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A case of ligneous conjunctivitis

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Summary

Ligneous conjunctivitis is a rare form of idiopathic membranous conjunctivitis. It occurs with type 1 plasminogen deficiency and is characterized by development of firm, fibrin-rich, woody-like, recurrent pseudomembranous lesions mainly on the tarsal conjunctiva. It may occur in other mucous membranes including oral cavity, tracheobronchial tree and upper gastrointestinal tract in addition to the conjunctiva. Due to plasminogen deficiency there is a defect in destruction of fibrin plaque which develops on the damaged mucosa as a result of minor trauma. Although autosomal recessive inheritence is described, most of the cases are sporadic. Generally, it develops during infancy and childhood, but can occur at any age. A 4 year-old male infant presented to the Opthalmology department with pink-red membranous lesion on his left eye extending from the conjunctiva to the iris. Histopathologic evaluation of the excised material was compatible with ligneous conjunctivitis and the diagnosis was confirmed with significantly decreased level of plasminogen in the patient. Despite topical prednisolone and cyclosporin treatment the lesion recurred. The patient was consulted with a hematologist and systemic and topical fresh frozen plasma (FFP) were administered. The case was discussed in terms of its histopathologic features and good response to FFP treatment in company with the literature. *(Turk Arch Ped 2012; 47: 131-3)*

Key words: Ligneous conjunctivitis, plazminogen deficiency

Introduction

The term ligneous conjunctivitis (LC) was used by Borel in 1933 for the first time to describe a rare form of chronic, bilateral, recurrent conjunctivitis which was characterized by development of fibrin-rich, woody-like, pseudomembranous lesions mainly on the upper tarsal conjunctiva and less frequently on the lower eye lid and bulbar conjunctiva. It occurs due to type 1 plasminogen deficiency and may present as a systemic disease involving other mucous membranes besides the conjunctiva (1,2).

Although autosomal recessive inheritance has been described, sporadic cases have been reported. Type 1 plasminogen deficiency has been found to be related to homozygous or combined heterozygous mutations in the plasminogen gene (2-4). These mutations lead to rapid destruction of plasminogen which is the key element of the fibrinolytic system. Thus, transient fibrin matrix which forms during wound healing can not be dissolved because of plasminogen deficiency. These fibrin deposits accumulate as under-epithelium masses and cause to mucosal ulcers. Ultimately, a visceous cycle of tissue damage and fibrin accumulation is observed (4,5). Here, a case of ligneous conjunctivitis involving the upper tarsal conjunctiva in a 4-year-old boy is presented.

Case

A 4-year-old male patient presented to the Opthalmology Clinic because of a pink-red membraneous lesion in the left upper eye lid which developed following varicella infection (Picture 1). It was learned that membrane was removed from the eyelid previously in the patient two times in a private hospital and histopathologic examination of the samples was not performed. The lesion extracted under general anesthesia was sent to the Pathology Clinic. On macroscopic examination, a pink colored lesion with a rigid consistency and smooth surface and with dimensions of 0.6x0.3x0.3 cm was observed. On histopathological examination, a rather thick, uncellular, eosinophilic and fibrinoid substance was observed just below the

