Role of intrastromal vancomycin in recalcitrant corneal abscess after phacoemulsification

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SUMMARY

Side port infection and corneal abscess after cataract surgery can produce devastating outcomes. Topical antibacterial drugs are the mainstay in management of these cases. Although intrastromal antifungal agents are an established modality for fungal keratitis, such use of antibacterial agents is rarely reported due to better pharmacokinetic profile of antibacterial agents.

We report a case of methicillin-resistant *Staphylococcus aureus* corneal abscess following phacoemulsification that responded to intrastromal vancomycin injection in addition to conventional therapy.

This case of postphacoemulsification corneal abscess highlights the importance of postoperative hygiene practices, use of anterior segment optical coherence tomography for monitoring these patients and use of intrastromal vancomycin as an adjunct to topical and systemic therapy.

BACKGROUND

Bacterial keratitis is a common cause of corneal blindness worldwide.[1] Aggressive institution of appropriate antibiotic therapy is the cornerstone of management.[2] However, patient factors and pathogenicity of causative organisms influence the final visual outcomes. Poor response to pharmacotherapy can lead to non-healing keratitis, culminating in thinning, perforation, descemetocele formation and even endophthalmitis.[1]

The possible sources of microorganisms for corneal wound infections and endophthalmitis may be patient's own eyelids and conjunctiva, minute foreign bodies clinging on to the instruments, contaminated intraoperative fluids, respiratory flora of operating room personnel and breach in sterility protocols.[3] Prolonged surgical duration, intraocular introduction of multiple instruments, diabetes mellitus, deficits in immune system, eyelid abnormalities, nasolacrimal duct obstruction, chronic dry eye and steroid use predispose to development of such infections.[4 5] The common causative organisms include *Streptococcus epidermidis*, *Streptococcus pneumoniae*, *Streptococcus viridans*, *Pseudomonas aeruginosa*, *Aspergillus flavus* and *Candida tropicalis*.[6]

Bacterial keratitis is conventionally managed by targeted antimicrobial therapy. Tectonic grafts performed in unresponsive cases are associated with high complication rates.[5] Alternatively, amniotic membrane transplant, tissue adhesives, autologous plasma-rich serum, tenon patch graft, conjunctival flaps, collagen crosslinking, corneal stromal lenticules, therapeutic contact lenses and tarsorrhaphy have been used in conjunction with antibiotics.[1 7]

The route of antibiotic delivery in bacterial keratitis, is primarily topical, intrastromal injections being used rarely.[8–11] We report the clinical course of a case of refractory methicillin-resistant *Staphylococcus aureus* (MRSA) corneal abscess following phacoemulsification. The intrastromal injection of vancomycin, in addition to the fortified drops and systemic medication, hastened the resolution of the keratitis. The case also highlights the role of anterior segment optical coherence tomography (ASOCT) in objectively monitoring the progress in such cases.

CASE REPORT

Case presentation

A 41-year-old woman, presented with diminution of vision in the left eye for the past 6 months. There was history of two episodes of left acute anterior uveitis in the last 1 year, that had resolved on topical steroids and cycloplegics. She underwent phacoemulsification with implantation of foldable posterior chamber intraocular lens. Antibiotic prophylaxis in the form of intracameral moxifloxacin (0.5%) was given at the end of surgery.

On the first postoperative day, her distance visual acuity was 20/20 and her clinical evaluation was unremarkable. The patient was advised ocular hygiene, topical tobramycin (0.3%) four times a day, topical prednisolone acetate (1%) six times a day, topical homatropine 2% two times a day, oral prednisolone 50 mg once a day and oral pantoprazole 40 mg. Oral steroids were prescribed in view of prior history of uveitis to minimise postoperative inflammation.

The patient reported back on the fourth postoperative day with the complaints of pain, redness and diminution of vision in the operated eye for the past 2 days. She had a habit of wiping her eye with her 'dupatta' around her neck. Her visual acuity had dropped to hand movement close to face with accurate projection of rays. Slit lamp examination revealed, diffuse corneal oedema and a corneal abscess of height 4 mm involving the inferior side port at 5 o'clock position and 4+ anterior chamber reaction (figure 1). On ASOCT, epithelium, descemet's membrane and endothelium appeared intact and no hypopyon was seen (figure 2). The intraocular pressure was raised digitally, and fundal glow was absent. There was no evidence of vitreous exudation on B-scan ultrasonography.

