Managing Intractable Acanthamoeba Keratitis with Collagen Cross-linking

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Acanthamoeba keratitis is a rare, sight-threatening corneal infection affecting mainly contact lens wearers.

A twenty-two-year-old male, known user of contact lenses presented with a painful red eye, photophobia, and excessive lacrimation. A diagnosis of acanthamoeba keratitis was made based on clinical examination, which revealed a discoid opacity at the center of the cornea. The response to anti-microbial and anti-amebic medications (Brolene) was poor; therefore collagen cross-linking (CXL) with exposure to riboflavin and UV-A light was performed which revealed a dramatic response.

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Acanthamoeba keratitis (AK) is a necrotizing corneal infection caused by tiny, free-living amoebae. It is typically uni-nucleated and mobile trophozoite, but they form a double-walled cyst when subjected to severe environmental circumstances[1]. The first AK case was recorded in 1974 and since then case reports had increased among contact lense users[2].

Acanthamoeba polyphagia, acanthamoeba Castellani, and acanthamoeba hatchetti are the most prevalent species of Acanthamoeba causing Acanthamoeba keratitis. Several predisposing factors can increase the risk of acanthamoeba keratitis, including poor hygiene whilst using soft contact lenses, trauma and stagnant water exposure. Epitheliitis, epitheliitis with radial neuritis, anterior stromal disease, deep stromal keratitis, or ring infiltrate are the slit-lamp biomicroscopy findings in these cases. However, the ring infiltrates of Acanthamoeba organism is seen in only 50% of the cases[3].

AK can be classified into the development stage, convalescence stage, or cicatricial stage. Marked conjunctival hyperemia, a corneal epithelial defect, infiltration, and progressive inflammation could be seen in the development stage. Less conjunctival hyperemia, corneal disciform structures develop, repair of the corneal epithelial defect and abundant neovascularization could be seen in convalescence stage. Keratoleukoma could be seen in the cicatricial stage[4].

AK is difficult to treat even with the use of topical antimicrobial agents. Currently, AK is treated with propamidine isethionate 0.1% (Brolene). Diamines could be transported by trypanosomes to bind with the DNA within the nucleus and kinetoplast. It interferes with DNA associated enzymes[4]. The collagen crosslinking method requires corneal epithelial removal and exposure to riboflavin and UV-A light for 10 to 30 min. The epithelial defect usually takes 2 to 5 days to heal completely[4].

The aim of this presentation is to report a rare case of AK resistant to medication which has been treated successfully with CXL.

THE CASE

A twenty-two-year-old male with a history of soft contact lens use, presented with redness, photophobia, and excessive tearing in the right eye. On examination, visual acuity in the right eye was 6/9 and 6/6 in the left eye. Conjunctiva showed congestion; the cornea showed punctate epithelial erosion (PEE) and radial perineurits, see figure 1.

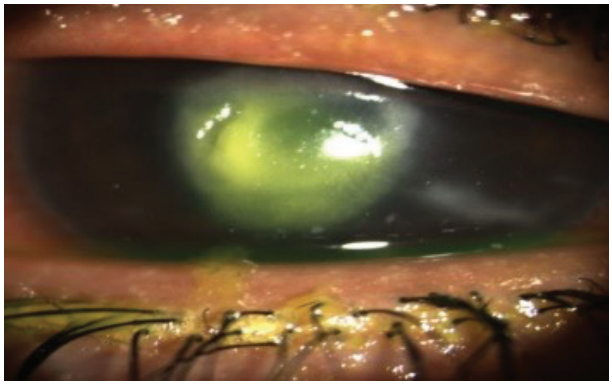

Figure 1: Contact Lens Related Acanthamoeba Keratitis

Differential diagnosis of acanthamoeba keratitis was considered. A swab was taken and Betadine 0.5 %, vigamox and lubricating eye drops were prescribed. Despite being followed up daily and aggressive antibiotic treatment (vigamox, gentamycin and maxitrol, frequent lubrication), the patient's condition worsened.

