

Can cryotherapy be used as an adjunct in select cases of recalcitrant endophthalmitis? - A case report

Shreyansh Doshi, Avinash Pathengay, Sharat Hegde, Bhavik Panchal

We report two cases of recalcitrant endophthalmitis, a delayed postoperative fungal endophthalmitis following cataract surgery and an atypical mycobacterial endogenous endophthalmitis associated with infective scleritis. Due to recalcitrant nature of the endophthalmitis, one or more sittings of double freeze and thaw cryotherapy was applied over and adjacent to the infective foci in each case. This cryotherapy was used as an adjunct alongside conventional endophthalmitis management following which resolution of infection was observed in both cases.

Key words: Cryotherapy, endophthalmitis, infective scleritis, linezolid

The visual outcome in cases of delayed fungal postoperative endophthalmitis and mycobacterial associated endogenous endophthalmitis is poor.^[1,2] Higher rates of enucleation/ evisceration or phthisis bulbi have been reported in such cases due to their recalcitrant nature.^[3,4]

In the current report, we present two patients with recalcitrant ocular infection due to fungus and atypical mycobacteria who were successfully managed using cryotherapy as an adjunct to the routine treatment modalities.

Case Reports

Case 1

A 62-year-old male with diabetes mellitus presented with blurring of vision, redness, and persistence of ocular inflammation 9 weeks following right eye cataract surgery. At presentation, his best corrected visual acuity (BCVA) in the right eye was 20/30 and left eye was 20/20. On evaluation of

the right eye, cells 1+, light brown feathery ball like exudate in the inferonasal quadrant of the anterior chamber with fluffy margins, a posterior chamber intraocular lens (IOL) with an intact posterior capsule [Fig. 1a], and normal fundus was noted. Left eye was unremarkable. A clinical diagnosis of right eye delayed postoperative endophthalmitis with a suspected fungal etiology was made.

The patient underwent an anterior chamber tap with removal of the feathery ball like exudate. Since the exudate involved the underlying iris and adjacent capsule, localized iridectomy and partial capsulectomy was performed in combination with intravitreal injections of amphotericin b (5 µg/0.1 ml) and voriconazole (100 µg/0.1 ml). Filamentous fungi belonging to genus *Cladophialophora* was identified in the aqueous sample [Fig. 2a and b - ×40 magnification, Fig. 2c - ×100 magnification].

The exudate started to reappear on the 4th postoperative day and increased in size even after two additional intravitreal injections of amphotericin b and voriconazole injected 4 days apart [Fig. 1b]. In view of persistence of anterior chamber exudates and the patient not consenting for IOL explantation, we repeated surgical debulking of the affected tissue with a fourth dose of intravitreal amphotericin b and voriconazole along with external cryotherapy application to the affected area [Fig. 1c]. A double freeze-thaw technique of external scleral cryotherapy was applied (1 mm from the limbus, covering one clock hour on either side of the affected uveal tissue to cover the clinically visible exudate). Two weeks after cryotherapy application, the BCVA in the right eye improved to baseline 20/30 with reduction of anterior chamber reaction and absence of anterior chamber exudates [Fig. 1d]. There was no recurrence of inflammation seen on subsequent follow-up visits upto 6 months from initial presentation. Table 1 summarizes the right eye vision and procedure performed with respect to day of presentation.

Case 2

A 42-year-old HIV positive male with CD4 counts of 46 per cubic millimeter on antiretroviral therapy was referred for management of right eye infective scleritis. On examination of the right eye, his BCVA was 20/80 with lid edema, conjunctival and scleral congestion, iris prolapse at site of scleral necrosis nasally, pus pointing at 6 o'clock, keratic precipitates on endothelium, and 1 mm hypopyon along with vitritis [Fig. 3a and b]. The left eye was unremarkable. A diagnosis of right eye infective scleritis with suspected endogenous endophthalmitis was made for which the patient underwent right eye scleral scraping, scleral derroofing, and an anterior chamber tap.

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Vitreoretina and Uveitis Services, LV Prasad Eye Institute, Visakhapatnam, Andhra Pradesh, India

Correspondence to: Dr. Shreyansh Doshi, Retina and Uveitis Services, GMR Varalakshmi Campus, LV Prasad Eye Institute, 11-113/1, Hanumanthawaka Junction, Visakhapatnam - 530 040, Andhra Pradesh, India. E-mail: shreyansh.doshi87@gmail.com

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He was started on topical fortified cefazoline (5%) 1 hourly, fortified amikacin (2.5%) 1 hourly, atropine sulphate (1%) three times a day along with broad spectrum oral antibiotics in the form of amoxicillin and clavulanate potassium (625 mg 3 times a day) covering mainly gram-positive antibiotics and ciprofloxacin (750 mg 2 times a day) covering mainly gram-negative organisms. The visual acuity continued to deteriorate with increase in intraocular inflammation and formation of nasal anterior chamber ball like exudates [Fig. 3c]. On day 11 of presentation, the scleral scraping showed growth of *Mycobacterium* species sensitive to chloramphenicol, vancomycin, amikacin and linezolid, and intermediate sensitivity to ciprofloxacin and moxifloxacin. Topical treatment including linezolid (0.2%) 1 hourly and fortified amikacin (2.5%) 1 hourly along with oral linezolid 600 mg twice a day were started, and oral ciprofloxacin 750 mg twice a day was continued.

