CASE REPORT

Ocular pseudopemphigoid with concomitant eyelid dermatitis secondary to rosacea

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INTRODUCTION

Ocular cicatrical pemphigoid (OCP) is a form of mucous membrane pemphigoid that is characterized by progressive inflammation and scarring of the conjunctiva. OCP may result in severe ocular complications and permanent vision loss if it is not recognized and managed early in its clinical course. Ocular pseudopemphigoid is a rare disorder that clinically mimics OCP. It has been primarily reported secondary to the long-term use of glaucoma medications but may also occur secondary to other diseases, such as rosacea, atopic dermatitis, and lichen planus. We present an unusual case of ocular pseudopemphigoid that concurrently developed with a rosaceiform eruption on the eyelids in a patient with a history of glaucoma.

CASE REPORT

A 58-year-old man with a history of glaucoma was referred for evaluation of chronic cicatrizine conjunctivitis and a rash on the eyelids. Three months earlier, he developed redness and irritation of the left eye, which was shortly followed by similar involvement of the right eye. During this period, a scaly erythematous eruption developed on both the eyelids. He had no history of atopy, including atopic keratoconjunctivitis. Since 2009, he had been treated for glaucoma in both the eyes with topical therapy, including brimonidine tartrate, timolol maleate, bimatoprost, and sodium chloride solutions. He had previously undergone 2 corneal transplants in the right eye for blindness secondary to glaucoma.

Following a presumptive clinical diagnosis of OCP, he was treated with a short course of oral prednisone. The eruption on his eyelids subsequently recurred, and he was referred to our clinic for further evaluation and management.

Physical examination showed marked bilateral conjunctival hyperemia with blunting of the conjunctival fornices bilaterally. Erythematous plaques with mild scale were present circumferentially on the bilateral upper and lower eyelids and associated with significant eyelid edema (Fig 1, A). No antecedent or concurrent vesicles, erosions, or scarring were identified on other mucosal or cutaneous sites.

A punch biopsy from the infraorbital skin revealed changes consistent with rosacea-type periorificial dermatitis (Fig 2). A biopsy of the inferior conjunctiva was also performed, which showed submucosal fibrosis associated with squamous metaplasia (Fig 3). There was no deposition of immunoglobulins along the epithelial basement membrane zone on direct immunofluorescence (DIF). Indirect immunofluorescence (IIF) studies did not detect circulating autoantibodies against the basement membrane zone or epithelial cell surface. Enzyme-linked immunoassay testing for bullous...

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Abbreviations used:

DIF: direct immunofluorescence
IIF: indirect immunofluorescence
OCP: ocular cicatrical pemphigoid
pemphigoid 180 and 230 IgG antibodies was negative. Patch testing was subsequently performed, which did not indicate any allergy to a standard series (American Contact Dermatitis Society Core Allergen Series), cosmetic series (Dormer Chemotechnique), or custom series of allergens that included the patient's 4 topical glaucoma medications.

Ocular pseudopemphigoid secondary to rosacea was suspected given the clinicopathologic findings and lack of resolution following trial discontinuation of topical glaucoma medications and treatment with triamcinolone 0.1% cream (Fig 1, B). Concurrently, the patient was started on acetazolamide therapy by his ophthalmologist for the management of his glaucoma. He was also started on oral doxycycline 50 mg and metronidazole 0.75% cream, both twice daily. One month later, the patient demonstrated significant improvement in his symptoms and ocular findings, along with resolution of his eyelid dermatitis. The patient's symptoms continued to improve over the following 8 months on oral doxycycline and topical metronidazole therapy (Fig 1, C).

**DISCUSSION**

Ocular pseudopemphigoid was first described in 1976 by Patteu and colleagues. While the pathogenesis of ocular pseudopemphigoid is not well understood, it has been primarily reported secondary to the prolonged use of topical antiglaucoma medications. Ocular pseudopemphigoid may also occur due to other diseases, such as rosacea, atopic keratoconjunctivitis, lichen planus, and Sjogren syndrome. In the largest retrospective study of this disorder, ocular pseudopemphigoid occurred secondary to topical glaucoma therapy in 28.3% of patients, followed by rosacea and atopic keratoconjunctivitis in 20% and 8.3% of patients, respectively.

The clinical findings of ocular pseudopemphigoid are indistinguishable from those of OCP. These features include chronic conjunctivitis and conjunctival scarring that may go unnoticed in early stages of the disease. As the clinical course progresses, conjunctival scarring leads to the shortening of the conjunctival fornices and formation of conjunctival adhesions (symblepharon). In severe cases, acute ulcerative lesions and permanent vision loss can occur.

Several histopathologic features of ocular pseudopemphigoid have been reported on conjunctival biopsy, which are also observed in OCP. These include subepithelial fibrosis, reduction/loss of goblet cells, chronic inflammation, squamous metaplasia, and keratinization of the conjunctiva. With regard to immunopathologic studies, DIF and IIF tend to be negative in ocular pseudopemphigoid. In contrast, DIF has a sensitivity of 60%-80% for OCP, while IIF has a sensitivity of 10%-40%.

We favor the diagnosis of ocular pseudopemphigoid in this patient due to lack of subepithelial split on histopathology of the conjunctiva, negative DIF/IIF and enzyme-linked immunosorbent assay, and absence of antecedent oral mucosa involvement, which occurs in the majority of patients with OCP.

While our patient had a history of topical glaucoma therapy, we believe that ocular pseudopemphigoid most likely occurred secondary to rosacea, given the clinical and histopathologic findings of the eyelid skin, in addition to the significant improvement after 1 month of treatment with oral doxycycline and topical metronidazole. Furthermore, in the aforementioned study by Thorne et al, a history of multidrug antiglaucoma therapy was present in 97.4% of patients with ocular pseudopemphigoid. Interestingly, the authors suggested that polypharmacy may confer an increased risk for the development of cicatrizing conjunctivitis.

Fig 1. A, Bilateral conjunctival hyperemia with scaly, erythematous circumferential plaques and marked edema on the bilateral upper and lower eyelids upon presentation, 5 months after the symptoms first developed. B, One month after the initial presentation and status post lack of improvement with triamcinolone 0.1% cream. C, Clinical improvement status post 8 months of treatment with oral doxycycline and metronidazole cream.
In patients presenting with clinical signs of OCP and negative immunofluorescence studies, it is important to consider both OCP with undetectable tissue-bound and/or circulating autoantibodies, as well as ocular pseudopemphigoid, given the sharp contrast in management.

For OCP, systemic corticosteroids and B-cell–depleting regimens with cyclophosphamide or rituximab are the mainstay of therapy. In contrast, if ocular pseudopemphigoid is suspected, a prompt management of the underlying cause is essential to stop the disease progression and the development of severe ocular complications and potential vision loss.

Furthermore, it is important to note that in patients suspected to have ocular pseudopemphigoid, including those with negative DIF and/or IIF, close monitoring for the progression of the disease is essential, as there may not be improvement despite the treatment of the underlying cause of ocular pseudopemphigoid. In such cases, patients should be managed with standard therapy for OCP. Given that no single test reliably differentiates these 2 disorders, clinical, historical, histopathologic, and immunopathologic findings are important to correlate.

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