

Case Report

Mucous membrane pemphigoid presenting after cataract surgery

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Abstract

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Mucous membrane pemphigoid is a rare autoimmune disorder of the ocular surface and other mucosa, causing scarring of the conjunctiva and cornea. Cataract surgery is yet considered a safe procedure in these cases. However we present a case of ocular pemphigoid manifested four weeks after an uneventful cataract procedure in both eyes. Clinical exam and histology excluded other causes of cicatrizing conjunctivitis or Sjogren syndrome. This may be the first reported mucous membrane pemphigoid presented after cataract surgery, in a previously asymptomatic patient.

Keywords: Cataract surgery, Dry eye, Mucous membrane pemphigoid, Ocular cicatricial pemphigoid, Ulcerative keratitis

INTRODUCTION

Mucous membrane pemphigoid (MMP) is a rare autoimmune disorder of the ocular surface. The incidence of MMP is unknown, many ophthalmologists seeing only a few cases during their practice (Scully et al., 1999). In ophthalmology centers the incidence is between 1:8000-1:46000 patients (Dart, 2005). It is characterized by chronic cicatrizing conjunctivitis and progressive conjunctival subepithelial fibrosis (Frith et al., 1989). MMP may also involve other mucosa, especially oral mucosa, or skin. Dry eye, keratinization of the ocular surface, corneal ulcer with pannus formation and limbal stem cells loss may be the cause for visual impairment in half of the patients, especially if not diagnosed or treated early (Dart, 2005; Lee et al., 2018; Williams et al., 2016). Ocular manifestations can also be referred to as ocular cicatricial pemphigoid. MMP is characterized by deposits of autoantibodies on the basement membrane zone at the epithelial-subepithelial junction of mucous membranes and occasionally the skin. Complement activation and infiltration of the conjunctiva by neutrophils, macrophages and activated T lymphocytes cause conjunctival and corneal scarring. (Georgoudis et al., 2019) Sometimes the immune response is caused by

drugs inducing MMP, like antiglaucomatous drops (Butt et al., 1998).

Clinical Case

A 79 years old male presented with bilateral ocular surface complaints, weeks after uneventful cataract surgery, performed in both eyes, one week apart. Complaints included dry eye, redness and intense foreign body sensation. He received multiple consultations, all concluded with a dry eye syndrome, which may have temporarily been induced by cataract surgery. Six months after moderate artificial tears use, the vision started to drop. The patient was then hospitalized with low vision, hand movement perception in both eyes. Eye exam showed perikeratic congestion, corneal ulcer covering most of the cornea in right eye and 2/3 of the cornea in left eye. In both eyes, a central corneal white plaque was soon observed, while the patient already receiving treatment (Figure 1).

Corneal vascularization became prominent, especially in the right eye. Discreet forniceal conjunctival fibrosis



Figure 1. Perikeratic congestion, epithelial defect covering most of the cornea, vascular invasion, and central white corneal plaque (left eye).



Figure 2. Same eye, after treatment.

was noticed. Schirmer test was zero mm. Xerostomy and parotid gland enlargement prompted for Sjogren syndrome evaluation. Small salivary glands biopsy and autoantibodies (anti-Ro, anti-La) were instead negative. Erythrocytes sedimentation rate, C-reactive protein, antinuclear antibodies, cytoplasmic and anti-neutrophil

cytoplasmic antibodies, immune circulating complex, complement (C3, C4) were normal. Calcium, D-vitamin, and parathormone were normal. Conjunctival biopsy showed signs of fibrosis in lamina propria and lymphoplasmocytic infiltration and confirmed the clinical picture of the mucous membrane pemphigoid (Figure 3).

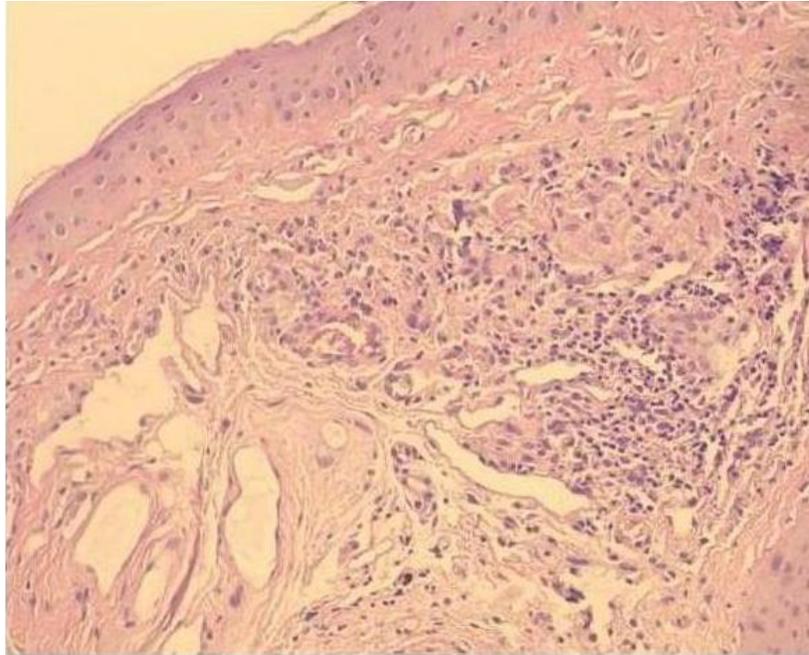


Figure 3. Goblet cells loss, lymphocytic infiltrate, and fibrosis. (Hematoxylin eosin, 200x)

