

Prevention of Recurrence of Ligneous Conjunctivitis with Subconjunctival and Topical Autologous Fresh Frozen Plasma-A Case Report

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Abstract

Objective: To report the case of a 6 year-old male child that presented ligneous conjunctivitis (LC) after infectious conjunctivitis, showing recurrent membranes after surgical removal; treatment with autologous fresh frozen plasma (AFFP) resulted in remission of the membranes.

Methods: Ophthalmologic examination, plasminogen functional activity and plasmatic plasminogen level were measured for LC diagnosis. Surgical removal of the membranes was performed and light microscopy was applied on biopsies from both eyes. Topical treatment with corticosteroids and aminoglycosides was administered on both eyes. Bilateral recurrence was treated with the administration of a single subconjunctival injection of 0.75 ml of AFFP, continued with topical application every four hours for four weeks, tapered to every 6 hours to present.

Results: The diagnosis of LC was confirmed with the 48% of plasminogen functional activity and supported with histological typical findings. Following surgical removal of membranes and topical treatment with corticosteroids, bilateral recurrence of membranes was observed after one month. Treatment with subconjunctival and topical AFFP revealed no recurrence of LC membranes after 4 years of follow-up.

Conclusion: In our patient a single subconjunctival injection associated with topical administration of the AFFP impeded the recurrence of hard wood-like membranes presented in LC.

Keywords: Ligneous conjunctivitis; Fresh frozen plasma; Plasminogen; Membranes

Introduction

Ligneous conjunctivitis (LC) is a rare and chronic disorder which is characterized by hard wood-like membranes on palpebral and bulbar conjunctiva [1-4]. It usually presents when plasminogen functional activity is under normal range (80-120%), usually below 52%, and plasminogen level in blood generally <1.2 mg/dl (normal range 6-25 mg/dl) [3-7]. Severity is associated with a low plasminogen functional activity, values below 5% can affect all mucous surfaces, and the disease could present as a systemic disorder [4,7,8]. LC may occur after infectious conjunctivitis or ophthalmic surgical treatment, associated with recurrence of membranes after removal [3,4,8]. Plasminogen topical administration has demonstrated a plausible efficient treatment for preventing the recurrence of LC [1-4]. The goal of our study is to report the case of a 6 year-old male child with post infectious LC, that when he was 2 years old presented recurrence of the disease after surgical resection and combined treatment with topical tobramycin, dexamethasone and cyclosporine A. Treatment with autologous fresh frozen plasma (AFFP) resulted in remission of the membranes.

Case and Methods

A 2 year-old male child with bilateral conjunctivitis, product of the second pregnancy of nonconsanguinous Mexican parents was attended

at the Service of Ophthalmology in the Hospital General Dr. Manuel Gea González 4 years ago. The first revision disclosed an inflammatory process and erythema of the conjunctiva. A culture of the conjunctival discharge confirmed a conjunctivitis produced by *Staphylococcus aureus*. The ophthalmic examination disclosed hard wood-like membranous lesions covering the upper and lower bulbar and tarsal conjunctiva of both eyes (Figure 1), rest of ocular examination was normal.



Figure 1: Two year-old male child with LC. Image showing the left eye of a two-year old male child disclosing hard wood-like membranous lesions in the left lower palpebral conjunctiva.

Diagnosis of LC was confirmed with plasminogen functional activity of 48% and plasminogen level of 1.2 mg/dl. The patient's

parents were aware of the disease, risks, and benefits of the procedures and signed informed consents were obtained. Research and Ethics Committees approval was also obtained.

Membranes were surgically excised and light microscopy was performed on formalin fixed, paraffin-embedded material (membranes), provided from the original biopsies from both eyes.

After surgery, topical dexamethasone and tobramycin were administered on both eyes and topical dexamethasone and cyclosporine A were indicated for 2 weeks based on treatments previously described in known literature [9-11].

One month later, bilateral recurrence of membranes was observed, and was treated with the administration of a subconjunctival injection of 0.75 ml of AFFP, continued with topical application in a regime of every four hours for four weeks, tapered to every 6 hours without suspension. The AFFP was prepared with a 20 ml sample of the patient's blood, collected in a sterile blood collection tube containing a coagulation activator and a polymer gel for serum separation. The sample is then subjected to a centrifugal process during 10 minutes. The 2 ml supernatant of fresh plasma were filtered and collected in a sterile dropper with 8 ml of hypromellose and refrigerated at 4°C [12].

