Cicatricial Conjunctivitis and Concurrent Clinical Features: A Case Study

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ABSTRACT

PURPOSE: We report a case of cicatricial conjunctivitis to illustrate the clinical approach for management of such a case. This is a 52-year-old Chinese man who presented with bilateral red eyes associated with itching for a year. He had a history of chronic itchy rash in the chest and the arms. Otherwise there was no history of autoimmune disease, asthma, sinusitis, or drug allergy. On examination, he had diffuse hyperemia over both conjunctivae, with symblepharon involving the inferior bulbar and palpebral conjunctivae, associated with cicatrization of the caruncles, and obliteration of inferior lacrimal puncta. There were mild subtarsal papillary reaction with Meibomian gland dysfunction and presence of inferior mis-directed eyelashes. The corneas showed multiple foci of superficial epitheliopathy. A clinical diagnosis of chronic cicatricial conjunctivitis was made, with differential diagnosis of chronic atopic allergic conjunctivitis. Conjunctival biopsy was performed from the inferior conjunctival adhesions and it showed patchy chronic stromal inflammation with focal lymphoplasmacytic sub-epithelial infiltrates and loss of goblet cells. The stroma shows marked fibrosis, with no evidence of mast cells or eosinophils. In particular, there were no deposits of IgA, IgM, C3, and fibrinogen in the basement membrane. The patient was treated with topical loteprednol, glucocorticoids and artificial tears, and his symptoms improved after treatment.

CONCLUSION: We present a man with cicatricial conjunctivitis with chronic subconjunctival inflammation and fibrosis but no immune deposits in the conjunctival basement membrane on histology, to illustrate the clinical approach and diagnostic challenges in managing such a case.

KEYWORDS: Cicatricial conjunctivitis, dry eye, conjunctival fibrosis, conjunctival biopsy

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Introduction

Cicatrizing conjunctivitis may be caused by physical or chemical trauma, infections, oculocutaneous disorders, drugs, or systemic disorders. Proper management is essential to avoid visual impairment, which may be severe and can lead to blindness in some cases. Moreover, patient's quality of life may be affected due to severe ocular irritation. We report a case of cicatricial conjunctivitis to illustrate the clinical approach for management of such a case.[1]

Case Presentation

We report a 52 years old Chinese male presenting with the complaint of bilateral red eyes associated with itching for a year. The redness of the eyes was constant, with intermittent watering, but no associated pain, grittiness, photophobia, or discharge. There was transient, episodic blurring of vision related to dry eyes, which was relieved with topical lubricants. There was no diplopia.

He has a history of chronic rash in the chest and arms that suggests atopy or eczema. There was no history of sinusitis or asthma.

He had been diagnosed with type 2 diabetes mellitus, hypertension, and dyslipidemia, and he was on medication for all of these conditions. There was no history of any other autoimmune or dermatological disease, and no family history of inherited ocular and skin diseases. He did not have any history of allergy to drugs or drug-related skin eruptions and did not have previous treatment with systemic immunosuppressive drugs. He did not smoke cigarettes.

There was no past history of ocular procedures such as diathermy, surgery or trauma, or contact lens wear. His intraocular pressures were known to be transiently elevated in response to topical corticosteroid eye drops.

On examination, this was a man with moderate build with normal hair distribution and facial appearance. There was maculopapular rash over the chest and arms involving both the flexor and extensor surfaces of the elbow. There were no excoriation marks. There were no rosacea or acneform lesions on the face, and no mouth ulcers.

His conjunctiva showed bilateral moderate diffuse bulbar hyperemia, with grade 1 subtarsal papillary reaction in each eye. Notably there was symblepharon in each eye (Figure 1) involving the inferior bulbar and palpebral conjunctiva involving up to 3 clock hours, and associated with cicatrization of the caruncle. There were no chemosis, deposits, pigmentation, or scleral nodules. The inferior lacrimal punctum was noted to be obliterated by scarring. There was no conjunctivochalasis, ankyloblepharon or lagophthalmos, and eye movements were normal.