Treatment

A provisional diagnosis of left eye bacterial corneal abscess was made, and swabs were sent from the

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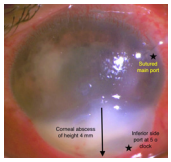

Figure 1 Slit lamp photograph of patient on postoperative day 4 showing diffuse corneal oedema, deep stromal infiltrate involving the inferior side port and anterior chamber exudates.

side port for gram staining and culture sensitivity. She was empirically started on intravenous vancomycin 500 mg four times a day and ceftazidime 1 g two times a day, topical fortified drops of vancomycin 5% and ceftazidime 5% administered one time an hour, ointment atropine sulfate 1% three times a day and tablet acetazolamide 250 mg three times a day. All forms of corticosteroids were stopped. On the sixth postoperative day, on microbial culture, MRSA was isolated. The growth was sensitive to vancomycin, moxifloxacin and ciprofloxacin and resistant to cefuroxime and tobramycin. The patient was continued on topical and intravenous vancomycin, topical atropine ointment and oral acetazolamide for the next 5 days. Despite maximal topical and systemic antibiotic therapy, the patient's condition did not improve; however, no vitreous exudation was seen on repeat B-scan ultrasonography.

In view of the non-responsive nature of the corneal abscess, intrastromal injection of vancomycin (1 mg/0.1 mL) was administered in the operating room under all aseptic precautions. The injections were given at four spots, 0.1 mL each, using 30-G needle, roughly 2 mm apart, just above the superior border of the abscess, taking care not to rupture the abscess or enter the anterior chamber.

Outcome and Follow-up

The height of the abscess reduced to 3 mm over the next 12 hours and the patient was continued on topical fortified vancomycin 5% one time an hour, ointment atropine sulfate 1% three times a day and oral acetazolamide 250 mg three times a day. On postoperative day 13, the height of the abscess was 3 mm with an overlying epithelial defect measuring 4 mm×3 mm (figure 3). Assuming toxic medicamentosa of the cornea due to frequent administration of vancomycin eye drops and the benzalkonium chloride in atropine ointment, the treatment was modified. The frequency of topical vancomycin was reduced to four times an hour and the atropine ointment was replaced by subconjunctival injection of mydricaine (6 mg lignocaine, 1.3 mg atropine sulfate and 0.12 mL epinephrine solution 1:1000) once a day. Height of the abscess progressively decreased and the epithelial defect completely resolved over the next 2 weeks. The patient had an uncorrected distance visual acuity of 20/60 with an inferior vascularised corneal opacity by fourth postoperative week (figures 4 and 5).

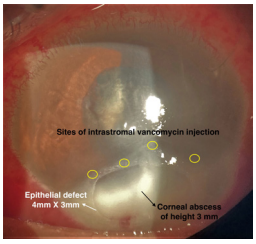

Figure 3 Slit lamp photograph of patient on postoperative day 13 showing resolving inferior corneal abscess with an overlying epithelial defect.

DISCUSSION

Corticosteroid intake is a known risk factor for occurrence of postoperative infections.[4] Poor ocular hygiene in addition to the steroid-induced immunosuppression possibly predisposed our patient to infection. Temporal clear corneal incisions lack the protection offered by the lid.[12] However, in this case, the main wound, though situated around 2 o'clock position, was sutured. The organism possibly tracked into the corneal stroma through the hydrated inferior side port at 5 o'clock position causing deep stromal keratitis.