As there was further deterioration with worsening of ocular inflammation, on day 23 of presentation intravitreal

vancomycin (1 mg/0.1 ml) and amikacin (0.4 mg/0.1 ml) along with external scleral cryotherapy application at the affected site of scleritis (double freeze and thaw technique) was performed [Fig. 2c] avoiding the site of scleral perforation. The patient received additional three doses of the same intravitreal antibiotics on day 26, 33, and 40 of presentation, respectively, along with a repeat cryotherapy application to the affected area on day 33 of presentation, following which the scleral infection and inflammation reduced.

Antibiotics were discontinued after resolution of ocular infection. At the last visit, 9 months after initial presentation the visual acuity in the right eye was hand motion, intraocular pressure was 2 mm Hg, the nasal scleral nodule had regressed with conjunctiva covering the area of scleral perforation and thinning. Deep corneal vascularization was seen nasally with neovascularization of iris and presence of total cataract [Fig. 3d]. B scan showed the retina was attached with a shallow peripheral choroidal detachment and shallow disc elevation. Table 2 summarizes right eye vision and procedure performed with respect to day of presentation.

Discussion

The main mechanisms by which cryotherapy causes cellular damage is during the process of freezing and thawing. During the process of freezing, intracellular ice formation causes intracellular organelle and cell membrane disruption, while during the process of thawing, ice formation and recrystallization causes cell swelling and destruction.^[5,6]

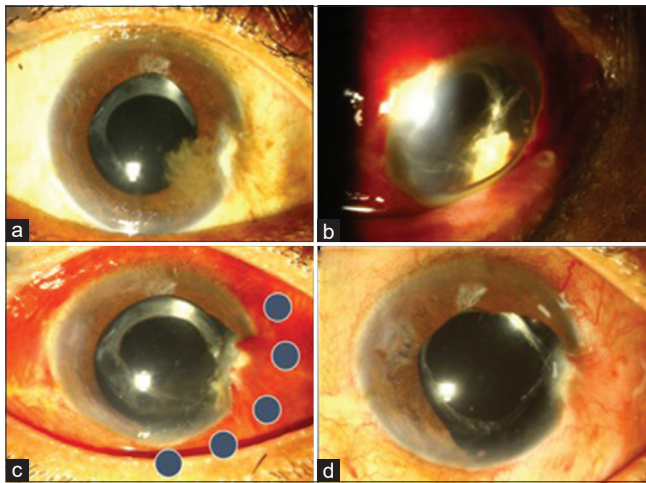


Figure 1: Patient 1, (a) Anterior segment picture of right eye at presentation showed a nasal pterygium, anterior chamber inflammation, light brown feathery exudate in the inferonasal quadrant of the anterior chamber, and a posterior chamber IOL with an intact posterior capsule. Right eye visual acuity at presentation was 20/30. (b) Day 8 of presentation, visual acuity dropped to 20/80 and anterior chamber inflammation further increased in size, (c) spots of external cryotherapy application (shown as blue dots) to the sclera in the affected area, (d) Two weeks after cryotherapy application, the best corrected visual acuity in the right eye improved to baseline 20/30 with reduction of anterior chamber reaction and absence of anterior chamber exudates

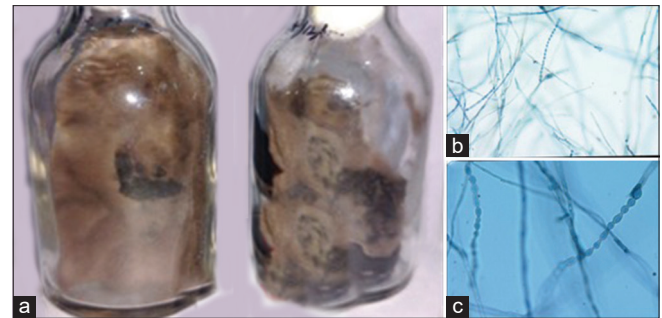


Figure 2: Patient 1, (a) Bottles with Sabouraud's dextrose agar and potato dextrose agar inoculated with anterior chamber fluid showed olive green growth with a black velvety texture indicating fungal growth, (b) Lactophenol cotton blue stain 40 × magnification- Conidia arranged in long, non-fragile chains, without apical branching, (c) Lactophenol cotton blue stain 100 × magnification- Smooth walled, single-celled, ellipsoidal conidia were noticed

