Anti-BP180-type oral mucous membrane pemphigoid reactive to both NC16a and C-terminal domains

Sir,

Mucous membrane pemphigoid is a chronic autoimmune blistering disease, commonly affecting oral and conjunctival mucosae.[1] We report a case reactive to both the BP180 NC16a and C-terminal domains of BP180.

A 23-year-old Japanese woman presented with a 3-month history of oral bullous lesions. Her past medical history was not significant. On examination, several blisters and erosions were observed on the gingivae [Figure 1a]; the conjunctivae and the skin were clear. A biopsy from the erosion on the gingivae showed subepithelial detachment with infiltration of lymphocytes and neutrophils in the lamina propria [Figure 1b]. Direct immunofluorescence demonstrated linear deposits of IgG and C3 in the epithelial basement membrane zone (BMZ) [Figure 1c]. Indirect immunofluorescence on 1M salt-split normal human skin demonstrated

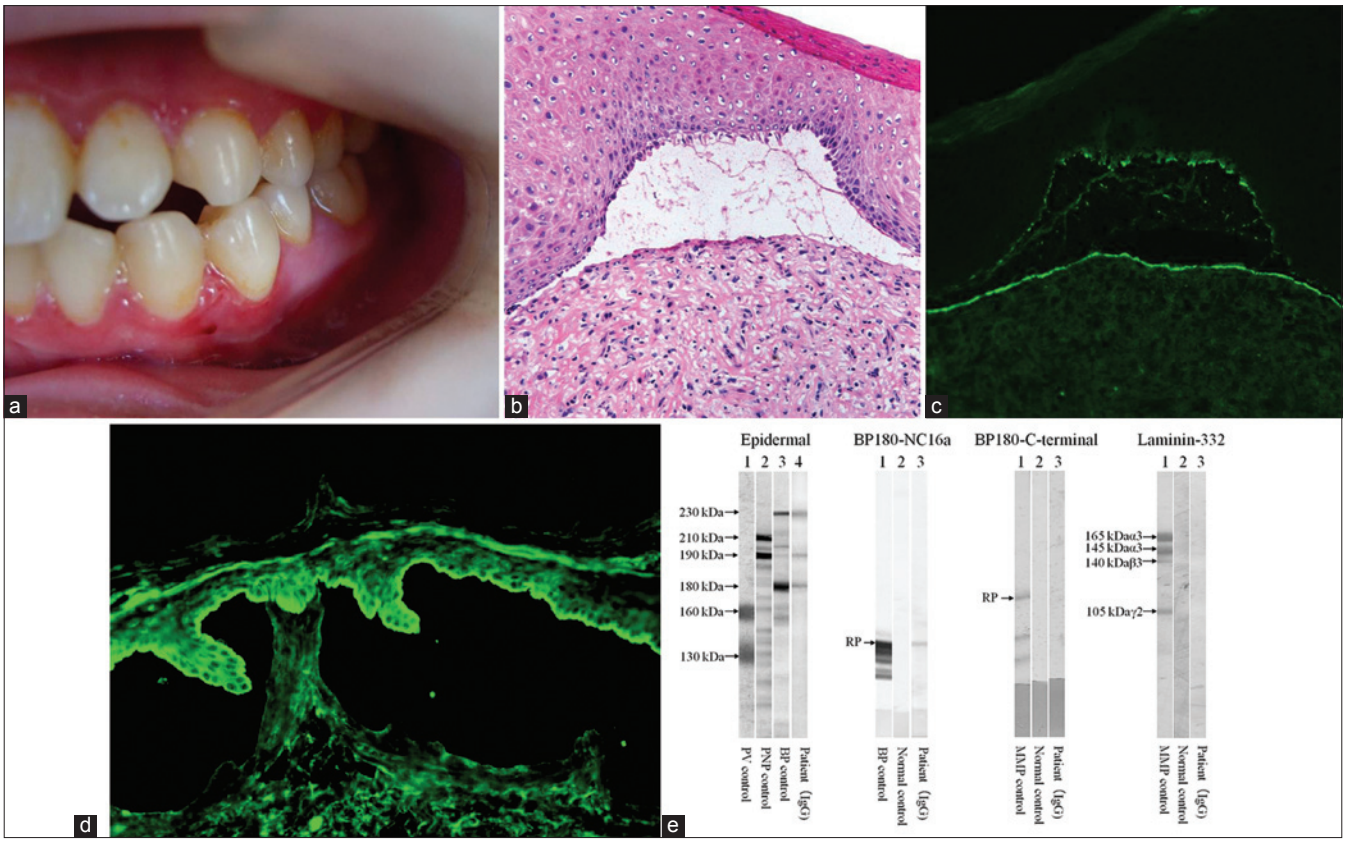

Figure 1: (a) Erosions and blisters on the gingivae. (b) Subepithelial cleft and inflammation in superficial lamina propria (H and E, ×200). (c) Linear band of IgG along the dermo-epidermal junction (×200). (d) IgG anti-basement membrane zone antibodies reacted with the epidermal side of 1M NaCl-split human skin (×200). (e) Immunoblotting (IB) of normal human epidermal extract detected IgG antibodies to BP180, BP230 and periplakin, and also showed IgG antibodies reactive with BP180 NC16a recombinant protein

IgG anti-BMZ antibodies reacting to the epidermal side [Figure 1d]. Immunoblotting of normal human epidermal extract detected IgG antibodies to BP180, BP230 and periplakin [Figure 1e]. Immunoblotting also showed IgG antibodies reactive to the BP180 NC16a recombinant protein (RP) [Figure 1e]. Immunoblotting of BP180 C-terminal domain recombinant protein and purified human laminin-332 showed negative results [Figure 1e]. Commercially available IgG enzyme-linked immunosorbent assays showed positive reactivity to BP180 NC16a domain recombinant protein (index 51: positive >15), but negative reactivity to BP230 recombinant proteins (index 1.31: positive >9) (MBL, Nagoya, Japan). A recently developed enzyme-linked immunosorbent assay of BP180 C-terminal domain recombinant protein showed a weakly positive reactivity (0.36: Positive ≥0.269).[2] The patient was diagnosed with anti-BP180-type mucous membrane pemphigoid. Monotherapy with oral nicotinamide controlled her symptoms well for the follow up duration of 5 years. No lesions on the other mucosae or the skin were observed during this time.

