Hyaluronidase-Induced Orbital Compartment Syndrome Following Sub-Tenon's Anaesthesia: Review of Literature and a Case Report

Dr. Claire Lim[1], Mr. Matthew Stahl[2], Mr. Christopher Holmes[2], Professor Lyndon DaCruz[2]

Royal Free London NHS Foundation Trust[1], Moorfields Eye Hospital NHS Foundation Trust[2]

INTRODUCTION/ BACKGROUND

- Hyaluronidase is used as an optional adjunct in ophthalmic local anaesthesia (sub-Tenon's, peribulbar blocks) to enhance anaesthetic diffusion by breaking down connective tissue, leading to faster onset and improved akinesia[1,2].
- Generally safe but can rarely cause hypersensitivity reactions-local or systemic[3].
- Reactions range from mild swelling to severe orbital inflammation and, in rare cases, orbital compartment syndrome.
- Early recognition and management are crucial to prevent permanent vision loss.

AIM

- To review the literature on hyaluronidase-induced orbital inflammation.
- To present a rare case of orbital compartment syndrome caused by a severe hypersensitivity reaction following sub-Tenon's anaesthesia.

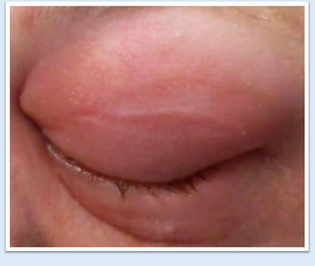


Fig 1: Day1 of presentation

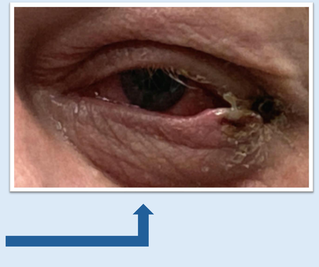


Fig 2: Day7 of presentation

References

1.Raichura, N. D., Alam, M. S., Jaichandran, V. V., Mistry, S., & Mukherjee, B. (2017). Hyaluronidase allergy mimicking orbital cellulitis. *Orbit*, *37*(2), 149–153. https://doi.org/10.1080/01676830.2017.1383465

2.Leibovitch, I., Tamblyn, D., Casson, R., & Selva, D. (2006). Allergic reaction to hyaluronidase: a rare cause of orbital inflammation after cataract surgery. *Graefe's Archive for Clinical and Experimental Ophthalmology*, *244*(8), 944–949. https://doi.org/10.1007/s00417-005-0190-5

3.L Delaere, Zeyen, T., Beatrijs Foets, J Van Calster, & Stalmans, I. (2008). Allergic reaction to hyaluronidase after retrobulbar anaesthesia: a case series and review. *International Ophthalmology*, *29*(6), 521–528. https://doi.org/10.1007/s10792-008-9258-7

4.Singh, A., Singh, K., Rana, J., Singh, U., Sharma, A., & Kumar, V. (2023). Vision-threatening reactions of hyaluronidase after local anesthesia: A case series and review of literature. *Indian Journal of Ophthalmology - Case Reports*, *3*(3), 888–891. https://doi.org/10.4103/jjo.jjo_2143_22

5.Minning, C. A. (1994). Hyaluronidase Allergy Simulating Expulsive Choroidal Hemorrhage. *Archives of Ophthalmology*, *112*(5), 585. https://doi.org/10.1001/archopht.1994.01090170029012

6.Ahluwalia, H. S., Lukaris, A., & Lane, C. M. (2003). Delayed allergic reaction to hyaluronidase: a rare sequel to cataract surgery. *Eye*, *17*(2), 263–266. https://doi.org/10.1038/sj.eye.6700243

CASE REPORT

Patient: 57-year-old female, post-op day 1 after uncomplicated left cataract surgery under sub-Tenon's anaesthesia (with hyaluronidase and lignocaine). Left only eye status.

