

LETTERS TO THE EDITOR

Mucous membrane pemphigoid reactive only with BP230

Dear Editor,

Mucous membrane pemphigoid (MMP) is defined as an autoimmune subepithelial blistering disease primarily affecting mucous membranes.¹ Here, we describe a case of MMP presenting with only anti-BP230 antibodies.

The patient was a 45-year-old Japanese woman, who developed ulcers on the oral mucosa and hard palate for 1 or 2 months (Fig. 1a,b). Other mucosae, including conjunctiva, and skin were not involved. A biopsy specimen taken from lip mucosa showed a submucosal blister with inflammatory cell

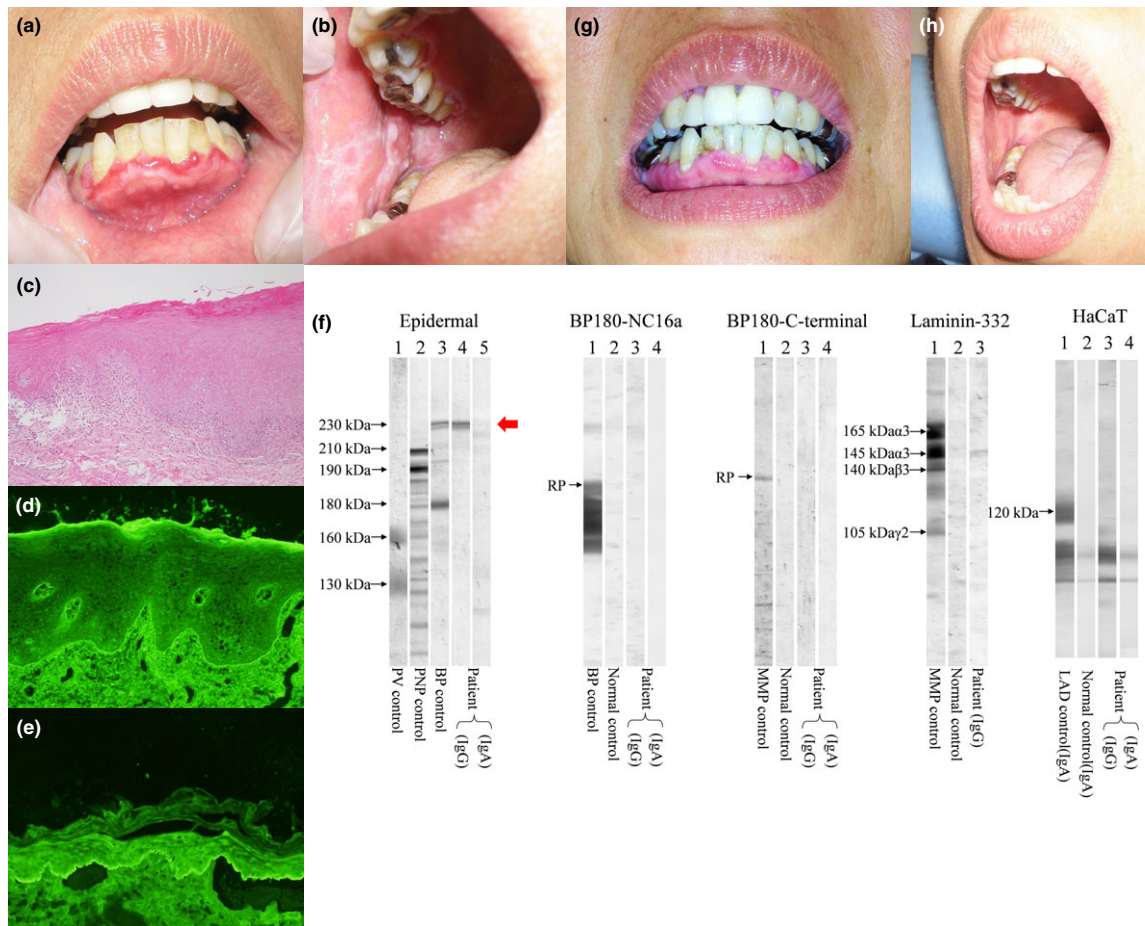


Figure 1. (a) Erythematous and atrophic changes along lower gingival mucosae. (b) Pseudomembrane-covered erosions on the buccal mucosae. (c) Histopathology demonstrates a subepithelial blister with inflammatory cell infiltrates (hematoxylin–eosin, original magnification $\times 100$). (d) Direct immunofluorescence (IF) reveals a linear deposition of immunoglobulin (Ig)G at the basement membrane zone (BMZ) ($\times 200$). (e) Indirect IF using 1 mol/L NaCl-split skin sections demonstrates serum IgG bound to the epidermal side of the split ($\times 200$). (f) Results of the immunoblot (IB) analyses. (Leftmost column) In IB using normal human epidermal extract (epidermal), IgG antibodies in the patient's serum reacted with the 230-kDa BP230 indicated with a red arrow (lane 4). Control pemphigus vulgaris (PV) serum reacted with the 160-kDa desmoglein (Dsg)1 and the 130-kDa Dsg3 (lane 1); control paraneoplastic pemphigus (PNP) serum reacted with the 210-kDa envoplakin and the 190-kDa periplakin (lane 2); and control bullous pemphigoid (BP) serum reacted with the 230-kDa BP230 and the 180-kDa BP180 (lane 3). (Second from left and central columns) IgG antibodies did not react with recombinant proteins (RP) of either the BP180 NC16a domain or the C-terminal domain. (Second from right column) IB of purified human laminin-332. The patient serum did not react with any subunits of laminin-332. (Rightmost column) IB of concentrated culture supernatant of HaCaT cells. The patient serum did not react with the 120-kDa LAD-1. (g,h) Oral mucosal lesions remarkably reduced after oral prednisolone therapy.

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infiltrates consisting of lymphocytes (Fig. 1c). Direct immunofluorescence (IF) revealed a linear deposition of immunoglobulin (Ig)G, IgA and C3 at the basement membrane zone (BMZ) (Fig. 1d).

Indirect IF using 1 mol/L NaCl-split skin sections demonstrated IgG and IgA antibodies reactive with the epidermal side of the split (Fig. 1e). Immunoblot (IB) analysis using normal human epidermal extract as a substrate showed positive IgG immunoreactivity with BP230, but not with BP180. IgG and IgA antibodies in the serum did not react with recombinant proteins (RP) of the NC16a or C-terminal domains of BP180. IB of purified human laminin-332, and concentrated culture supernatant for the 120-kDa LAD-1 showed negative results (Fig. 1f). In enzyme-linked immunosorbent assay (ELISA), IgG antibodies in the patient serum reacted with BP230 RP (index, 47.27; cut-off, <9), but not BP180 NC16a domain RP (index, <3; cut-off, <9).

