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Case Report

Management of recurrent acute bilateral corneal endotheliitis monitored by serial corneal pachymetry

Lt Col B.V. Rao^a, Devika S. Joshi^b, Lt Col Sandeep Gupta^{c,*},
Brig P.S. Moulick^d

^aClassified Specialist (Ophthalmology), Military Hospital, Kirkee, Pune 411003, India

^bResident, Department of Ophthalmology, Armed Forces Medical College, Pune 411040, India

^cAssociate Professor, Department of Ophthalmology, Armed Forces Medical College, Pune 411040, India

^dProfessor & Head, Department of Ophthalmology, Armed Forces Medical College, Pune 411040, India

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Introduction

Acute corneal edema can be caused by angle closure glaucoma, intraocular surgery, and trauma. In patients without prior history of trauma, surgery, or noxious agents, it is known to be caused by infectious agents, such as Cytomegalovirus,¹ Mumps virus,² Varicella zoster,³ and Herpes simplex virus (HSV).⁴

Bilateral corneal edema can be seen in endothelial dystrophies. Bilateral presentation due to viral causes, such as Herpes simplex,⁴ is rare and has been reported in

approximately 15% of cases.³ However, bilateral simultaneous presentation of corneal edema is rarer still. As most of these cases have an immunological etiology, they are known to respond well to medical treatment with topical steroids and cycloplegics.

Case report

A young healthy male patient presented with bilateral sudden onset diminution of vision. On examination, he was found to have distant visual acuity (DVA) of counting fingers close to

* Corresponding author. Tel.: +91 9130546336.

E-mail address: drsandygupta19@yahoo.com (S. Gupta).

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face in both eyes along with bilateral epithelial and stromal corneal edema in disciform pattern, Descemet's folds, and circumcorneal congestion with diminished corneal and conjunctival sensations in both eyes. Intraocular tension in both eyes was normal as measured by Tonopen (Reichert Avia, USA). Rest of the ocular examination was normal.

He was investigated for any underlying immunosuppression and was found to have normal routine investigations and negative HIV and VDRL. An aqueous tap by paracentesis was obtained from the right eye and was sent for detection of viral markers of Varicella zoster, Herpes simplex, and Cytomegalovirus, which was negative for all three viruses.

In view of his disciform lesions, diminished ocular sensations in phakic eyes, and absence of immune suppression, a presumed diagnosis of acute bilateral herpes simplex endotheliitis was made. Patient was started on tab Acyclovir 400 mg, 5 times a day, Prednisolone acetate 1% eye drops at 6 times a day, and Homatropine 2% eyedrops twice a day in both the eyes. There was rapid improvement in vision and reduction of corneal edema within 3 days. Bilateral fine keratic precipitates were noticed in central cornea after reduction of the corneal edema along with few cells in anterior chamber. Medications were then tapered over the next 2 months by seeing the clinical response to the above therapy. He was maintained on tab Acyclovir 400 mg twice daily.

The patient had a recurrence of corneal edema with similar findings to the first episode after 6 months of initial presentation and was once again started on therapy of antivirals, steroids, and cycloplegics with slow tapering over 3 months. There were two similar such episodes during tapering of topical steroids in spite of initiating full dose medical therapy in a period of 15 months pointing to a diagnosis of withdrawal of medication while the disease was active.

It was decided to monitor the corneal disease activity by measuring the corneal thickness and accordingly taper the

Fig. 1 – Specular microscopy: right eye showing polymegathism.

Fig. 2 – Specular microscopy: left eye showing focal loss of endothelial cells.

medicines after ascertaining disease quiescence. The subclinical corneal edema was monitored with ultrasound pachymetry (Pachette 2, DGH 550, DGH Technology, Inc, USA) and endothelial cell count was monitored with specular microscope (Topcon SP2000P Specular microscope) with some loss of endothelial cells noted at every episode of recurrence (Figs. 1 and 2). Topical steroids and cycloplegics were not tapered rapidly till a normal corneal pachymetry was obtained. Once two consecutive normal pachymetry readings were obtained $<530\ \mu\text{m}$, a slow taper of topical treatment was done and the patient was shifted to a prophylactic dose of Tab Acyclovir 400 mg PO BD.