Table 1: Case 1-Right eye vision and procedure performed with respect to day of presentation

Day	Vision	Procedure/Cause for reduced vision
Day 0 - Presentation	20/30	AC tap, intraocular antifungal agents, additional procedures
Postoperative day 1	20/160	Generalized corneal stromal edema
Postoperative day 3	20/125	2 nd intraocular antifungal agents
Postoperative day 7	20/80	3 rd intraocular antifungal agents
Postoperative day 9	20/80	Surgical debulking, 4 th intraocular antifungal agents, cryotherapy
Postoperative day 1	HMCF	Generalized corneal stromal edema and dispersed vitreous hemorrhage
Postoperative day 7	20/60	Reduced corneal edema and vitreous hemorrhage
Postoperative day 14	20/30	Resolved corneal edema and vitreous hemorrhage

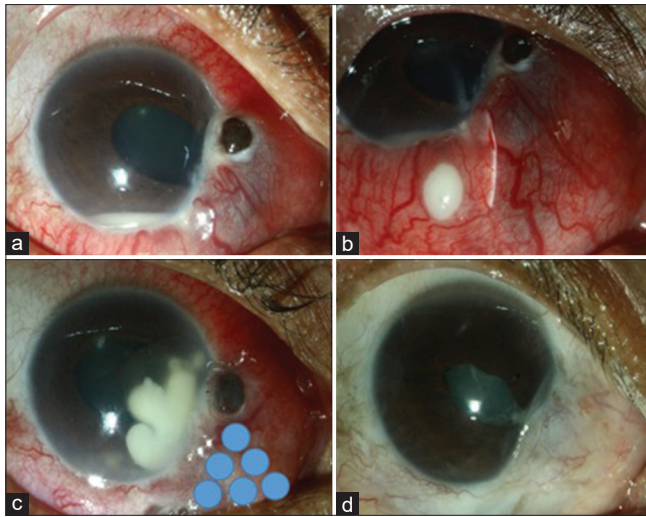


Figure 3: Patient 2, (a and b) Anterior segment picture of right eye showed marked conjunctival and scleral congestion, iris prolapse at site of scleral necrosis nasally with pus point at 6 o'clock, keratic precipitates on corneal endothelium and 1 mm hypopyon, (c) Day 17 of presentation, the infection increased further with formation of condensed exudates (like a ball) in the anterior chamber inferonasally. External cryotherapy (shown as blue dots) was applied to the sclera in the affected area, (d) At the last visit, 9 months from presentation, regressed nasal scleral nodule with conjunctiva covering the area of scleral perforation, thinning and iris prolapse, deep corneal vascularization was seen nasally with neovascularization of iris and total cataract

Table 2: Case 2-Right eye vision and procedure performed with respect to day of presentation

Day	Vision	Procedure
Day 0 - Presentation	20/80	Scleral scraping, scleral deroofting, anterior chamber tap
Postoperative day 23	CFCF	Intraocular antibiotics, cryotherapy
Postoperative day 26	20/800	Intraocular antibiotics
Postoperative day 33	20/800	Intraocular antibiotics, repeat cryotherapy
Postoperative day 40	20/500	Intraocular antibiotics

In an experimental study, cryotherapy when used as an adjunct to topical antifungal agents in treating fungal keratitis in rabbit eyes showed a positive response.^[7]

Unlike the first case, the second case, in addition to the routine medical and surgical management, required two applications of double freeze--thaw cryotherapy for resolution of the infective lesion. A study by Hodson *et al.* involving patients with infectious scleritis employed various antimicrobial treatment regimens. Medical therapy was adequate as the sole treatment in only 18% of patients, with most requiring surgical debridement and a higher rate of enucleation or evisceration was present in those treated solely with medical methods.^[4] Cryotherapy, lamellar or penetrating corneoscleral grafts in addition to intensive antibiotics improves the overall outcomes.^[8]

Also, in a retrospective study evaluating patients with endophthalmitis caused by nontuberculous mycobacterium, immunocompromised state is an important risk factor with almost 70% patient having an unfavorable outcome despite appropriate standard of care.^[2] Also long-term oral linezolid with a combination of macrolides, aminoglycoside, or fluoroquinolones can be tolerated well for treatment for nontuberculous mycobacterium infections.^[9]

To conclude, one or more external double freeze--thaw scleral cryotherapy could be used as an adjunctive therapy to treat localized peripheral recalcitrant infective lesion causing endophthalmitis.

Abbreviations

BCVA - best corrected visual acuity, IOL - intraocular lens, HIV - human immunodeficiency virus.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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