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**SHORT COMMUNICATION**

# Ocular involvement in anti-epiligrin cicatricial pemphigoid

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PURPOSE. *To report an anti-epiligrin cicatricial pemphigoid (AECP) patient with severe ocular involvement and to provide a practical approach to distinguishing AECP patients from those with other subepidermal blistering diseases.*
METHODS. *Techniques included direct and indirect immunofluorescence microscopy, Western blot and immunoprecipitation studies, as well as interdisciplinary examinations of mucous membranes and skin.*
RESULTS. *This study describes a patient with clinical features of cicatricial pemphigoid, circulating anti-basement membrane zone IgG antibodies, and subepidermal blisters. Histopathology and immunofluorescence analysis suggested the diagnosis of a cicatricial pemphigoid-like type of epidermolysis bullosa acquisita. However, Western blot and immunoprecipitation studies demonstrated that the patient's serum contained autoantibodies against laminin 5 $\alpha$3 subunit, leading to the diagnosis of an AECP.*
CONCLUSIONS. *Since patients with AECP have an increased relative risk for malignant tumors, it is important to distinguish this entity within the spectrum of cicatricial pemphigoid patients by additional studies such as Western blot or immunoprecipitation. (Eur J Ophthalmol 2006; 16: 867-9)*

KEY WORDS. *Anti-epiligrin, Laminin 5, Cicatricial pemphigoid, Symblepharon*

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## INTRODUCTION

Cicatricial pemphigoid (CP, mucous membrane pemphigoid) (1) refers to a group of rare, chronic autoimmune blistering disorders of mucous membranes and skin. Previous studies have shown that autoantibodies from CP patients that resemble each other clinically, histologically, and immunopathologically may target different autoantigens in epithelial basement membrane (BM). These include bullous pemphigoid antigens 1 and 2, laminin 5 (L5) and 6, type VII collagen, $\beta$4-integrin subunit, and antigens with unknown identities (1). Accordingly CP is now considered to be a disease phenotype rather than a single nosologic entity. Anti-epiligrin cicatricial pemphigoid (AECP) is a chronic, subepidermal autoimmune blistering disease of mucous membranes and skin. Patients with this form of CP have circulating IgG autoantibodies directed against L5, a protein localized within the lamina lucida of the epithelial BM. Anti-L5 autoantibodies are specific for patients with AECP and hence serve as a disease-specific marker. Ocular involvement is a sight-threatening aspect of AECP and can lead to symblepharon formation, shortening of the fornices, severe dry eye, ankyloblepharon, and potential blindness (2).

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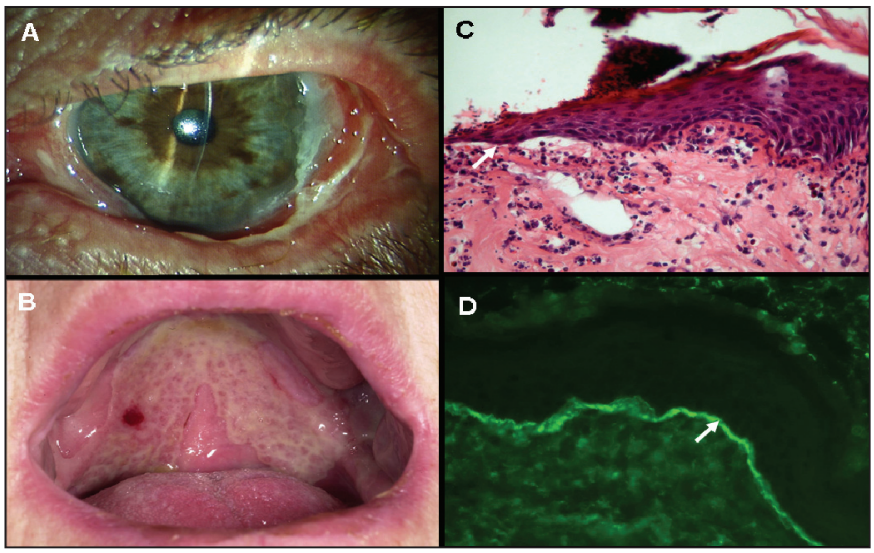


**Fig. 1 -** (**A**) *Scarring conjunctivitis with symblepharon formation (stage III a/1), corneal ulceration (temporal), bacterial superinfection of the ocular surface due to ectopia of the lower eyelid, and severe dry eye.* (**B**) *Erosive lesions and ulcerations of the oral mucosa.* (**C**) *Light microscopy of lesional skin: subepithelial separation (left side) with a dermal infiltrate along the basement membrane zone (BMZ).* (**D**) *Direct immunofluorescence of perilesional skin and mucosa: linear deposition of IgG along the BMZ (arrow).*