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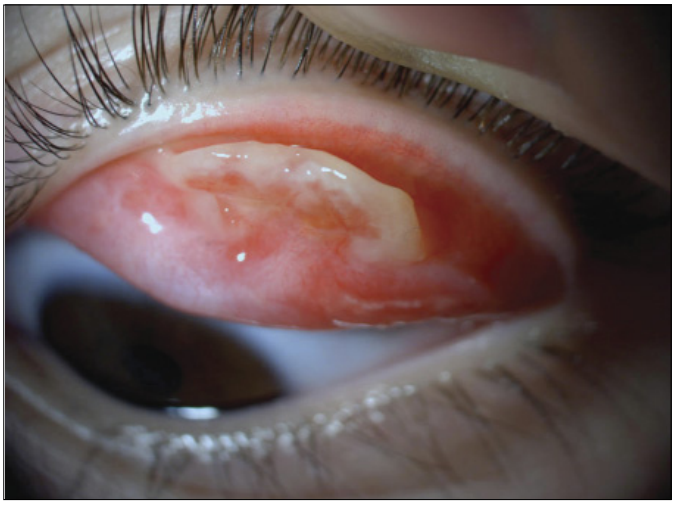
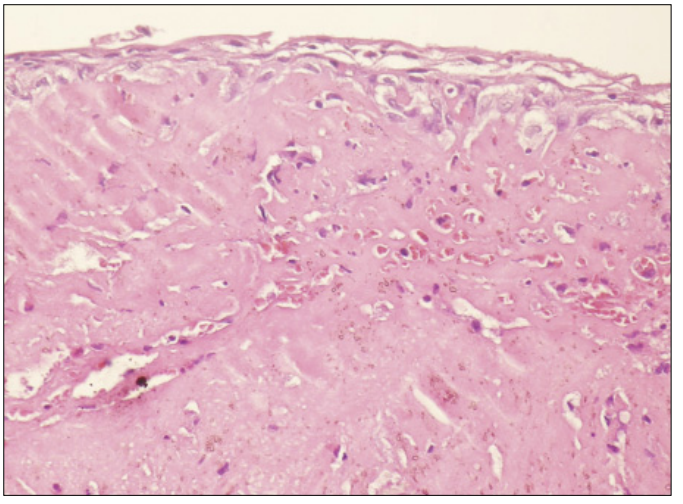
superficial epthelium which appeared damaged from place to place (Picture 2). Active chronic inflammation and focal hyalinization were present in the other areas. On histochemical study performed in terms of amyloid, Congored and Crezil violet stainings were found to be negative. This accumulated substance was assessed to be fibrin. Meanwhile, Ophtalmology Clinic was contacted and plasminogen levels were asked to be measured. When the level of free plasminogen was found to be low (16 mg/dl), a diagnosis of ligneous conjunctivitis was made with clinical, histopathological and biochemical findings. Plasminogen levels of the parents were also measured and were found to be within normal limits (the mother: 74 mg/dL, the father: 76 mg/dl). No other similar lesions were found in the other mucous membranes. No pathological finding was found on systemic examination. Prednisolone acetate 1% opthalmic suspension (4x1) and cyclosporine 0.05% ophtalmic emulsion (2x1) were given to to the patient in the Opthalmology Clinic and the patient was started to be followed up. The lesion recurred one month later and the patient was consulted with Cerrahpaşa Medical Faculty, Division of Pediatric Hematology. With the recommendation of the division fresh frozen plasma (FFP) (15 ml/kg) was infused as a single dose. In addition, topical FFP was prepared by drawing FFP into injectors of 5 ml to be kept at -18°C and topical FFP (4 x 1 ml/day) and cyclosporine 1% drop (2x1) was started. With this treatment the membrane was reduced, but recurred one month later. Thus, a single dose of systemic FFP (15 ml/kg), topical FFP (4x1) and cyclosporine 1% drop (2x1) were administered again. The treatment was continued for eight months. The membrane was reduced a great deal and no new membrane development was observed (Picture 3).

Discussion

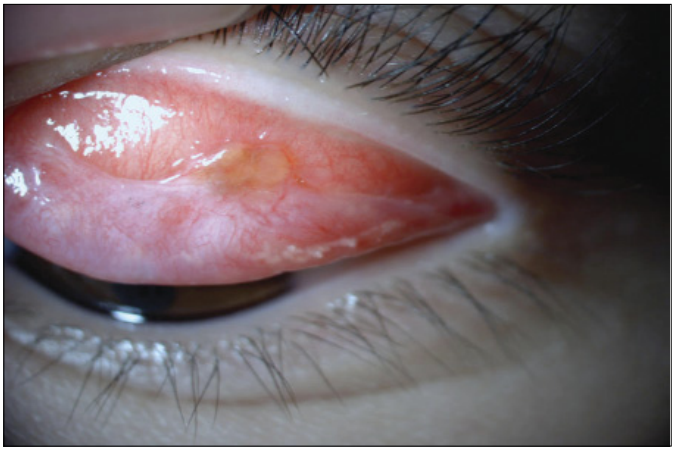
Ligneous conjunctivitis is a rare form of idiopathic membraneous conjunctivitis. More than 100 cases have been reported worldwide, but the actual frequency is not known (3). It was described by Biusson in 1847 for the first time and the term ligneous conjunctivitis was used by Borel in 1933 for the first time (1). Since similar lesions can be formed in other mucous membranes, Mingers et al. (1) recommended the term pseudomembraneous disease. The actual etiology is not known, but it has been associated with local damage, infections and surgical interventions (2,3). Although most cases with ligneous conjunctivitis occur sporadically, familial cases have also been reported. Familial cases show autosomal recessive inheritance. Mingers at al. (6) showed that this disease developed due to hereditary type 1 plasminogen deficiency in 1994 for the first time. Since 1997 Schuster et al.(2) have shown that homozygous and combined heterozygous mutations are frequent in the plasminogen gene in patients with ligneous conjunctivitis and this has confirmed that the disease is inherited autosomal recessively. The fact that plasminogen deficiency was not found in the mother or father of the patient and no similar lesions were found in close relatives suggests that it is a sporadic case.



