Isolated Conjunctival Lichen Planus

A Diagnostic Challenge

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Background: Lichen planus is a common inflammatory autoimmune condition of unknown etiology that commonly affects the skin and mucous membranes. Isolated ocular lichen planus is an extremely rare presentation that most commonly involves the eyelids, conjunctiva, and cornea, leading to severe scarring, and is clinically indistinguishable from other causes of cicatricial conjunctivitis.

Observations: A 79-year-old man complained of a chronic keratoconjunctivitis refractory to multiple topical treatments. Slit-lamp examination revealed diffuse bilateral conjunctival hyperemia, subepithelial fibrosis, and symblepharon, with a marked shortening of the lower conjunctival fornix. There were no other skin or mucosal lesions. Hematoxylin-eosin staining revealed acanthosis, focal thickening of the basement membrane, and a dense subepithelial mononuclear infiltrate. Direct immunofluorescence demonstrated a linear shaggy fibrinogen deposition along the basement membrane, suggestive of lichen planus. Ultrastructural examination revealed a marked widening of the epithelium–lamina propria interphase, with prominent fragmentation, reduplication, and reticulation of the lamina densa of the basement membrane. The patient was successfully treated with systemic immunosuppressive agents.

Conclusions: Isolated conjunctival lichen planus is an exceptional and severe cause of cicatricial conjunctivitis. Distinguishing this unusual presentation from other inflammatory diseases with conjunctival involvement is crucial to initiate an appropriate therapy early to avoid irreversible damage of the visual function.

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Lichen planus (LP) is a common inflammatory condition of unknown etiology that commonly affects the skin and mucous membranes, especially the mouth and genitalia. Ocular involvement is infrequent and very often associated with cutaneous or oral involvement. Isolated ocular LP is an extremely rare presentation that most commonly involves the eyelids, conjunctiva, and cornea and may lead to severe scarring, clinically indistinguishable from other causes of cicatizing conjunctivitis. Herein we report a case of LP with exclusive ocular involvement and characterize the immunopathological and ultrastructural features of this disease.

REPORT OF A CASE

A 79-year-old man was referred from the Department of Ophthalmology for evaluation of a chronic keratoconjunctivitis of unknown origin, refractory to multiple topical treatments (lubricants, antibiotics, and corticosteroids). A medical history review revealed chronic glaucoma treated with dorzolamide and timolol maleate and bilateral cataract surgery. The patient complained of severe photophobia and visual acuity impairment. Physical examination revealed a severe scarring conjunctivitis with symblepharon formation (Figure 1). Slit-lamp biomicroscopy demonstrated marked diffuse conjunctival hyperemia, subepithelial fibrosis, and fornical symblephara with foreshortening of the lower fornix. A thorough dermatological examination did not reveal any other lesion on skin or oral or genital mucosa.

A conjunctival biopsy specimen was obtained from the inferior fornix of the right eye. Histopathological examination disclosed epithelial acanthosis, focal thickening of the basement membrane, and a dense bandlike infiltrate of lymphocytes, histiocytes, and plasma cells, with exocytosis of mononuclear cells and scanty intraepithelial apoptotic cells (Civatte bodies).
Ultrastructural examination of the conjunctiva revealed a marked widening of the dermal-epidermal interphase, with prominent fragmentation, reduplication, and reticulation of the lamina densa. The fragmented and anastomosing layers of lamina densa were separated by a delicate fibrillary and branching material, with features consistent with reticulin fibers. Interposition of cytoplasmic fibers of fibroblasts and inflammatory cells between the thickened basement membrane layers could also be observed. A focal increase in collagen compaction in the papillary dermis was also observed along with an inflammatory dermal infiltrate composed mainly of scattered plasma cells and lymphocytes. Occasional intraepithelial exocytosis was also noted.

Direct immunofluorescence study from involved mucosa demonstrated linear shaggy fibrinogen deposition along the basement membrane zone, suggestive of LP (Figure 2). No IgG, IgA, IgM, or C3 deposition was detected, and indirect immunofluorescence examination of the patient’s serum revealed no evidence of circulating IgG against the epithelium or the basement membrane zone on salt-split skin. Antibodies against BP180, Dsg1, and Dsg3 were not detected by enzyme-linked immunosorbent assay.

Treatment with topical dexamethasone, 0.1%, 5 times a day was prescribed, which was discontinued when a trophic corneal ulcer appeared on the left eye. Then, topical cyclosporin, 2%, was administered; however, the patient did not tolerate it owing to an intense ocular burning sensation. Oral treatment with methylprednisolone (0.5 mg/kg/d) and azathioprine (dose adjusted to thiopurine S-methyltransferase enzymatic activity) was initiated. A progressive improvement was observed after 6 weeks of treatment. Systemic methylprednisolone therapy was withdrawn 4 weeks later, and treatment with oral azathioprine was maintained. No new flares of the disease have been observed after 8 months of follow-up.

