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# A Korean Case of Anti-p200 Pemphigoid

**Sung Bin Cho and Soo-Chan Kim**

*Department of Dermatology and Cutaneous Biology Research Institute, Yonsei University College of Medicine, Seoul, Korea.*

Anti-p200 pemphigoid is a newly defined autoimmune subepidermal blistering disease, which is characterized by the presence of IgG autoantibodies to the dermal side of 1M NaCl split skin as well as by the reactivity of these antibodies to a novel 200-kDa antigen on immunoblot analysis of a dermal extract. We describe a 49-year-old Korean male who presented with a bullous eruption on the whole body, which clinically resembled bullous pemphigoid or epidermolysis bullosa acquisita. A histopathological examination of a lesional skin biopsy specimen showed an area of dermal-epidermal separation and mixed dermal inflammatory infiltrates consisting of lymphocytes, neutrophils, and eosinophils. Direct immunofluorescence showed a linear deposition of IgG and C3 along the basement membrane zone. Indirect immunofluorescence demonstrated circulating IgG autoantibodies directed against the dermal side of the 1M NaCl split skin. Immunoblot analysis of dermal extracts revealed the patient's sera recognized the 200-kDa antigen. This is the first Korean case of an anti-p200 pemphigoid who showed good response to the treatment with systemic corticosteroids and dapsone.

**Key Words:** Anti-p200 pemphigoid, autoimmune subepidermal bullous disease, 200-kDa antigen

## INTRODUCTION

Autoimmune subepidermal bullous diseases, including bullous pemphigoid (BP), epidermolysis bullosa acquisita (EBA), pemphigoid gestationis, lichen planus pemphigoides, cicatricial pemphigoid, anti-p105 pemphigoid, linear IgA dermatosis (LAD), and bullous systemic lupus erythematosus, are classified by the autoantigenic molecules of the basement membrane zone (BMZ) which are recognized by their autoantibodies.[1-3] Recently, anti-p200 pemphigoid, a novel autoimmune subepidermal bullous disease with antibodies to a 200-kDa protein, has been described.[4-12] Thus far, 18 cases of anti-p200 pemphigoid have been reported in the English literature.[4-12] Most of the patients showed the clinical features of BP,[10,11] and some patients clinically resembled either dermatitis herpetiformis[6] or LAD.[11] Some cases are associated with psoriasis.[11] Histologically, there is a predominance of neutrophils in the infiltrate. Indirect immunofluorescence demonstrates circulating IgG antibodies reacting with the dermal side of the salt split skin. Electron microscopy shows IgG deposition at the lamina lucida-lamina densa interface. Moreover, immunoblot analysis of the human dermal extracts shows that the patient's sera recognizes the 200-kDa antigen.[12] Patients with anti-p200 pemphigoid respond well to systemic corticosteroids, dapsone, tetracycline, and colchicine treatments.[12] To the best of our knowledge, this is the first case of an anti-p200 pemphigoid diagnosed in Korea.

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*Reprint address: requests to Dr. Soo-Chan Kim, Department of Dermatology and Cutaneous Biology Research Institute, Yongdong Severance Hospital, Yonsei University College of Medicine, 146-92 Dogok-dong, Kangnam-gu, Seoul 135-270, Korea. Tel: 82-2-3497-3362, Fax: 82-2-3463-6136, E-mail: kimsc@yumc.yonsei.ac.kr*

## CASE REPORT

A 49-year-old Korean male was referred to this department with a one month history of tense blister formation over the whole body. He had been treated for schizophrenia and diabetes mellitus with haloperidol, lorazepam, and glimepiride, over the past two years. Two months before his visit, he was also diagnosed with pulmonary tuberculosis and he had been treated with isoniazid, rifampin, ethambutol, and pyrazinamide. A physical examination indicated that his

