A Case of Anti-BP180-type Mucous Membrane Pemphigoid with IgG and IgA Autoantibodies Showing Distinct Reactivities

Dear Editor,

Mucous membrane pemphigoid (MMP) is an autoimmune blistering disease characterized by erosive mucosal lesions mainly on the oral and ocular mucosae (1). We report a case of oral and ocular anti-BP180-type MMP with variable IgG and IgA reactivities and underlying dementia.

An 84-year-old Japanese man presented with a 4-year history of erosions in the oral cavity and on the conjunctivae, with progressive vision impairment. The medical history included benign prostatic hyperplasia, cataract, sinusitis, and dementia. Physical examination revealed erosions and white atrophic scars along the gingival mucosa and on the hard palate (Figure 1, a, b). Conjunctival inflammation and corneal scarring were also observed only on the left eye (Figure 1, c, d). No lesions were observed on the skin or on any other mucosae.

A skin biopsy from the patient's oral mucosa showed lymphocytic infiltration in the superficial dermis without apparent subepithelial blister. Direct immunofluorescence showed linear depositions of IgG, IgA, and C3 at the epithelial basement membrane zone (Figure 1, e-g).

Circulating IgG and IgA autoantibodies were not detected by indirect immunofluorescence of normal human skin, while circulating IgA, but not IgG, autoantibodies were bound to the epidermal side of 1M NaCl-split normal human skin at 1:10 serum dilution (Figure 1, h, i). Commercially available IgG enzyme-linked immunosorbent assays (ELISAs) of BP180 NC16a domain, BP230, and type VII collagen (MBL, Nagoya, Japan) showed negative results. IgG and IgA immunoblotting analyses of six different antigen sources, including BP180 C-terminal domain recombinant protein, were all negative. However, ELISA of full-length BP180 was slightly positive for IgG antibodies (index = 5.79; cut-off <4.64). Immunoblotting analysis of full-length BP180 was negative for both IgG and IgA antibodies (Figure 1, j, k). Immunoblotting analysis of hemidesmosome-rich fraction was negative for both IgG and IgA antibodies to integrin β4 (Figure 1, l). Based mainly on the clinical and immunological findings, we established a diagnosis of MMP with IgG and IgA autoantibodies, likely reactive with BP180.

Because the patient refused systemic treatments, we prescribed a mouth rinse sodium gualenate hydrate and eyedrops of fluorometholone and purified sodium hyaluronate, which did not improve the oral and ocular mucosal symptoms during the 8 month follow-up period (Figure 1, m, n).

Both IgG and IgA autoantibodies in anti-BP180-type MMP tend to react with the C-terminal domain of BP180 (2), and IgG autoantibodies in 39.7% of MMP patients reactive with the epidermal side of split skin were reported to be positive with BP180 C-terminal domain (3). The full-length BP180 ELISA shows excellent sensitivity for diagnosing BP180-type MMP (4). The different IgG and IgA reactivities among various methods used in the present study may be attributed either to different methodologies (i.e., immunoblotting or ELISA) or to the different substrates, since BP180-type MMP targets various regions of BP180, including the NC16a domain, the C-terminal domain, and the intracytoplasmic region (5).

Precise diagnosis for MMP by various immunological methods is critical, because urgent and extensive treatments are necessary for the ocular and laryngeal lesions, which may result in loss of eyesight and airway obstruction, respectively.

