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SHORT COMMUNICATION

Corneal ulcer as an atypical presentation of ocular cicatricial pemphigoid

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PURPOSE. *To describe three patients, each presenting noninfective corneal epithelial damage as first manifestation of ocular cicatricial pemphigoid (OCP).*
METHODS. *Case report.*
RESULTS. *Patients 1 and 2 were referred to the authors' clinic for corneal ulcer while Patient 3 for relapsed epithelial defects. All patients had negative history for systemic diseases and microbiological tests were negative. Topical steroid treatment induced the complete resolution of corneal damage. During the follow-up period, the onset of mild conjunctival fibrosis in the lower fornix allowed the authors to suspect OCP, confirmed by conjunctival biopsy.*
CONCLUSIONS. *In the three patients corneal damage was an early sign of OCP, in the absence of typical signs of conjunctival fibrosis. The authors thus suggest considering conjunctival biopsy as a useful additional test in the management of idiopathic corneal ulcers. (Eur J Ophthalmol 2007, 17: 121-3)*

KEY WORDS. *Corneal ulcer, Ocular cicatricial pemphigoid, Conjunctival biopsy*

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INTRODUCTION

Ocular cicatricial pemphigoid (OCP) is a chronic vision-threatening disease of the ocular surface characterized by inflammation, progressive fibrosis, corneal xerosis, and opacification (1). The clinical diagnosis is a major challenge for ophthalmologists in the early stages of the disease since subepithelial fibrosis and fornix foreshortening may be overlooked and the associated conjunctival inflammation may be confused with other clinical entities of a red eye (1). According to Foster and Mondino and Brown, corneal involvement has been generally described to occur in the late stages of the disease, as a consequence of dry eye and eyelid abnormalities (1, 2). In the present report, we describe noninfectious corneal ulcer, associated with normal Schirmer values, in three patients who subsequently developed conjunctival fibrosis, fornix foreshortening, and typical immunofluorescent staining of OCP 12 to 18 months after the initial corneal manifestations.

Case reports

Case 1

A 38-year-old man developed a central ulcer associated with intense conjunctival hyperemia, pain, and photophobia in the left eye (Fig.1, A and B). Systemic and ocular histories were unremarkable and the contralateral eye was normal. Microbiological investigation was negative for bacteria, herpes, fungi, and acanthamoeba. A rapid worsening of the ulcer caused corneal

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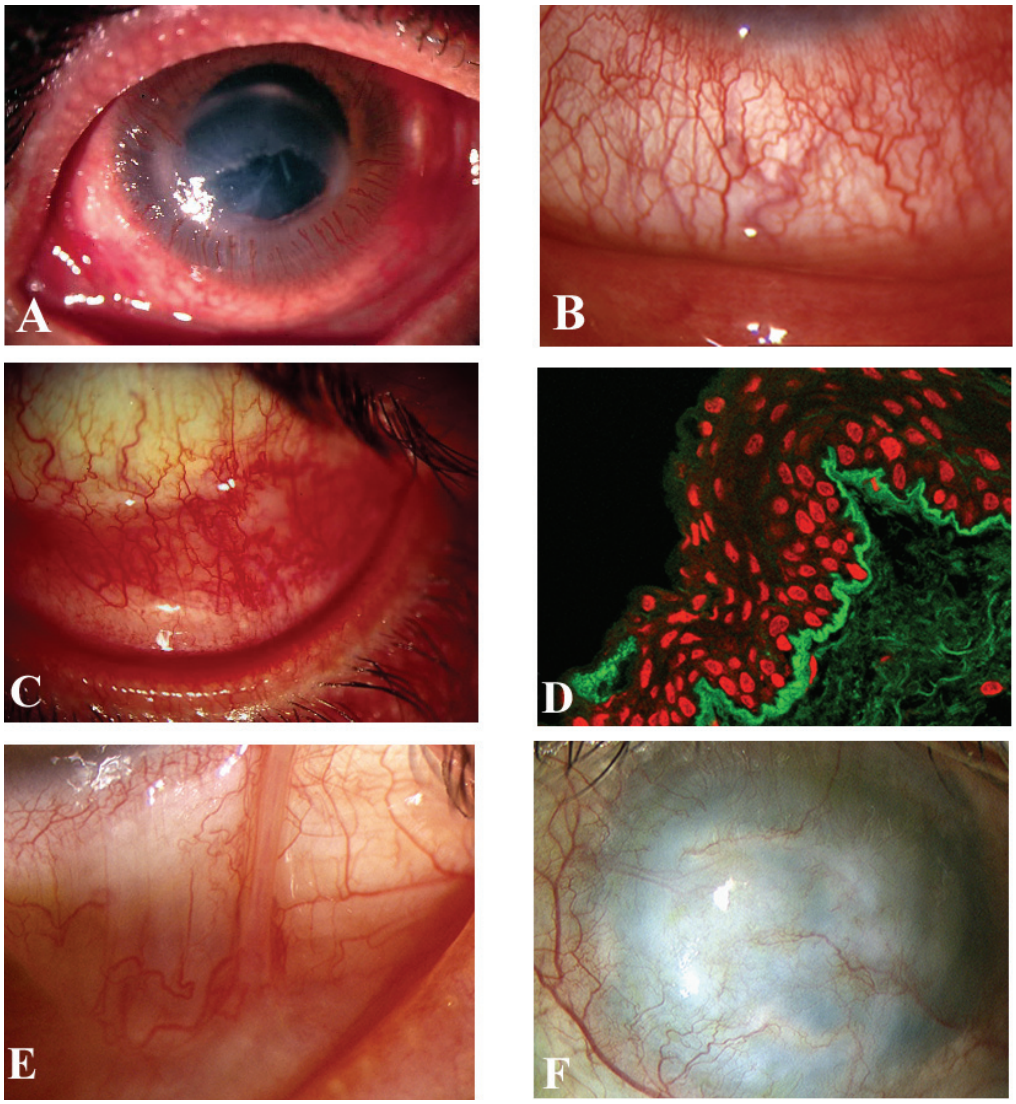