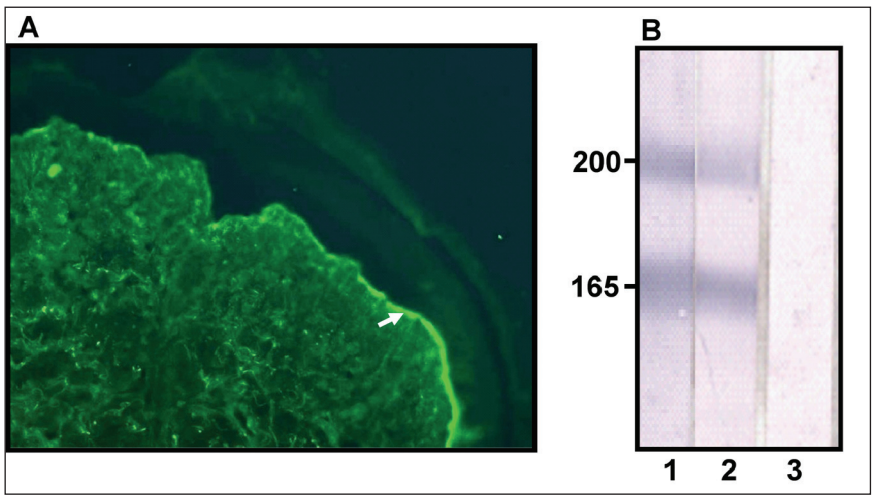


**Fig. 2 -** (**A**) *Dermal-binding of IgG antibodies on salt-split skin (arrow).* (**B**) *Western blot analysis of keratinocytes extracts with the patient's serum revealed IgG reactivity to the 200-kD unprocessed and 165-kD processed ?3 subunit of L5 (lane 1). Positive control (lane 2), negative control (lane 3).*

## Case report

A 59-year-old woman with extensive blistering on mucous membranes presented with red eyes and 4-week history of severe bilateral foreign body sensation. Best-corrected visual acuity was 20/25 in both eyes. Slit lamp examination (Fig. 1A) revealed bilateral keratitis and corneal ulcerations. Inferior fornix shortening and symblepharon formation in the medial aspect of the lower fornix was noted in both eyes. According to Tauber`s grading system (3) symblepharon formation was graded as stage III a/1 in both eyes. Additionally, bilateral chronic blepharitis with bacterial superinfection and ectropia of the lower eyelids were observed. A 5-minute Schirmer 1 test was 8 mm in the right eye and 5 mm in the left eye. Dilated fundus examination and intraocular pressures were normal in both eyes. Besides severe ocular involvement erosive lesions and/or ulcerations were found on oral (Fig. 1B), pharyngo-laryngeal, and genital mucous membranes and skin. Light microscopy studies of lesional skin (upper inner arm) demonstrated subepithelial separation with a dermal infiltrate along the basement membrane zone (BMZ) composed mainly of neutrophils and eosinophils (Fig. 1C). Direct immunofluorescence (DIF) of perilesional skin and oral mucosa demonstrated linear deposition of IgG (Fig. 1D) and C3 along the BMZ and indirect immunofluorescence revealed the presence of low titer (1:20) circulating IgG anti-BMZ antibodies. When tested on salt-split skin, dermal-binding IgG antibodies were detected (Fig. 2A). Histopathology and immunofluorescence (IF) analysis thus suggested the diagnosis of a CP-like type of epidermolysis bullosa acquisita (EBA) or AECP. Finally,

Western blot (WB) (Fig. 2B) and immunoprecipitation (IP) studies demonstrated that the patient's serum contains anti-L5 autoantibodies against $\alpha 3$ subunit leading to the diagnosis of an AECP. In our patient the treatment with systemic corticosteroids and colchicine led to marked reduction of disease activity within 2 weeks.

## DISCUSSION

Our patient showed common clinical signs of CP as cicatrizing conjunctivitis, oral mucosa erosions, and involvement of other mucous membranes as well. Results of histologic and IF analysis suggested the diagnosis of EBA or AECP. Therefore additional tests such as WB or IP are important to distinguish AECP within the spectrum of CP patients. In our patient WB and IP detected anti-L5 autoantibodies, whereas in patients with EBA autoantibodies against the N-terminal domain of type VII collagen can be found (4). An additional diagnostic tool to show the exact ultrastructural localization of immunoreactants in situ, even when the autoantibodies cannot be detected in the serum, is immunoelectron microscopy (5).

Treatment of AECP and other subsets of CP is usually chosen by site and severity of involvement (1, 6). Most patients start treatment with dapsone alone or in conjunction with systemic glucocorticosteroids. In the event of failure to respond or intolerance patients can be treated with the addition of or substitution with other immunosuppressive medications. While there is no standard regimen and we initially suspected a CP-like type of EBA or AECP, we favored as a steroid-sparing agent colchicine, a well-tolerated medication that is inexpensive and safer in moderate doses than most immunosuppressive agents (7, 8). Surgical procedures that may be needed in AECP are cryoepilations and fornix reconstruction with or without mucous membrane transplantation. Additionally, recent developments in surgical therapy like keratolimbal allografts and amniotic membrane transplantation, with or without penetrating keratoplasty, are important measures in cases with total limbal stem cell deficiency (6).

Finally, the increased risk for cancer (9) and immunosuppressive therapy with its possible complications necessitates regular screenings and a close cooperation of multiple physicians.

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*No author has a proprietary interest.*

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