Two weeks later, the patient started to develop a central corneal ulcer measuring 2×2 mm with diffuse infiltration. Visual acuity was 6/12 in the right eye and the results of the swab revealed Klebsiella oxytoca and stenotrophomonas maltophilia. The patient was commenced on anti-amoeba (Brolene) while continuing medications prescribed earlier. During the next two weeks, the dimensions of the punctate epithelial erosion was reduced (1.5×1.5 mm), and healing from the superior quadrant was noted. Corneal opacity due to the previously mentioned

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ulcer measured 2.5×4.5 mm with diffuse corneal haziness developed.

One week later, the patient developed an additional 3×3 mm epithelial defect in the inferior quadrant with surrounding infiltration. The patient followed the treatment protocol without improvement. In the following week, conjunctival injection and multiple infiltrations were noted inferiorly. A central ring ulcer measuring 4.5× 4.5 mm and a previously healed corneal ulcer with opacification were also noted. The visual acuity dropped to 6/30 in the right eye with severe pain and blurring of vision.

The patient underwent collagen cross-linking under topical anesthesia and was commenced on Ciprofloxacin, fortified vancomycin and Tobradex (tobramycin and dexamethasone ophthalmic eye drops). One week after collagen cross-linking, the pain had been significantly reduced and the corneal ulcer had healed with epithelialization. The patient's surrounding cornea was healthy. However, visual acuity reduced to 6/60 due to corneal opacity.

In the following two weeks, the eye showed no signs of active keratitis, showing central corneal stromal opacity for which keratoplasty can be performed but after a suitable period.

DISCUSSION

Corneal ulcers could be bacterial, viral or fungal. They are difficult to treat and may cause an opacity that requires keratoplasty. The unspecific presentation and rarity of acanthamoeba keratitis are the primary factors in delaying the diagnosis. The delay ranged from 7 weeks to 12 months. Besides, corticosteroid therapy if initiated can result in disease progression. The annual incidence of Acanthamoeba keratitis among contact lens users is increasing, which could be due to a lack of proper hygiene and contamination of lenses. Several trials have recently shown the effectiveness of UV light in treating AK resistant to medication[5]. The most frequently reported genotype in clinical practice is the T4 genotype[6].

The clinical presentation during the early stage could be punctate epitheliopathy, pseudo dendrites and herpes keratitis. Moreover, the toxicity of the anti-Acanthamoeba makes many physicians reluctant to start therapy without a definite diagnosis.

A study compared patients with acanthamoeba keratitis receiving either chlorhexidine or polyhexamethylene biguanide (PHMB); no significant difference was found in the resolution of the disease, visual acuity and need for keratoplasty[7].

A study highlighted two possible theories of the effectiveness of CXL in keratitis. First, CXL can boost the resistance of collagen in the eye to digestive enzymes like pepsin, trypsin, and collagenase. Second, cell apoptosis after CXL can happen for both human keratocytes and pathogens due to the UVA light antimicrobial effect[8,9]. Makdoumi et al used CXL as a first-line treatment for bacterial corneal ulcers, only two needed antibiotic treatment[10].

Several studies have identified the enhanced effectiveness of post-CXL antibiotic or non-steroidal anti-inflammatory (NSAIDs) ointment use[11,12,13]. The use of topical corticosteroids and/or NSAIDs can exacerbate infection and corneal melting, particularly in the presence of epithelial defects and hypoxic circumstances caused by bandage contact lens application. It is therefore advised to delay the use of steroids after the epithelial defect has been completely healed and the bandage contact lens has been removed[14,15,16].

Despite these promising outcomes, the relatively small number of participants in the previously published study makes further studies required before CXL can be integrated into routine clinical practice for keratitis treatment.

CONCLUSION

Our case suggests that CXL is a promising option in cases of medication-resistant AK with corneal melting. It provides rapid symptomatic relief and significant corneal improvement in a short period.

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