Lichen planus is an inflammatory mucocutaneous disease that can present with a variety of clinical manifestations. Pathogenetic mechanisms of LP still remain unknown; however, most of the present evidence supports that epithelial damage results from T-cell–mediated keratinocyte apoptosis triggered by a yet unidentified antigen on genetically predisposed individuals. Viruses, autoimmune phenomena, drugs, vaccines, and contact allergens have been reported as potential etiologic factors.1

The classic skin presentation of LP is characterized by shiny, violaceous, flat-topped polygonal papules with a superficial network of fine white lines (Wickham striae). Lesions may appear anywhere on the body surface, with a predilection for the anterior aspect of the wrists, ankles, and the lumbar region. Involvement of mucous membranes in cutaneous LP is a common phenomenon and occurs as reticul:ar whitish macules, predominantly on the buccal mucosa, lips, and genitalia. This subtype of LP usually follows a benign course, with spontaneous remission in most cases after 1 to 2 years. Oral LP without skin lesions is considered a distinct entity with a chronic unremitting course, occasionally associated with hepatitis C viral infection. The buccal mucosa and tongue are the most frequently involved sites, and lesions on other mucosal surfaces, such as the anus, genitalia, and upper aerodigestive tract, may also occur. Conjunctival involvement is rare, and it usually presents as a chronic cicatriz:ing keratoconjunctivitis in association with other clinical manifestations of LP.1-12 Lichen planus with exclusive involvement of the conjunctiva is exceptional. According to our review criteria, only 6 cases of isolated conjunctival LP have been previously reported.

Pakravan et al13 reported 2 cases: (1) a 57-year-old woman with a history of rheumatoid arthritis and secondary Sjögren syndrome, who was referred for further management of severe keratoconjunctivitis sicca that was refractory to treatment with multiple topical medications and (2) an 86-year-old man with a history of postoperative endophthalmitis following combined cataract extraction and trabeculectomy, who had chronic keratoconjunctivitis and blepharitis attributed to acne rosacea that was refractory to combined treatment with oral tetracyclines and topical corticosteroids. Slit-lamp biomicroscopy of both patients revealed signs of cicatrical conjunctivitis, and a detailed medical examination did
not reveal any other lesions on the skin or oral or genital mucosae. Both cases underwent a conjunctival biopsy for histopathological and immunofluorescence study, the results of which confirmed the diagnosis of LP. Symptoms were controlled with topical prednisolone acetate, 1%, and topical cyclosporin, 0.05%. These patients had been free of disease after 20 and 18 months of follow-up, respectively.

Thorne et al characterized 6 cases of LP with cicatrizing conjunctivitis. Only one of them, a 51-year-old woman with bilateral symblepharon, presented with exclusive ocular involvement. Diagnosis was confirmed by the immunopathologic findings. Symptoms were controlled with topical cyclosporin, 2%, 4 times daily. After a 6-month follow-up, she had not developed any other ocular symptoms.

Brewer et al recently described a series of 11 patients with ocular LP, 3 of whom presented with isolated ocular disease. All 3 patients had cicatricial conjunctivitis and responded to topical treatment.

The differential diagnosis of this unusual and severe subtype of LP should be established with other clinically indistinguishable diseases manifested as cicatrizing conjunctivitis, such as mucous membrane pemphigoid, pemphigus vulgaris, graft-vs-host disease, Stevens-Johnson syndrome, and paraneoplastic pemphigus. A definitive diagnosis is crucial because persistent and chronic inflammation may lead to progressive subepithelial fibrosis, synechia, secondary ocular dryness, entropion, trichiasis, and corneal opacification, which are invariably associated with a severe loss of visual acuity and blindness.

First-line medications include topical corticosteroids and cyclosporin. Those patients not responding to topical treatments may benefit from systemic therapy with systemic corticosteroids and other immunosuppressive agents, such as cyclosporin, azathioprine, or mycophenolate mofetil. Our patient did not respond or tolerate topical treatment, and a good clinical response was obtained with oral corticosteroids and azathioprine.

In conclusion, isolated conjunctival LP is an uncommon disorder to be added to the list of diseases leading to irreversible scarring keratoconjunctivitis. To achieve a correct diagnosis, clinical suspicion should be confirmed by the performance of a conjunctival biopsy for histopathological and immunofluorescence study. An increased awareness with regard to this unlikely diagnosis by both dermatologists and ophthalmologists seems important in order to start an aggressive, early anti-inflammatory treatment to avoid an irreversible visual loss.

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