Bacterial stromal keratitis usually responds to fortified topical antibiotics with few refractory cases mandating excision of infected cornea and replacement with tectonic grafts.[8] Unlike fungal corneal infections, where intrastromal antifungal agents are commonly used, intrastromal antibacterial agents are rarely employed due to better pharmacokinetic profile of topical antibacterial agents in cornea. Also, there are concerns with regards to the choice of safest intrastromal antibiotic and the minimum effective dosage and concentration required.[8]

Khan *et al*[10] were the first to report the role of intrastromal cefuroxime 250 mL/mL in treating patient of infectious crystalline keratopathy secondary to *Streptococcus parasanguis*. Subsequently, 0.02 mL of intrastromal tobramycin 0.3% was successfully used for treatment of recalcitrant deep stromal keratitis.[8] The organism isolated in our case was resistant to both cefuroxime and tobramycin. Although the isolate was sensitive to ciprofloxacin, intrastromal injection of fluoroquinolones is reported to cause intracorneal crystal deposition.[13] Both

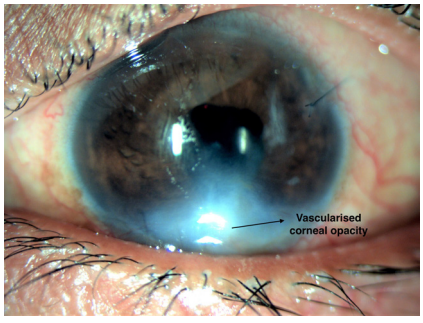

Figure 4 Slit lamp photograph of patient on postoperative day 28 showing inferior vascularised corneal opacity.

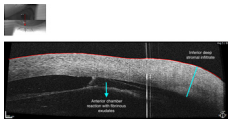

Figure 2 ASOCT image of patient on postoperative day 4. ASOCT, anterior segment optical coherence tomography.

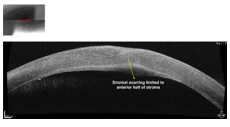

Figure 5 ASOCT image of patient on postoperative day 28. ASOCT, anterior segment optical coherence tomography.

teicoplanin and vancomycin, administered intrastromally, have been found to be effective in treatment of MRSA in rabbit model.[9] No adverse effect was observed by inadvertent injection of 1 mg/0.1 mL vancomycin intrastromally, post phacoemulsification, intended for antibiotic prophylaxis.[14] Therefore, we decided to inject vancomycin intrastromally, when the abscess failed to resolve even after 7 days of topical and systemic therapy. The continuation of topical vancomycin could have resolved the infection eventually. However, administration by intrastromal route enabled a faster recovery by directly targeting the bacterial nidus.

Despite its advantages, use of intrastromal antibiotics must be undertaken after due consideration to possible complications like endothelial toxicity, Descemet's membrane detachment, corneal perforation and inadvertent intracameral injections which may end up in intraocular seeding of microbes and endophthalmitis.[8]

The occurrence of an epithelial defect when the infiltration was subsiding, during the course of treatment, posed a significant challenge. Assuming drug toxicity of vancomycin and benzalkonium chloride preservative to be the cause, the frequency of topical instillation of vancomycin was reduced and ointment atropine was replaced by injection mydricaine. Management modalities for refractive epithelial defects include ointments, bandage contact lenses, autologous serum, platelet-rich plasma and amniotic membrane grafting.[7] As our patient recovered within 2 weeks of modifying the treatment, these therapies were not employed.

Although this case had multiple factors associated with poor visual outcomes like immunosuppression, topical steroid use, poor visual acuity at presentation, inferior location of infiltrate and severe anterior chamber reaction,[15] she finally gained a visual acuity of 20/60. The timely administration of intrastromal vancomycin possibly targeted the deep stromal focus of infection, restricting its spread and facilitating complete resolution.

To conclude, this case describes the safe and effective use of intrastromal vancomycin in postsurgical MRSA corneal abscess non-responsive to conventional medical therapy. It also highlights the adjunctive use of ASOCT to monitor the progress of such patients.

Patient's perspective

After successful cataract surgery, it was very scary to get infection in my eye which caused loss of vision and severe pain. Intially, the treatment helped in relieving the pain but my vision took a lot of time to improve. Treating doctors worked very patiently and tried different methods to cure the infection. Thanks to their efforts, I regained my vision at the end of treatment.

Learning points

- Poor ocular hygiene can predispose to post-operative intraocular infections even through adequately hydrated sideports in phacoemulsification.
- ASOCT serves as a useful objective tool to determine the response to therapy.
- Intrastromal vancomycin can be used safely for treatment of postsurgical MRSA corneal abscess

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