mental status was drowsy due to his underlying psychiatric diseases and medications. Multiple variable sized erythematous tense vesicles and bullae, which resembled BP or EBA, were found over the whole body, particularly on the upper and lower extremities (Fig. 1A and 1B). Both the oral and ocular mucous membranes were preserved. A histopathological examination of a lesional skin biopsy specimen showed an area of dermal-epidermal separation with a mixture of dermal inflammatory infiltrates consisting of lymphocytes, neutrophils, and eosinophils (Fig. 2). Direct immunofluorescence showed a linear deposition of IgG and C3 along the BMZ. Indirect immunofluorescence demonstrated circulating IgG antibodies reacting with the dermal side of the salt split skin (Fig. 3). Immunoblot analysis of the human dermal extracts showed that patient's sera recognized a 200-kDa protein (Fig. 4). Based on a diagnosis of anti-p200 pemphigoid, the patient was treated with systemic dexamethasone (5 mg/day) and dapsone (100 mg/day), as well as with topical prednicarbate ointment. The skin lesions responded promptly to the treatment, and no new blisters had developed after a week. The patient was then maintained with oral prednisolone (10 to 20 mg/day) and dapsone (75 mg/day).

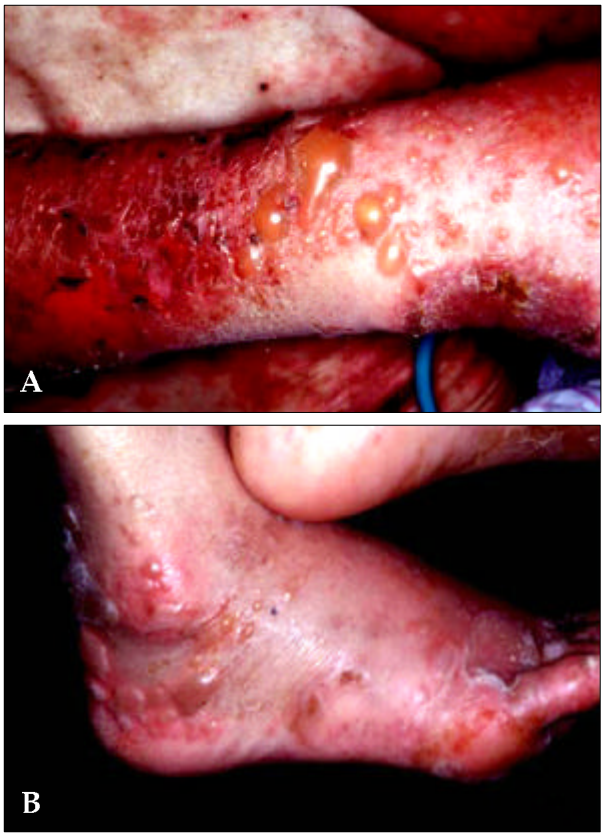


**Fig. 1.** Multiple variable sized erythematous tense vesicles and bullae over the whole body, particularly on both (A) the upper and (B) lower extremities.

## DISCUSSION

Indirect immunofluorescence of 1 M NaCl split skin is essential for making a proper diagnosis of subepidermal bullous disease. This technique has proven to be particularly important for making a distinction between patients with inflammatory EBA and those with BP or LAD.[12] Indeed, for a

