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CASE REPORT

Case report: acute hydrops and spontaneous corneal perforation in a patient with keratoconus treated with colchicine for familial Mediterranean fever

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Abstract
Purpose To report a rare case of spontaneous corneal perforation after hydrops in keratoconus patients who suffer from familial Mediterranean fever and was treated systemically with Colchicine.
Methods Case report.
Results We report a case of a 30-year-old male with keratoconus and familial Mediterranean fever treated with colchicine, presented with acute hydrops in his left eye, which progressed to a spontaneous corneal perforation. Attempts to treat the perforation with cyanoacrylate glue failed, and he underwent penetrating keratoplasty with an excellent visual outcome.
Conclusion Colchicine treatment may have had a role in the pathogenesis of this rare case.

Keywords Keratoconus · Hydrops · Corneal perforation · Colchicine · Familial Mediterranean fever

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Abbreviation
FMF Familial Mediterranean fever

Introduction

Keratoconus is a condition in which the cornea assumes a conical shape due to non-inflammatory thinning of the corneal stroma. The corneal thinning induces irregular astigmatism, myopia, and protrusion, leading to mild to marked impairment in the quality of vision [1]. Hydrops is an uncommon complication of advanced keratoconus. It occurs in less than 3% of patients [2] usually presenting with acute visual loss and pain. Hydrops relates to breaks in Descemet's membrane. The breaks are characterized by separation and the rolling of the edges of the torn Descemet's membrane. This exposes the bare corneal stroma to the aqueous humor that penetrates the stroma and causes separation of the collagen lamellae due to edema. This leads to the formation of large fluid filled intra-stromal clefts or cysts. The adjacent endothelium usually grows over the defect, forming a seal with the resolution of the stromal edema [3]. The edema may persist for weeks or months and usually resolves gradually with relief of the pain and resolution of the conjunctival hyperemia, but the edema is ultimately replaced by scar tissue [1]. Hypertonic saline can be used as an initial treatment for hydrops, whereas in refractory cases, intra-cameral injection of

air, SF6, or C3F8 may be used depending on the severity of the case [3]. Nearly 60% of keratoconus patients who develop hydrops will require penetrating keratoplasty for visual rehabilitation [4].

Case presentation

A 30-year-old patient with keratoconus presented to our outpatient clinic due to 4 days of pain in his left eye. His past ocular history was significant only for keratoconus. His medical history was significant for familial Mediterranean fever (FMF), treated systemically with colchicine. On presentation, his uncorrected visual acuity was 20/20 in his right eye and count fingers at 1.5 ft in his left eye. A slit lamp examination was consistent with signs of keratoconus in his right eye and acute hydrops with edema of the central cornea in the left eye. Treatment with topical steroid eye drops (Lotemax; Bausch & Lomb Incorporated, Rochester, NY, USA) combined with hypertonic saline four times per day in the left eye was initiated. Four months later, the patient presented to our emergency department due to acute exacerbation of pain in his left eye with no history of trauma or eye rubbing. On examination of the anterior segment, a positive Seidel test was found, indicating aqueous humor leakage with an inflammatory reaction in the anterior chamber of the eye (Fig. 1). Cyanoacrylate glue with a polyethylene disk was applied in combination with a therapeutic contact lens (Fig. 2) to seal

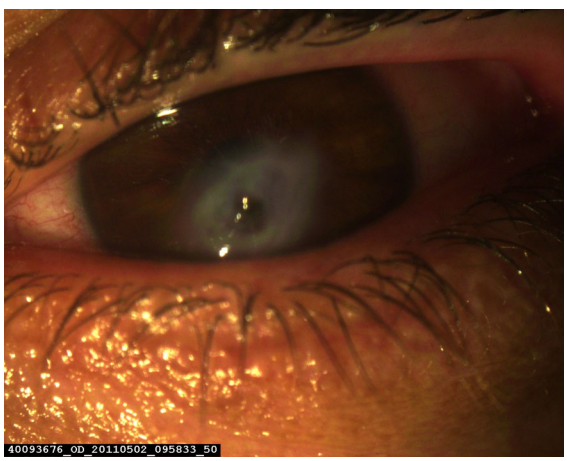

Fig. 1 Slit lamp photograph of the patient 4 months after the initial presentation of hydrops with extreme thinning and aqueous leakage at the site of the hydrops