After treatment with AFFP, with the regime previously mentioned, there has not been recurrence of membranes in the past 4 years of follow-up.

Results

The diagnosis of LC was confirmed with the 48% of plasminogen functional activity.

Surgical excision was performed, and topical treatment with dexamethasone and cyclosporine A was indicated.

The tissue sections obtained from surgery, subjected to light microscopy, disclosed subepithelial deposits of extracellular eosinophilic, amorphous, hyaline material, surrounded by an inflammatory infiltrate composed of lymphocytes, plasma cells, neutrophils, eosinophils and mast cells. The subepithelial deposits stained for periodic acid-Schiff (PAS), Masson's trichrome, and were negative for Congo red (Figure 2).

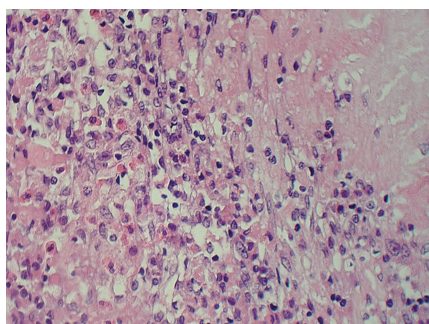


Figure 2: Histopathological observations. Subepithelial deposits of extracellular eosinophilic, amorphous, hyaline material, surrounded by an inflammatory infiltrate composed of lymphocytes, plasma cells, neutrophils, eosinophils and mast cells.

Recurrence of membranes was observed after surgical resection and topical anti-inflammatory combined treatment; therefore, we decided

an AFFP-based therapy, administered directly by a subconjunctival injection, followed by a continuous topical application. Following this treatment complete recovery has been observed for the past 4 years (Figure 3).



Figure 3: Six-year old male child without recurrence of membranes. Picture showing the right eye of the patient after 4 years of follow-up for a subconjunctival and topical treatment with AFFP.

Discussion

LC is a rare disease, which may cause important decrease in visual acuity, severe blepharoptosis, and amblyopia. It has been reported that surgical treatment of the lesions plus topical heparin, corticosteroids, and cyclosporine A may reduce recurrences [1-3,8,11]. Our patient was locally treated with corticosteroids and cyclosporine A after the surgery according to effectiveness reported; nevertheless recurrence was noted one month later. It has been recently shown that repeated intravenous replacement therapy with purified plasminogen leads to a rapid resolution of the membranes from the respiratory tract, palpebral and bulbar conjunctiva, but it needs repeated applications because of plasminogen's very short half-life [4,12]. Our patient did not present a systemic disease that could require intravenous plasminogen therapy. According to evidence, it has been demonstrated that combined subconjunctival and topical administration of fresh frozen plasma impedes the recurrence of membranes after excision [1,3-5]. Moreover, these studies employed plasma concentrates, which contained normal levels of plasminogen functional activity [1-3]. It has been suggested that AFFP has positive results in LC treatment because patients with this disease suffer from an inability to degrade fibrin aggregates adequately, which can be degraded and removed by proteolytic enzymes present in plasma, like elastase and plasminogen [8,12]. Interestingly, although the plasminogen functional activity in our patient was 48%, the autologous fresh plasma concentrate used in this study demonstrated sufficient plasminogen activity to cause a complete recovery of the patient's disease. Hence, the results in this report demonstrate that AFFP obtained from a plasminogen deficient patient could prevent the recurrence of LC membranes, when used as subconjunctival and constant topical treatment. We believe that the reason for this favorable outcome might be related to the plasminogen levels in our patient and the increased delivery of plasminogen by the AFFP drops applied directly in the affected conjunctiva [4,12]. Furthermore, usage of autologous plasma decreases the probability of the occurrence of an adverse immune response towards the plasmatic antigens of a normal plasminogen activity donor.

Conclusion

AFFP has been so far an effective therapy for LC in this patient, with no recurrence of the disease for 4 years. Therapy with AFFP clearly presents significant benefits such as easy collection of plasma, low cost, efficacy and availability.

According to our results and due to the small amount of evidence in treatments based in fresh frozen plasma, the scope of this report should be limited to certain situations specifically considering plasminogen level, plasminogen functional activity, and merely ophthalmic presentation.

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