Fig. 1 - *Patient 1 presented with a corneal ulcer* **(A)** *and no signs of conjunctival fibrosis* **(B)**. *Six months later, the same patient developed a subtle linear fibrosis on the lower fornix* **(C)** *indicative of an ocular cicatricial pemphigoid diagnosis. Confocal microscopy demonstrated the presence of linear deposition of Ig along the epithelial basal membrane zone, confirming the diagnosis of ocular cicatricial pemphigoid* **(D)**. *During the follow-up period, the patient developed symblepharon* **(E)** *and progressive corneal scarring with neovascularization* **(F)**.

perforation treated with both conjunctival flap and topical steroids. No signs of inflammation were observed during 16 months of follow-up and a lamellar keratoplasty was performed to improve visual acuity. The patient was free from signs and symptoms of inflammation for approximately 12 months when he returned complaining of ocular hyperemia, foreign body sensation, and mild photophobia in the left eye. Slit lamp examination showed mild punctate superficial keratitis, conjunctival hyperemia, and presence of linear subconjunctival fibrosis on the lower fornix (Fig.1C). A conjunctival biopsy was performed and immunohistochemistry supported a diagnosis of OCP (Fig. 1D). Systemic immunosuppressive treatment was promptly initiated. During 5 years of follow-up, despite systemic therapy, the left eye showed a slow but progressive worsening with the onset of symblepharon (Fig. 1E), entropion, corneal neovascularization, and opacity (Fig. 1F) and severe dry eye. The contralateral eye showed signs of dry eye and conjunctival fornix foreshortening.

Case 2

A 62-year-old woman was referred to our clinic with a noninfectious corneal ulcer in the right eye that was treated with topical and systemic steroid therapy for 4 weeks, after which time the corneal defect was completely healed. Steroids were decreased and then dis-

continued and the patient was treated with preservative-free artificial tears for an extended period. After 1-year, we observed some striae of subconjunctival fibrosis in her right lower fornix. Ocular cicatricial pemphigoid was suspected and conjunctival biopsy confirmed the diagnosis. Systemic immunosuppressive therapy was effective during the 4 years of follow-up.

Case 3

A 61-year-old woman was admitted to our department with a 1-year history of relapsing epithelial defects, despite preservative-free tear substitute therapy. The slit lamp examination showed diffuse bilateral superficial punctate keratopathy and the presence of a paracentral corneal ulcer in the left eye associated with limbal superficial neovascularization and moderate conjunctival hyperemia. Complete epithelial healing was achieved after 2 weeks of topical steroid treatment. After 6 months, mild subconjunctival fibrosis was observed and a conjunctival biopsy was performed. The diagnosis of OCP was confirmed by direct immunofluorescence and systemic immunosuppressive therapy was initiated.

DISCUSSION

In these three patients, the typical early manifestations of OCP such as subepithelial fibrosis and fornix foreshortening (1, 3) occurred 12 to 18 months after corneal ulcer, suggesting that the latter may have been the first clinical manifestation of OCP. These patients with early corneal involvement comprise 10.7% of our series of 28 OCP cases observed between 1998 and 2004, indicating that in some patients this may be a warning sign for early diagnosis of OCP, later confirmed by conjunctival biopsy of the ensuing conjunctival fibrosis (4). Corneal involvement in OCP is described as a common feature during the late stages of the disease (1, 5). In fact, superficial punctate keratitis, epithelial defects or noninfective ulcers, conjunctivalization, and keratinization are considered a consequence of eyelid abnormalities and severe dry eye (1, 5). However, in our three patients the corneal epithelial defects and ulcers, associated with intense pain, developed even in the absence of dry eye (normal Schirmer values) or eyelid abnormalities. The presence of early corneal epithelial damage may have been related to a subclinical chronic inflammatory reaction. We cannot exclude that at the time of the first examination a conjunctival biopsy would have revealed the presence of the underlying conjunctival autoimmune disease (4) . However, an alternative theory involving a primary autoimmune reaction against corneal antigens cannot be excluded. In line with this hypothesis, experimental studies have demonstrated that injection of IgG from patients with bullous pemphigoid into the corneal stroma of rabbits induces corneal opacity and linear deposition of IgG along the basal membrane zone (6).
This report demonstrates that noninfective corneal ulcer may be an atypical indication of the onset of OCP, suggesting that conjunctival biopsy may be a useful supplementary test in the management of idiopathic corneal ulcer.

No author has a proprietary interest.

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