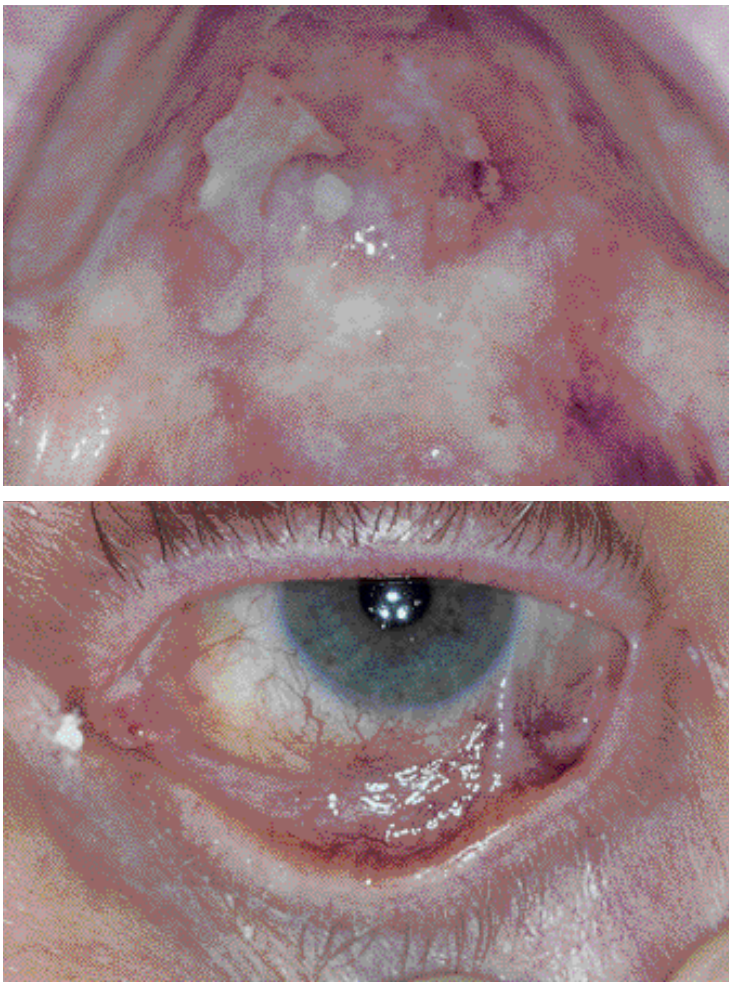
What Is Your Diagnosis?



A 59-year-old woman presented with oral ulcerations and conjunctival scarring of her left eye.

PLEASE TURN TO PAGE 68 FOR DISCUSSION

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The Diagnosis: Cicatricial Pemphigoid

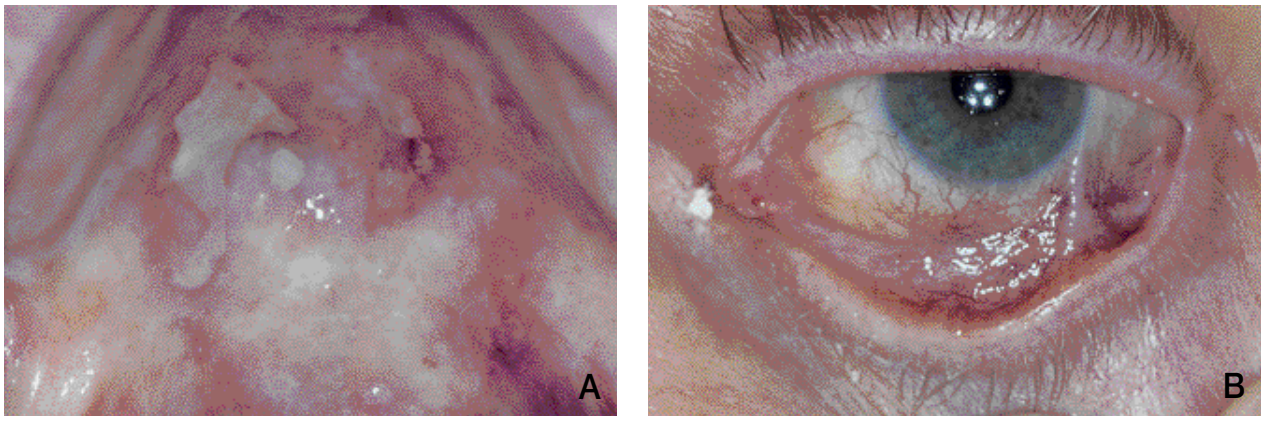

Figure 1. Oral ulcerations (A) and conjunctival scarring of the eye (B).

