

A challenging case of keratoconjunctivitis medicamentosa with necrotizing scleritis

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ABSTRACT

We report a case of keratoconjunctivitis medicamentosa in a 64-year-old female. She was operated for cataract 4 months back and treated for viral keratitis at present. Ocular examination revealed inferior sterile corneal melt with ischemic necrotizing scleritis and ischemic necrosis of tarsal and lower fornix conjunctiva. Keratoconjunctivitis medicamentosa was diagnosed. Tenoplasty with multilayered amniotic membrane grafting and mucous membrane grating of the tarsal plate was done to which she responded well. Chemical irritation of the ocular surface by topical drops may result in keratoconjunctivitis medicamentosa. A high index of suspicion is required for the accurate diagnosis of such a visually debilitating condition.

Key words: Ischemia, Keratoconjunctivitis, Medicamentosa, Scleritis

Progressive cicatrizing keratoconjunctivitis may arise as a rare adverse effect of certain drugs. Preservatives such as thiomersal and benzalkonium chloride are well documented to cause ocular toxicity [1]. The toxicity of drug combinations may be synergistic [2]. Clinical features may range from non-specific conjunctival hyperemia and papillary reaction to thickening, subepithelial fibrosis, inferior fornix shortening, shallowing of canthal recess, and punctual stenosis [1]. Associated keratopathy becomes an inevitable manifestation in misdiagnosed and improperly managed cases resulting in persistent epithelial defects, ring keratitis, stromal infiltration, corneal melting, and perforation with poor prognosis [3]. Primarily, the suspected drug should be withdrawn which may result in resolution. However, if irreparable sequelae have set in, a tailored approach to management would be required.

Here, we report a challenging case of keratoconjunctivitis medicamentosa with necrotizing scleritis and tarsal ischemia which required aggressive surgical management.

CASE REPORT


A 64-year-old female patient presented with gradual, painful diminution of vision in the right eye (RE) post-cataract surgery which was done 4 months back. She developed pain, burning sensation, and watering in her RE 3 days after surgery, for which a diagnosis

of viral keratitis was made. Acyclovir eye ointment (3%) was added to the ongoing treatment (gatifloxacin (0.5%), loteprednol (0.5%), homatropine bromide (5%), and sodium hyaluronate (0.1%) eye drops). She continued using the medication inadvertently.

On ocular examination, her best-corrected visual acuity (BCVA) in the RE was the perception of light (PL). A 9×7 mm inferior, sterile, hypopyon corneal ulcer, adjacent necrotizing scleritis extending up to 4 mm from the limbus in the 4–7 o'clock quadrant, tarsal ischemia, and a fibrotic scar in the lower tarsus were noted with macerated lower lid skin (Fig. 1a-c).

Ultrasound B scan was found normal. The patient's left eye was PL negative with anterior staphyloma (post-trauma). Systemic investigations revealed normal blood counts. Erythrocyte sedimentation rate and C-reactive protein were raised. Serological workup (rheumatoid arthritis factor, Venereal disease research laboratory test, antinuclear antibodies, and antineutrophil cytoplasmic antibodies profile) and chest X-ray was unremarkable. Corneal slough examination on Gram stain and 10% KOH mount showed no growth.

After excluding autoimmune and infectious etiology, a diagnosis of drug-induced cicatrizing keratoconjunctivitis was made since the examination findings were typical of post-chemical injury. The history of instillation of any irritants in the eye was repeatedly denied by the patient and she kept mentioning about a burning sensation on instillation of prescribed eye drops. Our diagnosis was further supported by a simple litmus paper test which showed an acidic pH (1–2) for eye drops loteprednol and sodium hyaluronate (Fig. 2a-b).

Access this article online	
Received - 12 September 2022 Initial Review - 30 September 2022 Accepted - 16 October 2022	Quick Response code 
DOI: 10.32677/ijcr.v8i10.3626	

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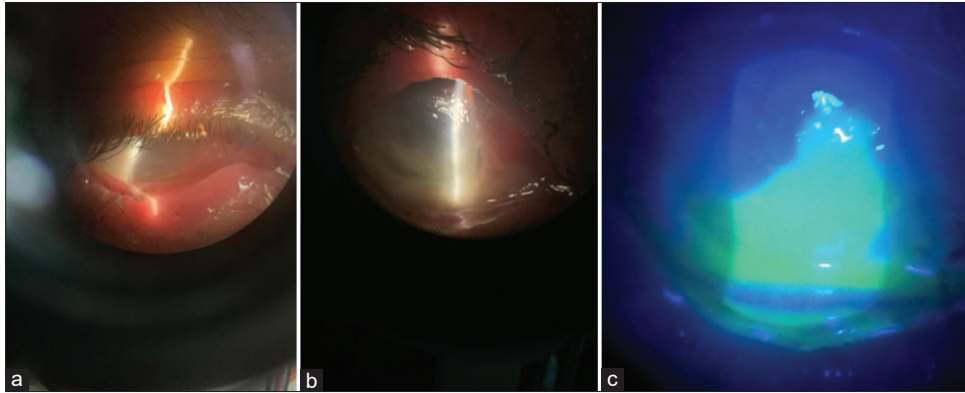


Figure 1: (a) Pre-operative total obliteration of the lower fornix and lower lid skin maceration, lid margin keratinization of right eye (RE); (b) inferior corneal ulcer RE; and (c) adjoining scleral ischemia RE