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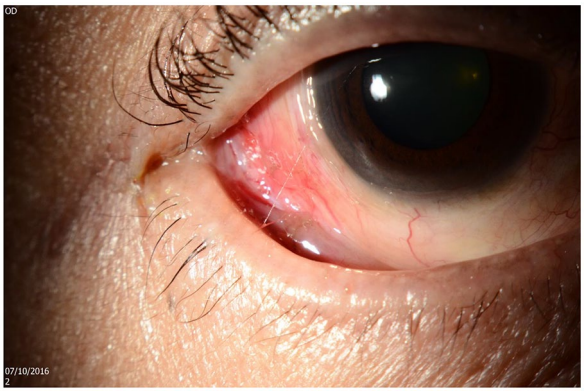

Figure 1. A Slit-Lamp photo showing the remaining conjunctival adhesions after conjunctival biopsy.

There was faint inferior corneal punctate fluorescein dye staining in both eyes, without any confluent epithelial defects or filaments. There was no corneal infiltrate or edema. There were multiple foci of inferonasal superficial right corneal scarring, not associated with thinning, vascularization, or calcification. Corneal sensation was normal on screening.

The fluorescein tear break up times was 4 and 5 seconds in the right and left eyes respectively. The Schirmer I test (without anesthesia) was 20 mm and 25 mm/5 minutes respectively. There were a few misdirected small eyelashes in the lower eyelids nasally, but with no corneal touch.

There was mild advancement of the Marx's line in the upper eyelids bilaterally, with borderline changes in the Marx's line in the lower eyelids, and no entropion or scalloping of the lid margins. On meibomian gland evaluator assessment, none of the glands demonstrated liquid meibum. With diagnostic force manual expression, only one meibomian gland orifice produced whitish viscous meibum in the right lower eyelid.

He had excellent presenting uncorrected Snellen visual acuity of 6/7.5 in each eye. His intraocular pressures were 17 and 19 mmHg in each eye respectively. Anterior chambers were deep and quiet, the vitreous chamber and posterior segments were normal on examination.

A clinical diagnosis of chronic cicatricial conjunctivitis was made, with differential diagnosis of chronic atopic allergic conjunctivitis. He was cautiously started on loteprednol eyedrops once a day, cyclosporine 0.5% eyedrops 4 times a day, preservative free lubricants hourly, and carbomer gel at night in both eyes.

In order to obtain a more definitive diagnosis, conjunctival biopsy was performed from the inferior conjunctival adhesions. The histology section showed patchy chronic stromal inflammation with focal interface inflammation (Figure 2A and B). There was a mild lichenoid chronic lymphoplasmacytic inflammatory infiltrate in the subepithelial stroma. Focal interface inflammation was present that suggested a possible underlying autoimmune cause. The stroma showed marked fibrosis. There was loss of goblet cells and mild squamous metaplasia of the epithelium suggestive of dry eye. Vascular dilatation was observed in the conjunctival stroma.

Features suggestive of allergic conjunctivitis such as mast cells and eosinophils were not observed (Figure 2B). Intraepithelial bullae or full thickness separation of the epithelium from the stroma were not seen. There were no features of ocular cicatricial pemphigoid on the immunofluorescence or immunohistochemistry findings (Figure 2C–K). Linear deposits of IgA, IgM, C3, and fibrinogen were not seen in the sub-epithelial basement membrane zone (Figure 2C–K). Although intercellular staining may be present in pemphigus disease of the skin, this staining in the conjunctiva is non-specific and not diagnostic of pemphigus (Figure 2C and D) without relevant clinical correlation. Lack of fibrinogen staining in the basement membrane suggests that lichen planus is unlikely. There was no evidence of dysplasia or malignancy.

Discussion

This patient has cicatricial conjunctivitis confirmed with histological features of chronic inflammation and subconjunctival fibrosis. One month after starting topical loteprednol, a glucocorticoid medication, the hyperemia in the conjunctiva has subsided. He will need review in the future because of the relapsing nature of the hyperemia that he described in the history, and possibility of worsening eyelash misdirection. We prescribed artificial tears for dry eye and topical mast cell stabilizer to prevent any allergic episodes. Common presentations of cicatricial conjunctivitis includes dry eye, conjunctival injection, symblepharon, ankyloblepharon, cicatricial entropion and trichiasis, and corneal complications such as punctate corneal opacification, persistent corneal epithelial defects leading to non-infectious and secondary infectious corneal ulcers. Some causes of cicatricial conjunctivitis that may not be so apparent include rosacea keratoconjunctivitis and atopic keratoconjunctivitis, and certainly in this case, the skin lesions suggest that some allergic conjunctivitis in the past may have contributed to the ocular fibrosis.[1,2]