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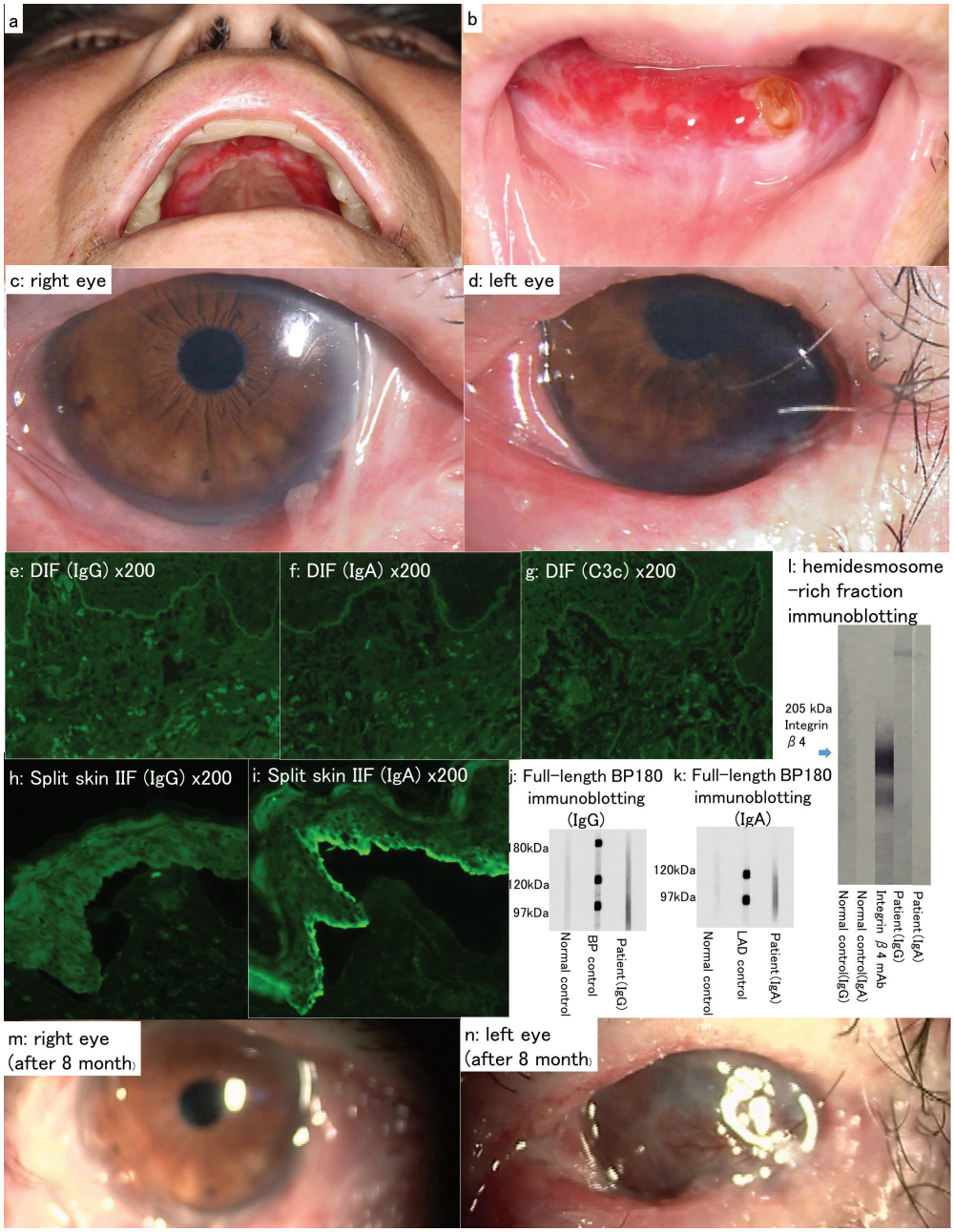

Figure 1. (a, b) Mucosal lesions on the gingivae and hard palate. (c, d) mucosal lesion on the right eye (c), as well as normal left eye (d). (e-g) The results of direct immunofluorescence for IgG (e), IgA (f), and C3 (g) (original magnification ´200). (h, i) The results of indirect immunofluorescence of 1M NaCl-split normal human skin for IgG (h) and IgA (i) antibodies (original magnification ´200). (j, k) The results of immunoblotting analysis of full-length BP180 for IgG (j) and IgA (k). (l) The results of hemidesmosome-rich fraction immunoblotting analysis; IgG and IgA antibodies in the serum from the patient were negative for integrin β4. (m, n) Ocular mucosal lesions 8 months after the initiation of treatments with rapid deterioration on the left eye.

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