Picture 1. Bright pink colored membraneous mass located in the conjunctiva of the upper eye lid



Picture 2. Amyloid-like fibrinoid substance containing erythrocytes and inflammatory cells accumulated below the epithelium (HEX200)



Picture 3. The final appearance of the lesion which was found to be regressed markedly with systemic and topical fresh frozen plasma treatment

Initially, the disease is manifested by lacrimation, hyperemia in the conjunctiva and mucopurulent discharge. Afterwards, yellow-white or pink colored woody-like firm pseudomembranes develop in the internal surfaces of the eyelids. It may recur after being removed locally. In most cases, infants or children have been affected, but the disease may occur at any age (2,7,8). In our case, the lesion which developed following varicella infection recurred a short time after removal.

Both eyes are involved in 51% of the cases. In 26-30% of the cases, vascularization, scarring, keratomalacia and corneal involvement which may lead to blindness as a result of corneal perforation are present (2,8). Involvement of the oral mucosa (especially gingiva) (9,10), the female reproduction system (4,11), the ear (12), the upper digestive system (2), the kidney (2) and even the skin has been reported in patients with ligneous conjunctivitis. In our case, no involvement was found in the other eye, cornea and another organ.

On histopathologic examination of the pseudomembranes, amorphous hyaline-like substance and lymphocytes, plasma cells and granulation tissue accompanied by granulocytes below the thinned or damaged epithelium are observed. Amorphous hyaline-like eosinophilic substance is similar to amyloid, but Congo red and Crezil violet stainings are negative. It has been shown to contain plasma proteins including fibrin, albumin and immunoglobulins (especially IgG) (14). In our case, the same morphological appearance was present histopathologically and amyloid stainings were found to be negative.

Mainly, extravasation of plasma proteins following mechanical damage and rapid fibrin(ogen) coagulation are involved in the formation of pseudomembranes. This fibrin-rich clot provides hemostasis in the damaged area of tissue and forms a transient matrix in the surface. In the process of normal wound healing, the fibrin matrix is replaced by granulation tissue with activation of inflammatory cells. Finally, granulation tissue is replaced by secondary matrix which is rich in connective tissue. Plasmin is involved in the destruction of the extracellular matrix which is rich in fibrin. Destruction of the granulation tissue is dependent on the plasminogen activator system and matrix metalloproteases (MMPler). In patients with ligneous conjunctivitis, wound healing in the mucous membranes is disrupted and seems to be interrupted at the stage of formation of granulation tissue. The main component of the pseudomembranes is fibrin (ogen). This shows deficiency of plasmin-mediated extracellular fibrinolysin (1,2). Development of pseudomembranes in the conjunctiva in a patient who receives tranexamic acid which is an antifibrinolytic drug, supports the role of deficiency of plasminogen in the pathogenesis of ligneous conjunctivitis (15).

Spontaneous regression in ligneous conjunctivitis is observed rarely. Since hypoplasminogenemia is a strong etiological factor, surgical interventions should be avoided as much as possible to prevent membrane formation in such cases (2,3). In our case, the lesion recurred in a short time after surgical excision. Although many local treatment methods are performed, the outcomes are usually disappointing. When cyclosporin A which is an immunosuppresive drug is used locally in combination with topical corticosteroids, the frequency and severity of recurrences is decreased after surgical excision (2). In our case, cyclosporine drop was started following excision of the lesion, but the membrane developed again after a while. In recent years, Watta et al. (16) observed that the membranes disappeared completely in 2 of 3 patients with ligneous conjunctivitis and marked reduction developed in one patient with topical plasminogen treatment of fresh frozen plasma. This treatment facilitates elimination of the membranes by softening them, but its cost is rather high. Treatment with topical fresh frozen plasma prepared from fresh frozen plasma resulted in hopeful outcomes (17). In our case, marked reduction was obtained with this treatment and no new membrane formation was observed. Replacement treatment with extended-release plasminogen preparations and gene treatment will probably provide definite cure for these patients (2).

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