The differential diagnosis of chronic cicatricial conjunctivitis includes autoimmune diseases such as ocular pemphigoid (OCP) and other different etiologies. OCP is characterized by chronic fibrosis and subepithelial blistering,[3,4] but the latter was not seen in this patient. Another possibility is lichen planus[5,6] although the skin features of this patient were not typical and fibrinogen immunofluorescence of the basement membrane was not seen. Other non-autoimmune causes include thermal and chemical burns, post-infectious conjunctivitis, and Stevens-Johnson syndrome.[7] He did not have any triggers in the presenting history to suggest any of these.

The management of cicatricial conjunctivitis is according to the underlying etiology. However, it may not be always possible to identify the underlying cause and in cases similar to ours, one should manage contributing factors such as allergy and potential complications such as trichiasis, meibomian gland dysfunction, and dry eye.[2]

Interestingly, co-existence of atopy in patients with OCP has recently been reported. Out of 230 patients with biopsy proven

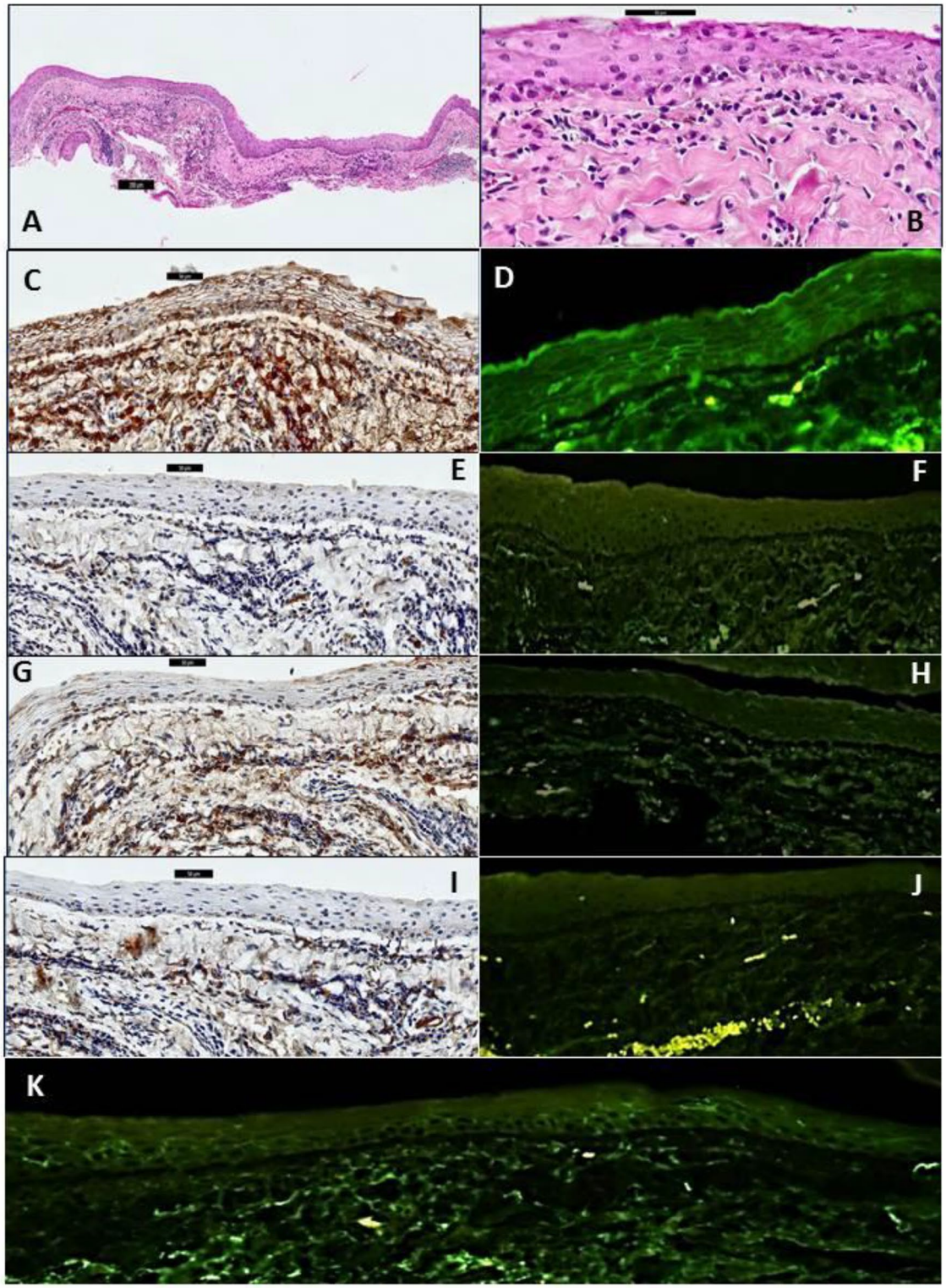

Figure 2. (A) Conjunctival biopsy: Patchy chronic stromal inflammation with focal interface inflammation. No intra epithelial or full thickness bullae. Squamous metaplasia of the epithelium with loss of goblet cells. Histological features are not suggestive of blistering disorders. Focal interface inflammation may be associated lichen planus. (Hematoxylin and Eosin, 4×). (B) Conjunctiva: Lymphocytic inflammation without eosinophils or mast cells. Stromal fibrosis, bands of collagen instead of normal loose conjunctival stroma. (Hematoxylin and Eosin, 40×). (C, E, G, and I) Immunohistochemistry stains with IgG, IgA, IgM, and C3 respectively. There is no linear basement membrane staining of IgG (C), IgA (E), IgM (G), and C3 (I). There is patchy intercellular staining of IgG (C). No intracellular staining is seen. (D, F, H, J, and K) Immunofluorescence stains with IgG, IgA, IgM, C3, and Fibrinogen respectively. There is no linear basement membrane staining of IgG (D), IgA (F), IgM (H), C3 (J), and Fibrinogen (K). There is patchy intercellular staining of IgG (D). No intracellular staining is seen. This staining profile excludes ocular cicatricial pemphigoid and other blistering conditions such as pemphigus. The lack of linear and thickened basement membrane immunofluorescence with fibrinogen excludes lichen planus.