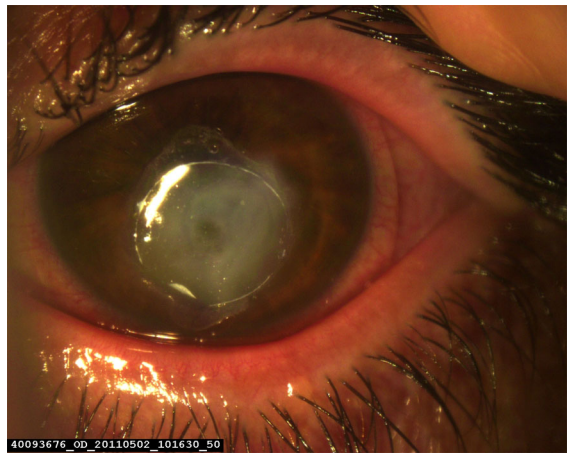

Fig. 2 Slit lamp photograph of the patient after gluing of the leaking area with cyanoacrylate glue

the area of the leaking hydrops. Topical moxifloxacin (Vigamox; Alcon, Ft. Worth, TX, USA) was prescribed four times per day. Due to the dislocation of the glue, the second attempt to glue the leaking site was made within a few hours of the first attempt. Two weeks later, the patient presented again with severe, intolerable pain and decreased visual acuity to hand motion. On slit lamp examination, the glue was displaced and a corneal perforation with iris prolapse and a shallow anterior chamber was found. Emergent full thickness penetrating keratoplasty was successfully performed. Three years after the surgery, his distance uncorrected visual acuity was 20/25 (+ 2) with a clear corneal graft.

Discussion

We describe a rare case of spontaneous corneal perforation following acute hydrops in a patient with keratoconus. Our patient suffered from FMF, which is one of the most common forms of hereditary autoinflammatory disorders characterized by recurrent episodes of fever and sterile inflammation resulting in peritonitis, pleuritis, arthritis, and/or erysipelas like erythema. Colchicine is the standard care for prophylactic treatment of the inflammatory episodes [5]. Our patient was treated systemically with colchicine, an antimitotic alkaloid agent, which in fact inhibits neutrophil mobility and activity, and it is the anti-inflammatory effect that helps it work for gout. This effect would actually help wound healing, and it is

probably its antimitotic effect by affecting the microtubules that interferes with other aspects of wound healing [5]. Colchicine for the most part affects cells with a high replication rate, such as epithelial cells, during the metaphase cycle of mitosis, and the lack of epithelial movement would compromise wound healing. The effect on the replication rate of the corneal epithelial cells was previously described by Buschke et al. [6]. In addition, although epithelial cells tend to have higher replication rate, keratocytes also tend to increase their replication rate usually following corneal insult [7]. Therefore, although highly effective for inflammation it may also interfere and impair wound healing [8]. Leibovitch et al. [9] described the access of colchicine to the corneal surface via the tear fluid, thus exerting its inhibitory effect on the corneal wound healing process. This suggests that colchicine may have a role in the pathogenesis of the corneal perforation in our case. To our knowledge, only a few cases have been reported describing spontaneous corneal perforations due to hydrops among keratoconus patients. The perforations were described to be associated with pregnancy, topical steroids treatment [10], eye rubbing [11, 12], elevated intraocular pressure [13], in the association with post-LASIK ectasia [14, 15] and even spontaneously [16–19]. However, an association with colchicine treatment was not suggested. Our case suggests that colchicine treatment may had a role in the pathogenesis of the perforation, but it is important to emphasize that other possibility is that this case represents a spontaneous perforation as noted in other papers and colchicine was not a precipitating factor. Thus, patients with hydrops and systemic treatment of colchicine should be followed closely and cessation of colchicine treatment should be considered carefully until a resolution of the hydrops is achieved.

Compliance with ethical standards

Conflict of interest Assaf Hilely and Guy Kleinmann declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent The patient has consented to the submission of the case report for submission to the journal.

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