Cicatricial pemphigoid (CP) was first described in 1794 by Wichmann as a chronic blistering disease associated with the eye.[1] In 1911, Thost coined the term *benign mucosal pemphigoid*, and Lever suggested the term *cicatricial pemphigoid* in the early 1960s.[1]

CP is a rare, chronic blistering disease of the mucosal surfaces. The surfaces most frequently affected are the oral and conjunctival mucosa (Figure 1).[1-2] Other mucosal membranes that can be involved are the nasopharynx, larynx, esophagus, genitalia, and rectum.[2] Only one third of patients with CP have skin involvement in areas such as the scalp, face, and extremities. The subepithelial blister characteristic of this condition is caused by the deposition of autoantibodies in the basement membrane zone.[3] Many autoantibodies have been associated with CP. To date, the best characterized are the IgG autoantibodies directed against epiligrin (laminin-5) and bullous pemphigoid antigen II with a weight of 180 kd (BP180).[1,4]

The incidence of CP is 1 in 12,000.[1] No racial or geographic predilection has been reported; however, there is a predominance in women. CP typically affects patients between the ages of 60 and 80 years, though some extremely rare cases have been reported in children.[1]

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Oral mucosal lesions of CP are tense blisters that rupture easily and leave painful erosions.[1] Ocular involvement includes chronic conjunctivitis that leads to decreased vision, photosensitivity, and scarring that can cause blindness.[5] Skin lesions are tense bullae located on an erythematous or urticarial base that often rupture within hours of onset.

An incisional biopsy specimen of unaffected and perilesional skin can demonstrate subepithelial clefting with a mixed inflammatory infiltrate and scarring on hematoxylin-eosin staining. The mucosal lesion infiltrate is primarily made up of mononuclear cells, histiocytes, and plasma cells, whereas the cutaneous lesion infiltrate is predominately composed of eosinophils and neutrophils.[1-2] Direct immunofluorescence staining often reveals linear deposition of C3 and IgG along the basement membrane (Figure 2); IgA and IgM also may be detected. Indirect immunofluorescence serum antibody levels are of no diagnostic significance.[3]

Treatment is predicated on the extent and severity of disease, with careful consideration given to the tissues involved. Laboratory tests are only needed as indicated for the management of systemic therapy. Mild lesions of the skin and oral mucosa initially are treated with topical steroids and/or topical anesthetics. First-line systemic therapy consists of corticosteroids, immunosuppressive agents (azathioprine and cyclophosphamide), dapsone, and sulfapyridine. A systemic corticosteroid and one of the corticosteroid-sparing agents are used concomitantly.

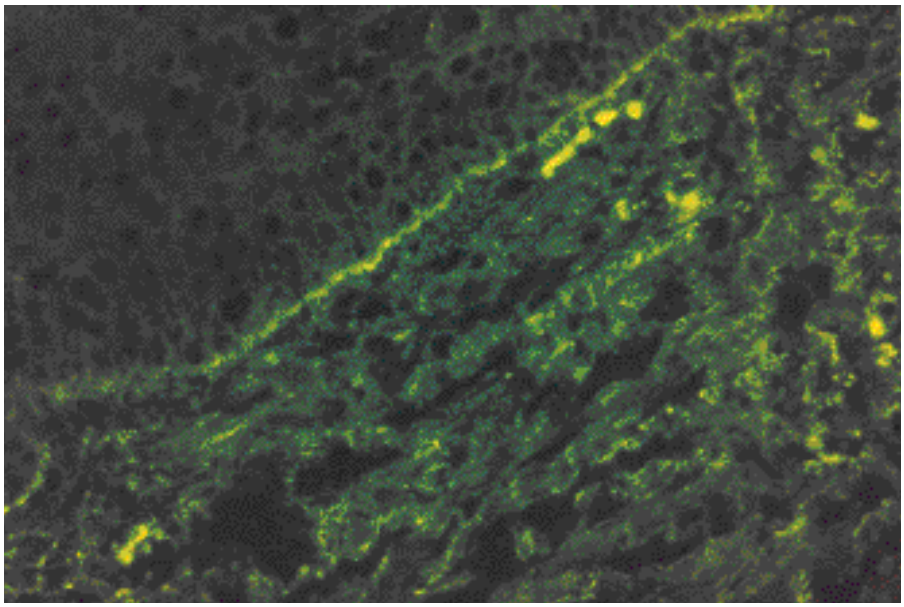

Figure 2. Linear deposit of C3 on direct immunofluorescence (original magnification ×40).

After the condition is controlled, the corticosteroid is tapered and discontinued. Second-line therapies for the treatment of CP are tetracycline and niacinamide. A third-line therapy is intravenous immunoglobulin.[6] Etanercept and mycophenolate mofetil have been reported effective in anecdotal case reports.[7-8]

Typically, patients with severe ocular involvement are treated initially with systemic steroids combined with an immunosuppressant agent. Topical ophthalmic therapy using cyclosporine has been reported to be of benefit when used with systemic steroids or immunosuppressant therapy. Eye lubrication and lid hygiene are important.[1-5]

Surgical intervention may be required for severe scarring involving the conjunctivae, esophagus, or larynx. Surgery should not be undertaken before the disease is under control, as it may lead to more severe scarring.[1]

CP usually is limited to the oral mucosa. Localized disease may be more responsive to treatment than extensive disease. Some patients may go into remission after treatment, while in others, the disease is chronic and progressive. A multispecialty evaluation and initiation of early aggressive therapy is needed to optimize outcomes. Coordination of supportive measures to ensure adequate nutrition and activities of daily living should be considered. Little is known about the factors that determine disease progression of CP. Further investigation into the pathophysiology of the disease is necessary to better identify prognostic factors.[1]

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