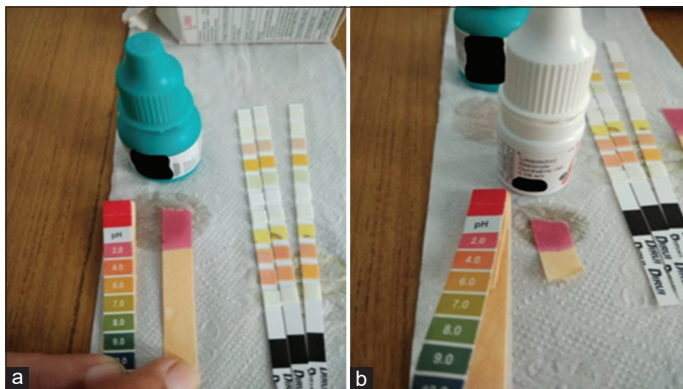


Figure 2: (a) Litmus paper test showing acidic pH of loteprednol (0.5%) eye drops; (b) litmus paper test showing acidic pH of sodium hyaluronate (0.1%) eye drops

Thereafter, lower lid tenonplasty with mucous membrane and multilayered amniotic membrane grafting (AMG) with bandage contact lens was done (Fig. 3a-c). Postoperatively, loteprednol (0.2%), homatropine bromide (5%), chloramphenicol (0.5%), and carboxymethylcellulose (0.5%) eye drops, azithromycin eye ointment (1%) for lid massage, tablet omnacortil, and oral doxycycline were given. At 1-week follow-up, the patient was asymptomatic and BCVA in the RE was counting finger at 1 m. There was a resolution of corneal ulcer with a well-formed lower lid margin and fornix (Fig. 4a-b). The patient did not turn up for subsequent follow-ups due to the COVID pandemic.

DISCUSSION

The clinical signs of iatrogenic disease are usually non-specific and identical to those resulting from other causes of surface disease. One epidemiological study identified 13% of keratoconjunctivitis cases as iatrogenic [4]. Iatrogenic toxicity occurs in patients with acute or chronic ocular surface disorders as a result of both short-term and long-term use of topical medications [4,5]. In advanced cases, progression cannot be arrested by discontinuation of the inciting agent alone. Obtaining a detailed history aids in differentiating it from chemical, thermal or radiation trauma, infectious conjunctivitis, Steven Johnson syndrome, trachoma, and mucous membrane pemphigoid. The inferior location, the

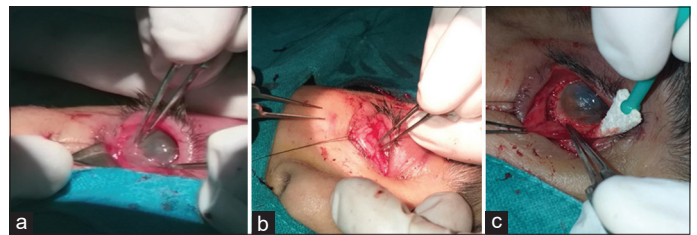


Figure 3: (a) Intraoperative picture showing multilayered amniotic membrane grafting with glue right eye (RE); (b) intraoperative picture of RE showing mucous membrane grating spread over tarsal plate; and (c) intraoperative picture of RE showing tenonplasty

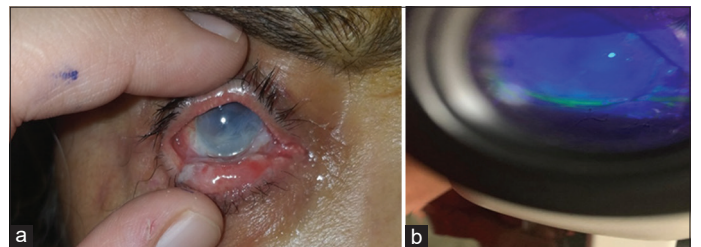


Figure 4: (a) Mucous membrane grating, amniotic membrane grafting, and BCL *in situ* RE on 1st post-operative day; (b) ocular surface of RE on 7th post-operative day

relatively normal superior bulbar conjunctiva, and the history of severe irritation on instillation of the drops are further indicators of keratoconjunctivitis medicamentosa as in this case.

Late occurring peripheral ulcerative sclerokeratitis can occur years after chemical injury [6], though the clinical picture would resemble that of necrotizing scleritis without tarsal involvement with a definite history of chemical injury. The presence of tarsal ischemia and tarsal conjunctival defect in our case differentiated it from a case of scleritis alone [7]. Ulceration and maceration of skin of the lower lid and its margin were additionally present in our case which is a tell-tale sign of keratoconjunctivitis medicamentosa.

The normal physiological pH of the ocular surface in humans is noted to be 7.11 ± 1.5 . Antibiotic eye drops contain HCl, phosphoric acid, or sodium hydroxide to adjust pH. For example, ofloxacin ophthalmic solution is unbuffered and formulated with a pH of 6.4 (range: 6.0–6.8) [8,9]. It is unusual to have a pH of <3 or >9 in ophthalmic medications and a value beyond these should

be viewed with suspicion [10]. In this case also, two eye drops had an acidic pH of 1–2 on a simple litmus paper test.

Placing an amniotic membrane on a severely ischemic sclera without a tenoplasty does not lead to epithelisation [10]. Hence, mucous membrane grating (for fornix reconstruction) with multilayered AMG and tenoplasty (to promote epithelization) was done in this case.

CONCLUSION

This case highlights the importance of having a high index of suspicion for the possibility of an underlying chemical injury in eyes that present with features suggestive of necrotizing scleritis, especially when associated with tarsal ischemia. A simple litmus paper test can be used to clinch the diagnosis. A well-tailored approach to management in cases with advanced scleral ischemia to prevent permanent ocular morbidity is required.

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Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Shakeel T, Dasgupta S. A challenging case of keratoconjunctivitis medicamentosa with necrotizing scleritis. *Indian J Case Reports*. 2022;8(10):314-316.