OCP, 33 have features of atopy such as asthma, hay fever and eczema, out of these 23 also have features of atopy in the conjunctival biopsy. The authors emphasized the use of anti-allergic treatment to treat residual symptoms in such OCP patients.[8]

The need for a routine conjunctival biopsy in cases of cicatricial conjunctivitis has been debated,[9] since a negative finding for basement membrane immunoglobulins does not exclude OCP or the need to begin systemic immunosuppression.[10] However, the prognosis of cicatricial conjunctivitis is worse in cases of autoimmune disease uncovered through biopsy. In some cases, conjunctival biopsies may only be clinically warranted after partial or non-resolution of conjunctival inflammation and therefore findings may be masked by treatment effects. Yet despite the risk of a negative biopsy result, it remains important for the exclusion of masquerades like sebaceous cell carcinoma. His diabetic status, lack of active corneal inflammation, chronicity of clinical findings and subsequent response to topical treatment were reasons for not commencing systemic therapy. In this case and in general, follow up consultations are necessary in view of potential recurrences with serious cornea complications. Further recurrences would require a dermatological referral, as it was reported that rituxamb and/or intravenous immunoglobulin is a preferred strategy for OCP patients with evidence of atopy.[8] Patients with OCP can also develop extraocular disease even if extraocular features are absent in initial presentation.[11]

In conclusion, we present a man with cicatricial conjunctivitis with chronic subconjunctival inflammation and fibrosis but no immune deposits in the conjunctival basement membrane on histology, to illustrate the clinical approach and diagnostic challenges in managing such a case.

Author Contributions

AF: wrote discussion, edited and revised manuscript, literature search.
AC: performed sectioning and histology, provided histological images, discussed case, edited manuscript.
LT: performed biopsy, examined patient, wrote first draft, taken images and edited manuscript.

Patient Consent

Consent to publish the case report was obtained. This report does not contain any personal information that could lead to the identification of the patient. Photographs and figures have no identifying features.

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