Collectively, the results of the IF studies indicated that this case was anti-BP180 type MMP, while the results of IB and ELISA studies indicated that the target antigen in this case was BP230.

The patient was treated with oral prednisolone at a dose of 20 mg/day (0.5 mg/kg per day) and the mucosal lesions improved markedly. Minocycline (100 mg/day) and nicotinamide (800 mg/day) were used to help tapering of oral prednisolone to 5 mg/day. Lesions of the patient were well controlled without recurrence (Fig. 1g,h).

Anti-BP180 type MMP was reported to react with epitopes on the BP180 C-terminal domain.² In this case, both IB and ELISA detected only anti-BP230 antibodies in the patient's serum.

Immunoglobulin G autoantibodies to the transmembrane protein BP180 are believed to be pathogenic in BP and MMP. Production of autoantibodies to the cytoplasmic protein BP230 is thought to be a secondary phenomenon because IgG antibodies cannot access intracellular proteins in intact cells.

There are no previous reports describing MMP presenting with only anti-BP230 antibodies, whereas bullous pemphigoid cases reactive with only BP230 have been reported.³⁻⁵ The possible three reasons for the immunoreactivity in our case are as follows: (i) although both anti-BP180 and anti-BP230 antibodies were present in the patient's serum, autoantibodies

against C-terminal domains of BP180 could not be detected due to low titer;⁴ (ii) intermolecular epitope spreading could occur during the clinical course, and if so, autoantibodies against NC16a and C-terminal domains of BP180 may be detected at the onset of the disease; and (iii) ulcerations in the oral mucosa triggered the production of IgG autoantibodies to BP230. However, we may also consider the possibility that anti-BP230 antibodies play a role in certain MMP patients.

CONFLICT OF INTEREST: None declared.

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doi: 10.1111/1346-8138.13361

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First case of redness and erosion at bacillus Calmette–Guérin inoculation site after vaccination against influenza

Dear Editor,

A 2-year-old healthy and allergy-free boy was vaccinated for the current year's influenza on his left arm near the bacillus Calmette–Guérin (BCG) inoculation site. He had received two doses of the influenza vaccine each previous year but had had

no adverse events related to vaccination other than swelling of the vaccination site. The day after vaccination, he presented to an emergency department because his left arm had swollen rapidly. He was treated with an i.v. anti-allergic drug. Approximately 36 h after vaccination, he returned to our hospital

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