

Treatment of ligneous conjunctivitis with amniotic membrane transplantation and topical cyclosporine

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Ligneous conjunctivitis (LC) is a rare form of bilateral chronic recurrent disease in which thick membranes form on the

palpebral conjunctiva and other mucosal sites. We report the clinical features and describe the management of two cases. Case 1 was an 8-month-old patient with bilateral membranous conjunctivitis. Case 2 was a 5-year-old patient with unilateral membranous conjunctivitis, esotropia, mechanical ptosis and complicated cataract, and had been treated with a number of medications. Histological investigation of the membrane in both cases showed LC. Treatments with amniotic membrane transplantation and institution of topical cyclosporine have shown good response. There has been complete resolution of the membranes with no recurrence at the end of 40- and 28-month follow-ups, respectively. No treatment related side effects were seen. Thus, it appears that amniotic membrane transplantation and topical cyclosporine are effective alternatives for the treatment of LC.

Key words: Amniotic membrane transplantation, ligneous conjunctivitis, pseudomembrane, topical cyclosporine

Ligneous conjunctivitis (LC) is a rare type of chronic and recurrent pseudomembranous and membranous conjunctivitis. In most cases, infants and children are affected, but the disease may manifest at any age.^[1] Both eyes are affected in up to 51% of cases, and corneal involvement, a complication that may lead to blindness, occurs in 20–30% of cases. Similar lesions in LC can occur on other mucous surfaces.^[1]

The management of LC is difficult, and no satisfactory treatment exists. Tabbara reported that fresh frozen plasma

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applied topically and subconjunctivally after membrane excision was effective.^[2] Heidemann and associates treated a case of LC with topical plasminogen.^[3] Treatment with topical heparin and cyclosporine A (CsA) was favorable in a case of LC and cataracts in a 10-year-old boy.^[4]

In this paper, we describe the clinical features and management of two cases of recalcitrant LC.

Case Reports

Case 1

An 8-month-old male child was referred to our service with a history of membrane formation on the upper and lower palpebral conjunctiva of both eyes since 2 months after birth. *Hemophilus influenzae* was cultured from the conjunctival smear. Examination under general anesthesia revealed firmly thickened, sessile membrane and papillomatous lesion on the upper and lower tarsal conjunctiva in both eyes [Fig. 1]. There was no involvement of the bulbar conjunctiva and cornea in both eyes, and the membranes and papillomatous lesions were excised. Postoperatively, the patient was treated with corticosteroid and antibiotic eye drops. Histological

examination of the membrane was suggestive of LC [Fig. 2]. Three months after the surgery, membrane and papillomatous lesion recurrence was noted in both eyes. The patient was started with CsA 2% drops in olive oil, four times daily. Local tolerability was excellent. The patient complained of a mild burning and sensation of a foreign body in the eye for a few minutes after application of the CsA drop. Excision of the membranes together with amniotic membrane (AM) transplantation for conjunctival reconstruction was decided upon. Before surgery, the ethics committee of our department approved the treatment, and the family provided written informed consent. The human AM was prepared according to Tseng *et al.*'s method.^[5] The new membrane and papillomatous lesion were excised under general anesthesia. The AM epithelium was secured up to the conjunctival edge at the mucocutaneous junction and the fornices with 8-0 polyglactin sutures in both upper and lower tarsal conjunctiva [Fig. 3]. Two months postoperatively, the AM had dissolved. Topical application of CsA 2% four times daily was continued for 6 months. The patient was examined monthly for the first 6



Figure 1: Case 1, ligneous conjunctivitis of right eyelid (a) and papillomatous lesion of left eyelid (b)

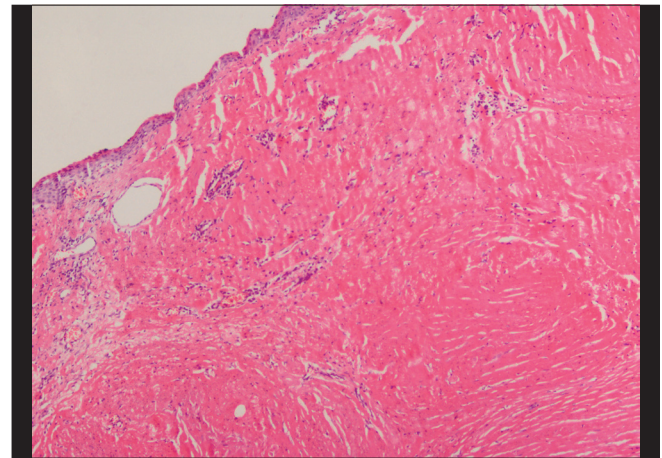


Figure 2: Case 1, subepithelial deposits of amorphous hyaline-like eosinophilic material, vessel proliferation and mixed inflammatory cell infiltration are noted in the histological section of the conjunctiva (original magnification $\times 10$, hematoxylin and eosin)

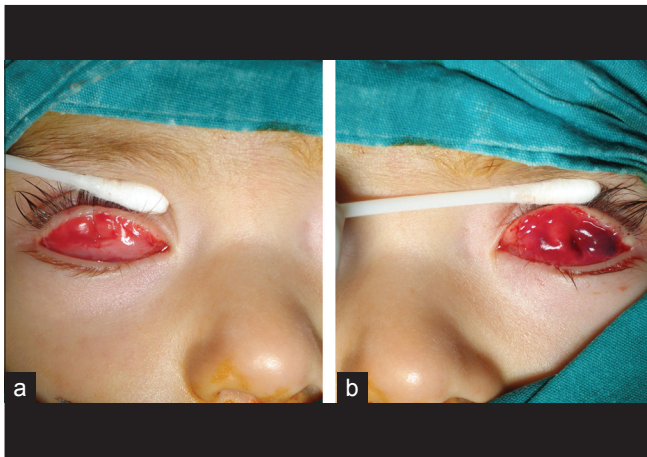


Figure 3: Case 1, intraoperative photographs, amniotic membrane transplantation of right (a) and left (b) upper tarsal plate



Figure 4: Case 1, postoperative 40th month view, the membrane disappeared, leaving moderate residual conjunctival scarring

months and then quarterly by the same ophthalmologist. At the end of 40 months follow-up, the membrane had resolved, leaving moderate residual conjunctival scarring on the upper and lower conjunctiva in both eyes [Fig. 4].