Presentation: Nausea, worsening pain, left eye swelling. Afebrile

Examination findings:
- Severe periorbital swelling, chemosis, proptosis (Fig 1)
- Restricted ocular motility
- IOP: 50 mmHg
- No signs of endophthalmitis

Initial management:
- Systemic and topical IOP-lowering treatment
- Emergency lateral canthotomy and cantholysis
- IV antibiotics for presumed orbital cellulitis

History: Similar, milder episode of left periorbital inflammation in 2018 post-op

Imaging (CT orbit):
- Marked orbital soft tissue oedema
- Proptosis and fat stranding
- No abscess or sinus pathology

Investigations: Inflammatory markers mildly raised – WCC 14, CRP 6, ESR normal; Eye swab culture**:** no growth

Outcome:
- Admitted for monitoring and treated with topical steroids within 24hours
- Remained afebrile throughout
- At 1-week: resolution of pain, improved vision, normalised IOP and eye movements (Fig 2)
- Later underwent reconstruction post-canthotomy and cantholysis

Author (Year)	Patient Details/ Setting	Symptoms, Timing	Management	Outcome
Raichura et al. (2018)[1]	5 patients; Peribulbar	Periorbital swelling, chemosis; Immediate – Intermediate onset(Days)	1 required canthotomy + cantholysis, Systemic steroids, antihistamines	4 out of 5 full recovery, Allergy confirmed in all
Leibovitch et al. (2006)[2]	5 patients; Peribulbar	Periorbital oedema, proptosis, EOM restriction, pruritus; Early – Intermediate onset(12 -72hours)	Systemic steroids and antibiotics	Full recovery; Allergy confirmed in all
Delaere et al. (2008)[3]	3 patients; Retrobulbar	Periorbital swelling, proptosis, EOM restriction, chemosis; Early onset (within 24hours)	IV antibiotics, systemic steroids, antihistamine	Full recovery; Allergy confirmed in 1 out of 3, not carried out in other 2
Singh et al. (2023)[4]	3 patients; Peribulbar	Pain, periorbital oedema, proptosis, restricted EOM, skin blisters and necrosis; Immediate – Early onset (4hours)	Lateral canthotomy, Systemic steroids, IV antibiotics, antihistamine	Residual corneal anaesthesia in 1. Allergy testing not carried out
Minning (1994)[5]	1 patient; Retrobulbar	Periorbital oedema, pruritus, intraoperative increase in posterior pressure; Immediate onset	Antihistamine	Full recovery; Allergy confirmed
Ahluwalia et al. (2003)[6]	1 patient; Peribulbar	Periorbital swelling, reduced VA (HM), EOM restriction, proptosis; Intermediate onset (28hours)	IV antibiotics, antihistamine, topical steroids	No improvement in VA, developed RAPD; Allergy confirmed

Fig 3: Key Published Case Reports

DISCUSSION

Key literature findings:

- **Incidence and mechanisms:** Hypersensitivity to hyaluronidase is rare (~1 in 2,000 cases), involving immediate (Type I, IgE-mediated) and delayed (Type IV, T-cell mediated) reactions[1,3].
- **Risk factors:** Previous hyaluronidase exposure and allergies to bee or wasp venom due to cross-reactive enzymes[1].
- **Clinical manifestations**: Symptoms range from mild periorbital oedema to severe orbital inflammation with proptosis, chemosis, pain, restricted motility, and raised IOP. Onset can be immediate or delayed by days to weeks[1,3,4].
- **Diagnosis:** Based on clinical assessment, imaging (CT to exclude abscess or haemorrhage), and allergy testing (skin prick and intradermal tests) when indicated[1,3]. Differentiation from orbital cellulitis or retrobulbar haemorrhage is essential as management differs.
- **Treatment:** Systemic corticosteroids and antihistamines are standard. Urgent surgical decompression (canthotomy and cantholysis) is required in orbital compartment syndrome. Empirical antibiotics may be used until infection is excluded[1-3].

A hypersensitivity reaction to hyaluronidase is the most likely cause of orbital compartment syndrome in this case. Although a reaction to lignocaine or other perioperative factors cannot be entirely excluded, hyaluronidase was one of only two agents used in the sub-Tenon's anaesthetic, and the rapid symptom onset, coupled with a similar but milder reaction after a previous procedure, raises suspicion of a delayed-type hypersensitivity response. Infection is considered unlikely, given the absence of systemic signs, negative cultures, and lack of radiological evidence of abscess or sinus involvement.

Although rare, hypersensitivity reactions to hyaluronidase have been documented and can present with rapid orbital swelling, chemosis, pain, and raised intraocular pressure—features consistent with this case. Prompt recognition and management, including IOP-lowering medications, systemic steroids, and surgical decompression when indicated, are critical. Most reported cases in the literature recover well with timely treatment, although severe presentations, such as this one, may pose a threat to vision if not urgently addressed. Hyaluronidase use should be carefully considered in patients with risk factors such as previous sensitising reactions, multiple allergies, bee/wasp sting allergy, or only eye status.