Bullous pemphigoid and mucous membrane pemphigoid mostly occur in the older age groups; involvement in younger age groups is rare, as in this case. The oral cavity, particularly the gingivae, is most frequently affected in mucous membrane pemphigoid, as seen in our case. Oral mucous membrane pemphigoid localized to the oral cavity is categorized as low-risk compared to disease affecting other sites and needs minimal therapy such as oral tetracycline and topical corticosteroids.[1] Our patient was well controlled with oral nicotinamide alone.

The major autoantigens in mucous membrane pemphigoid are BP180 C-terminal domain and laminin-332.[3,4] In addition, IgG antibodies to beta 4 integrin and alpha 6 integrin have been reported in ocular and oral mucous membrane pemphigoid, respectively, though these were not tested in our case.[1] In our case, immunoblotting of normal human epidermal extract detected IgG antibodies to BP230 in addition to BP180, in contrast to the negative results of enzyme-linked immunosorbent assays on BP230 recombinant protein. It is suggested that the discordance of the results was due to the lower sensitivity of enzyme-linked immunosorbent

assays because the central domain of BP230 is not detected with enzyme-linked immunosorbent assays on BP230 recombinant protein. A unique finding in our case was that commercially available enzyme-linked immunosorbent assays showed positive reactivity with BP180 NC16a domain recombinant protein, which is known as the autoantigen for bullous pemphigoid. However, we have recently reported that 30% of patients with oral mucous membrane pemphigoid were positive on enzyme-linked immunosorbent assays of BP180 NC16a domain.[5] Therefore, when patients with mucosal lesions show positive results in BP180 NC16a domain enzyme-linked immunosorbent assays, the diagnosis of anti-BP180-type mucous membrane pemphigoid should be considered. In addition, although our patient showed negative results in immunoblotting of BP180 C-terminal domain recombinant protein, a newly developed enzyme-linked immunosorbent assay of the same recombinant protein showed positive reactivity. Therefore, the novel enzyme-linked immunosorbent assays of BP180 C-terminal domain may be more sensitive than immunoblotting and may be useful for the diagnosis of anti-BP180-type mucous membrane pemphigoid.

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Conflicts of interest
There are no conflicts of interest.

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