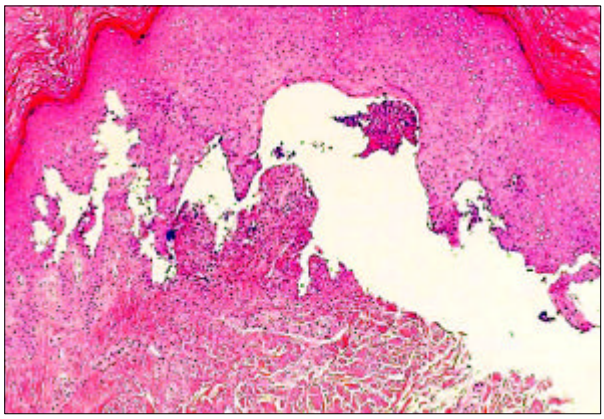

**Fig. 2.** Subepidermal blister with an infiltration of neutrophils and eosinophils in the dermis (H&E, × 40).

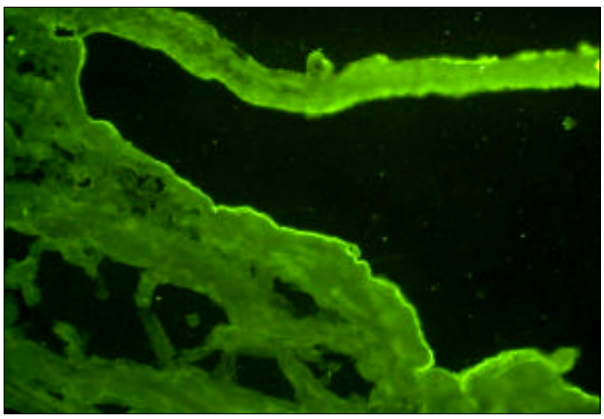

**Fig. 3.** Indirect immunofluorescence of the 1M NaCl split skin. Circulating IgG antibodies of the patient reacted with the dermal side of the split skin.

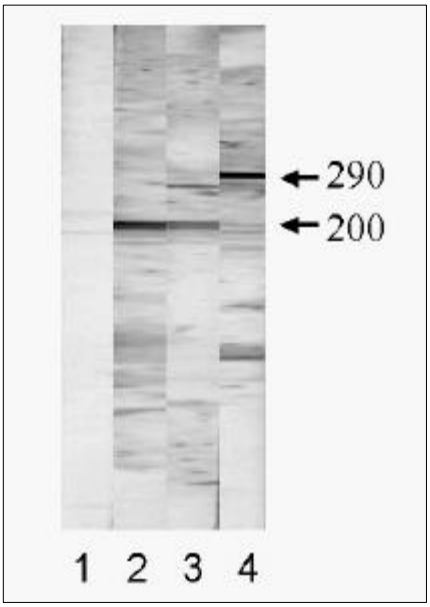


**Fig. 4.** Immunoblot analysis of the human dermal extracts. IgG from a control serum sample showed no reactivity (lane 1), our patient's serum demonstrated reactivity to a 200-kDa protein (lane 2). The reference serum of the patient with anti-p200 pemphigoid showed reactivity to a 200-kDa protein (lane 3), the control EBA serum recognized the 290-kDa antigen (lane 4).

number of years, anti-BMZ IgG against the dermal side of the 1 M NaCl split skin is believed to diagnostic for EBA because patients with EBA have circulating autoantibodies against type VII collagen (290-kDa antigen), which is a major component of the anchoring fibril.[13,14] However, recent studies have reported subsets of patients with IgG anti-BMZ autoantibodies against the dermal side of the salt split skin that specially binds the autoantigens other than type VII collagen. Some of these patients who have IgG anti-BMZ autoantibodies, which demonstrated reactivity with a unique 200-kDa antigen in dermal extracts on immunoblot analysis, were defined as being anti-p200 pemphigoid by Zillikens, et al.[4] in 1996 as a novel subepidermal blistering disease. In addition, anti-epiligrin cicatrical pemphigoid and anti-p105 pemphigoid are additional cases of subepidermal blistering diseases whose autoantibodies specifically bind the dermal side of the salt split skin.[15-18] Therefore, immunoblotting and/or immunoprecipitation analyses are essential for making a correct diagnosis of subepidermal blistering disease. It has been confirmed that the 200-kDa dermal antigen is not a fragment of either 290-kDa type VII collagen[10] or 200-kDa chain of laminin 5. However, the identity and function of the 200-kDa antigen have not been elucidated.[4,19,20]

The precise diagnosis of autoimmune subepidermal blistering diseases is also important for determining the adequate therapy and determining the prognosis. While both EBA and anti-epiligrin cicatricial pemphigoid can be insidiously progressive and tissue destructive despite the therapeutic interventions, anti-p200 pemphigoid shows a relatively favorable response to systemic corticosteroids, dapsone and cyclosporin A therapy.[5,6,12] In conclusion, immunoblotting and/or immunoprecipitation analyses must be performed in patients with subepidermal blistering disease.

## ACKNOWLEDGEMENT

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