Case 2

A 5-year-old female child was brought to us with a right sessile and dense membrane on the right upper eyelid since 1 month after birth. The membrane had previously been removed, and she had received long-term topical steroid treatment in another clinic. Upon examination, we found that she had right mechanical ptosis, esotropia, corneal leukoma, and complicated cataract, possibly steroid induced. The membrane had a firm, fibrous consistency with elevated edges and measured 20 × 14 mm in the right upper eyelid [Fig. 5]. There was minimal inflammation in the lower eyelid. Her visual acuity was motion hand-20/20 in her right and left eyes, respectively. The membrane was excised from the upper eyelid. Histopathological analysis of the removed pseudomembrane showed eroded epithelium with massive subepithelial deposits of amorphous hyaline-like eosinophilic

material and granulation tissue together with inflammatory cell which consisted of plasma cells and lymphocytes [Fig. 6]. The eosinophilic materials were negative for Congo red stain. After surgery, she was treated with CsA 2% drops in olive oil, four times daily. Recurrence of the conjunctival lesion was noted at the site of excision 2 months later. The lesion was again excised. The child did not come back for follow-up. The patient returned 2 years later with the same lesion. The lesion was excised and the AM epithelium was secured up to the conjunctival edge at the mucocutaneous junction and the fornices with 8-0 polyglactin sutures in the right upper eyelid [Fig. 7]. The right eye was treated with topical CsA four times daily and tobramycin eye drops six times daily.

Four months after AM transplantation (AMT), the patient showed new recurrence at the same site. The new pseudomembranous lesion was much smaller and softer; it was removed and the AM was used to cover the excision site. Treatment with topical CsA four times daily was continued for 6 months postoperatively. There was no recurrence of the membranes at the end of 28-months follow-up [Fig. 8].



Figure 5: Case 2, ligneous conjunctivitis with dense membrane on the upper tarsal plate

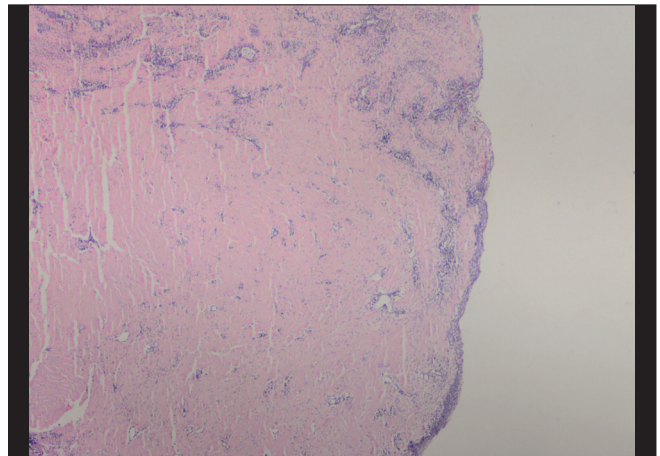


Figure 6: Case 2, histopathological appearance of ligneous conjunctivitis. Large amorphous hyaline-like eosinophilic deposits are present in the stroma (H and E, ×4)



Figure 7: Case 2, intraoperative photograph, amniotic membrane transplantation and corneal leukoma at presentation



Figure 8: Case 2, complete resolution of the conjunctival membranes on the upper tarsal plate 28 months after the treatment

Discussion

Until recently, the etiology of LC has largely been unknown. In patients with LC, there is a major deficiency of plasmin-mediated extracellular fibrinolysis that is required in the normal process of wound healing and is required for initial removal of the fibrin-rich matrix as well as for the remodeling of the granulation tissue and completion of wound healing as well as the capacity of cellular migration.^[1,6] Molecular genetic studies in 38 patients with LC revealed distinct mutations in the plasminogen gene. The most common genetic alteration was a K19E mutation found in 34% of patients.^[7]

AMT effectively facilitates epithelialization and reduces inflammation and scarring. The exact mechanism is not known. The AM probably acts as a physical barrier against polymorphonuclear leukocytes and inflammatory mediators in tear films.^[8] Highly potent proinflammatory cytokines are suppressed by AM stromal matrix. Some of the anti-inflammatory and anti-scarring effects of AM are believed to be due its effect on apoptosis.^[9] Since the distribution of α subchains of type IV collagen in the basal membrane of the AM is similar to that of the conjunctiva, the AM can be a more effective replacement for the conjunctiva.^[10] Barabino *et al.*^[11] were the first to carry out AMT in the case of LC successfully. Rodríguez-Ares *et al.*^[12] reported no recurrence in patients with LC who were followed up 39 months after AMT.

Immunohistochemical studies of these membranes have revealed a predominance of T-cells and focal accumulation of plasma cells and B-lymphocytes in the inflammatory infiltrate, particularly with IL-2 receptor expression.^[13] CsA is a highly specific immunomodulator that inhibits primarily T-lymphocyte proliferation.^[14] Several small, uncontrolled case series of CsA therapy have indicated improvement in patients with LC that is refractory to other models of treatment.^[13,15]

In summary, the present paper describes the clinical treatment for two cases of LC. AMT and topical CsA provide a favorable outcome as an alternative treatment for the treatment of LC.

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