Treatment was focused on lubrication and inflammation. This included artificial tears (gels, ointments, vitamin A), autologous serum, topical Cyclosporine A, high dose Methylprednisolone iv. Topical fluoroquinolones (Ofloxacin) were discontinued when the corneal white infiltration was observed. Infection prophylaxis continued with topical tobramycin. Amniotic membrane patching of the right eye showed no benefits. Because the ocular surface showed no signs of relief, systemic immunosuppression was administered. Methotrexate and Cyclosporine A were not tolerated because of systemic reactions. The patient received Azathioprine with a positive ocular response after four weeks of treatment. The white corneal plaques disappeared under treatment (Figure 2). Epithelium defect diminished very slowly, with vessels invading the limbus circumferentially in right eye and in the inferior half on the left eye. Visual acuity has stabilized at 1/50 in right eye and 4/50 in left eye, until present. The high level of inflammation and epithelial defect extended over a period of at least 5 months, from hospitalization until the slow remission.

DISCUSSIONS

MMP diagnosis was based mainly on clinical evaluation completed with a positive histopathological exam. Clinical appearance should meet the criteria of inclusion in MMP: bilateral conjunctival scarring, forniceal shortening, symblepharon formation, persistent epithelial defects, corneal ulceration, and limbal stem cell deficiency. The

presence of conjunctival scarring without forniceal shortening should place our case in an early stage MMP. Immunofluorescence microscopy is not mandatory if other causes of cicatricial conjunctivitis can be ruled out, including with biopsy (Georgoudis et al., 2019).

Undiagnosed Sjogren syndrome causing bilateral corneal ulceration was the main differential in our case, given the acute corneal presentation with the highly severe dry eye. Immunology and minor salivary gland biopsy ruled out this diagnosis. A multidisciplinary team was essential in managing this type of patient. The rheumatologist assisted us in the diagnosis process and established the dosing for the immunosuppression.

Differential diagnosis excluded other causes of cicatrizing conjunctivitis: infectious diseases, immune disorders or previous medication (Table 1) (Georgoudis et al., 2019; Kiire et al., 2011). The patient presented no history of atopic disorders, no atopic dermatitis and there were no prominent papillae on the conjunctiva. Atopic keratoconjunctivitis could have explained the corneal centrally located white plaques (corneal shields). However, corneal epithelial defect covered a larger area than the plaques and these formed while the patient was receiving high doses of systemic steroids. Finally, the biopsy was not suggestive for atopic disease. The white bilateral plaques could have been areas of keratinization, calcification or fluoroquinolone deposits. Fluoroquinolones were interrupted when the plaques were observed and the plaques eventually disappeared, leaving a thinner cornea due to deeper ulceration. Calcium metabolism was found to be normal.

Table 1. Differential diagnosis in Cicatricial Conjunctivitis

Causes of cicatrizing conjunctivitis
Infectious: chlamidia, adenovirus
Atopic keratoconjunctivitis
Rosacea
Trauma: burns, radiation
Drug-induced pemphigoid: topical antiglaucomatous drops
Stevens Johnson syndrome
Bulous disorders with rare ocular involvement: pemphigus vulgaris, epidermolysis bullosa

MMP may be triggered by topical medication, antiglaucomatous drops for instance (Butt et al., 1998). The trigger in our case seems to have been the cataract surgery. There is no other case report of a pemphigoid triggered by cataract surgery in a previously asymptomatic patient, to our knowledge. Cataract surgery is known to increase the inflammation on the eye surface and mild dry eye syndrome following the surgery is well established. Dry eye management is important before the intervention. Active conjunctival inflammation needs to be controlled also. Sangwan (Sangwan et al., 2018) summarized the outcomes of cataract surgery from three different studies, noting significant improvement of visual acuity early postoperatively, and general worsening afterwards due to natural disease progression.

There are a series of reports (Puranik et al., 2013) suggesting the safety of cataract surgery in patients already diagnosed with MMP. There is though a case report (Kiire et al., 2011) where cataract surgery precipitated a peripheral ulcerative keratitis in a well-established MMP patient, with a disease followed for 6 years. Sainz (Sainz et al., 1988) reported cataract surgery in 20 patients with biopsy-proven cicatricial pemphigoid, with no patient progressing in disease stage. Corneal ulcers did develop in 3 patients with systemic immunosuppression no longer tolerated after surgery, linking the outcome to inflammatory exacerbation after surgery. He indicates that after successful abolition of all conjunctival inflammation through chemotherapy, cataract surgery may be safely performed in patients with cicatricial pemphigoid.

CONCLUSION

This case highlights the challenges to establish a diagnosis in MMP and the lack of immediate response to treatment in MMP, in this case also because of the late presentation. Multidisciplinary approach was needed for the proper management of MMP. Dry eye signs after cataract surgery should be carefully evaluated in order to exclude a more serious ocular surface condition.

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Declaration of Conflicting Interests

The Authors declare that there is no conflict of interest

Author Declaration

Written informed consent was obtained from the patient for his anonymized information and images to be published in this article. Our institution does not require ethical approval for reporting individual cases.

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