cataract surgery. *Eye* 17:263–266. doi: [10.1038/sj.eye.6700243](https://doi.org/10.1038/sj.eye.6700243)
- Musa F, Srinivasan S, King CM, Kamal A (2006) Raised intraocular pressure and orbital inflammation: a rare IgE-mediated allergic reaction to sub-Tenon's hyaluronidase. *J Cataract Refract Surg* 32:177–178. doi: [10.1016/j.jcrs.2005.11.024](https://doi.org/10.1016/j.jcrs.2005.11.024)
- Kirby B, Butt A, Morrison AM, Beck MH (2001) Type I allergic reaction to hyaluronidase during ophthalmic surgery. *Contact Dermatitis* 44:52. doi: [10.1034/j.1600-0536.2001.440107-19.x](https://doi.org/10.1034/j.1600-0536.2001.440107-19.x)
- Leibovitch I, Tamblyn D, Casson R, Selva D (2006) Allergic reaction to hyaluronidase: a rare cause of orbital inflammation after cataract surgery. *Graefes Arch Clin Exp Ophthalmol* 244:944–949. doi: [10.1007/s00417-005-0190-5](https://doi.org/10.1007/s00417-005-0190-5)
- Ebo DG, Goossens S, Opsomer F, Bridts CH, Stevens WJ (2005) Flow-assisted diagnosis of anaphylaxis to hyaluronidase. *Allergy* 60:1333–1334. doi: [10.1111/j.1398-9995.2005.00891.x](https://doi.org/10.1111/j.1398-9995.2005.00891.x)
- Szépfolusi Z, Nentwich I, Dobner M, Pillwein K, Urbanek R (1997) IgE-mediated allergic reaction to hyaluronidase

- in paediatric oncological patients. *Eur J Pediatr* 156:199–203. doi:[10.1007/s004310050582](https://doi.org/10.1007/s004310050582)
14. Kallio H, Paloheimo M, Maunuksela E (2000) Hyaluronidase as an adjuvant in bupivacaine–lidocaine mixture for retrobulbar/peribulbar block. *Anesth Analg* 91:934–937. doi:[10.1097/00000539-200010000-00031](https://doi.org/10.1097/00000539-200010000-00031)
 15. Guise P, Laurent S (1999) Sub-Tenon's block: the effect of hyaluronidase on speed of onset and block quality. *Anaesth Intensive Care* 27:179–181
 16. Sarvela J, Nikki P (1992) Hyaluronidase improves regional anaesthesia with etidocaine. *Can J Anaesth* 39:920–924
 17. Dempsey GA, Barret PJ, Kirby IJ (1997) Hyaluronidase and peribulbar block. *Br J Anaesth* 78:671–674
 18. Krohn J, Seland JH, Høvdig G, Bertelsen T, Aasved H, Haugen OH (1993) Retrobulbar anesthesia with and without hyaluronidase in extracapsular cataract surgery. A prospective, randomized, double-blind study. *Acta Ophthalmol (Copenh)* 71:791–795
 19. Sarvela J, Nikki P (1992) Hyaluronidase improves regional anaesthesia with etidocaine. *Can J Anaesth* 39:920–924
 20. Nicoll JMV, Treuren B, Arun Acharya P, Ahlen K, James M (1986) Retrobulbar anesthesia. The role of hyaluronidase. *Anesth Analg* 65:1324–1328. doi:[10.1213/00000539-198612000-00013](https://doi.org/10.1213/00000539-198612000-00013)
 21. Crawford M, Kerr W (1994) The effect of hyaluronidase on peribulbar block. *Anaesthesia* 49:907–908
 22. Prosser DP, Rodney GE, Mian T, Jones HM, Khan MY (1996) Re-evaluation of hyaluronidase in peribulbar anaesthesia. *Br J Ophthalmol* 80:827–830. doi:[10.1136/bjo.80.9.827](https://doi.org/10.1136/bjo.80.9.827)
 23. Bowman RJ, Newman DK, Richardson EC, Callear AB, Flanagan DW (1997) Is hyaluronidase helpful for peribulbar anaesthesia? *Eye* 11:385–388
 24. Schulenburg HE, Sri-Chandana C, Lyons G, Columb MO, McLure HA (2007) Hyaluronidase reduces local anaesthetic volumes for sub-Tenon's anaesthesia. *Br J Anaesth* 99:717–720. doi:[10.1093/bja/aem272](https://doi.org/10.1093/bja/aem272)
 25. Escolano F, Pares N, Gonzalez I, Castillo J, Valero A, Bartolome B (2005) Allergic reaction to hyaluronidase in cataract surgery. *Eur J Anaesthesiol* 22:729–730. doi:[10.1017/S0265021505251190](https://doi.org/10.1017/S0265021505251190)
 26. Nicholson G, Hall GM (2003) Allergic reaction to hyaluronidase after a peribulbar injection. *Anaesthesia* 58:814–815. doi:[10.1046/j.1365-2044.2003.03295_18.x](https://doi.org/10.1046/j.1365-2044.2003.03295_18.x)
 27. Varma D, Metcalfe TW (2003) Orbital cellulitis after peribulbar anaesthesia for cataract surgery. *Eye* 17:105–107. doi:[10.1038/sj.eye.6700238](https://doi.org/10.1038/sj.eye.6700238)
 28. Minning CA Jr (1994) Hyaluronidase allergy simulating expulsive choroidal hemorrhage. *Arch Ophthalmol* 112:585–586
 29. Taylor IS, Pollowitz JA (1984) A little known phenomenon: allergic reaction to hyaluronidase. *Ophthalmology* 91:1003