At 8 weeks of follow-up, post-latest recurrence, the patient had DVA of 6/6 in both eyes with endothelial counts stable at $2305/\text{mm}^2$ in right eye and $2962/\text{mm}^2$ in left eye (Table 1). The patient is currently on tab Acyclovir 400 mg twice daily, eye drops Fluorometholone 0.1% three times a day, and eye drops Cyclosporine 0.5% twice daily in both eyes with monthly follow-up and to report SOS.

Discussion

The causes of corneal edema include any insult to the corneal endothelium or a raised intraocular pressure. The corneal endothelium can be involved in cases of endothelial dystrophies, iatrogenic surgical trauma, or viral endotheliitis. In a phakic patient, in absence of corneal changes suggestive of endothelial dystrophies, a diagnosis of viral endotheliitis is most likely. Infectious causes include viruses, mainly Cytomegalovirus,¹ Mumps virus,² Varicella zoster,³ HSV,⁴ and drugs like Amantadine,⁵ Amiodarone,⁶ or acute alcohol intake.⁷

Table 1 – Specular microscopy and pachymetry.

Follow up	Specular count (cells/mm ²) RE	Specular count (cells/mm ²) LE	Pachymetry (μm) RE	Pachymetry (μm) LE
Day 7 after 3rd recurrence on treatment	1729	3100	561	554
Week 4 on Treatment	2154	3010	542	545
Week 8 on treatment (tapering started)	2305	2962	510	520

Most of these diseases are unilateral, and rarely when bilateral disease is seen, it is usually asymmetric and/or sequential. Acute simultaneous bilateral corneal edema is rare. Bilateral endothelial disease in herpes has been seen in 15% of the cases as noted by Madhavan et al.³ Average age of patients developing bilateral disease was 40 years as compared to the younger age of patient in the present case. Also none of them had showed simultaneous involvement of both the eyes. As most of the patients with viral endotheliitis have an underlying immune process in endothelium and anterior chamber, such acute onset bilateral stromal edema appears to respond well to topical steroid therapy and oral Acyclovir, and slow tapering of these drugs is advocated. Recurrences are seen in cases with rapid and early tapering of steroids; hence, timing of drug withdrawal is of paramount importance.

Clinical improvement of visual acuity and corneal clearing may give a false picture of disease inactivity and corneal thickness may be a more objective and true indicator of corneal disease activity. Traditionally, corneal pachymetry has been used to measure graft edema after penetrating keratoplasty⁸ and to monitor for graft rejection. Pachymetry-guided treatment is useful in objective assessment of resolution of subclinical corneal edema and inversely the disease activity. Once the pachymetry is in normal range, topical steroid treatment may very well be tapered safely with less chances of recurrence.

According to Vannas et al., patients who had experienced severe keratouveitis showed marked pleomorphism of the endothelial cells and a 15% lower central endothelial cell density on average than the healthy fellow eyes.⁹ O'Brien et al. also report other findings, such as focal endothelial cell loss, multinucleate giant cells, and increased mean cell area based on direct observation of the endothelium of HSV-infected specific pathogen-free male New Zealand white rabbits.¹⁰

Due to repeated recurrences in spite of good response to treatment in this presumed case of herpes simplex bilateral endotheliitis, it was extremely important to quantify and monitor the corneal edema with ultrasound pachymetry as well as assess the status of corneal endothelium. Repeated measurements of the above parameters helped decide tapering point of treatment. Tapering of topical steroids was of utmost importance due to risk of development of complications, such as secondary glaucoma. Alternative immunosuppression in the form of Topical Cyclosporine or Tacrolimus may be considered as steroid sparing agents so as to avoid steroid-induced complications in case the objective parameters showed slow response and need for longer duration of immune suppression.

Conclusion

Bilateral simultaneous presentation of H. Simplex endotheliitis is uncommon but should be kept in mind in phakic patients without any signs of endothelial dystrophy. The diagnosis is clinical in spite of negative aqueous tap for virus and it shows good rapid response to topical steroids and specific antiviral therapy. The tapering of steroids to prevent its complications should be slow, and here, ultrasound pachymetry can be an important tool in monitoring the treatment response and point for starting tapering as early reduction of steroids may cause a recurrence, which leads to further loss of endothelial cells, starting a vicious cycle. Serial specular microscopy may also help assess endothelial cell loss in such cases.

Conflicts of interest

The authors have none to declare.

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