

CLINICAL REPORT

Bullous Eruption Associated with Scabies: Evidence for Scabetic Induction of True Bullous Pemphigoid

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Some patients with scabies develop bullae concomitantly with, or subsequently after, the occurrence of scabetic lesions. Although several immunofluorescence studies have demonstrated immunoglobulin deposition in the basement membrane zone of bullous lesions, it remained unclear whether these antibodies are directed to bullous pemphigoid antigens. We clearly show that two scabetic patients with bullous eruptions had circulating antibodies against BP180 and/or BP230 as determined by Western blotting analysis. This is the first report to demonstrate that at least some of the bullous eruptions occurring in scabetics are true bullous pemphigoid. Key words: bullous pemphigoid; scabies.

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Various agents and conditions have been reported to be causative for, or associated with, the occurrence of bullous pemphigoid (BP) (1), including drugs (2), psoralen/ultraviolet A chemotherapy (3), psoriasis (4, 5) and malignancies (6). In addition, a considerable number of reports have suggested that some patients with scabies develop BP-like eruptions concomitantly with, or subsequently after, the occurrence of scabetic lesions (7–15). As the detection of anti-basement membrane zone (BMZ) antibody by the immunofluorescence technique is not sufficient for the definite diagnosis of BP, it remains unclear whether the scabies-associated bullous lesions are BP or a BP-like disorder. In this report, we provide evidence that the bullous eruption occurring in scabetics is BP as determined by Western blotting of sera from 2 patients.

CASE REPORT

Case 1

A 75-year-old Japanese man, who had suffered from cerebral infarction, was referred and admitted to our hospital because of a 1-month history of pruritic blisters. Three months before the occurrence of bullous eruption, the patient developed an itchy eruption from which scabies mites were identified. He had been treated with topical application of crotamiton cream. On admission, there were tense blisters and erosions on his 4 extremities and abdomen, but scabies mites could no longer be found on either bullae or the interdigital spaces of the hands. An indirect immunofluorescence (IIF) study using normal human skin as a substrate revealed the presence of IgG anti-BMZ antibody at a titer of 1:160 in the

patient's serum. IgG bound to the roof of the skin of the patient was split by 1 M NaCl. Using Western immunoblot analysis (16) his serum reacted with a 180 kDa antigen (BP180) (Fig. 1). He was treated with prednisolone, 20 mg daily, followed by combination therapy with betamethasone, 6 mg daily, and mizoripine, 150 mg daily. One month later, no blisters developed and betamethasone dosage was tapered to 3 mg daily.

Case 2

A 72-year-old Japanese man consulted us for an itchy scaly eruption. Because of a history of scabies, he had previously been treated with crotamiton cream for 4 months. No scabies mite was found when we first saw the patient. One week later, he developed tense bullae on his legs. Biopsy specimens exhibited a subepidermal blister with an infiltrate of many eosinophils. Peripheral blood counts showed moderate eosinophilia. IIF studies using normal and split skin specimens demonstrated the presence of circulating anti-BMZ IgG antibodies at a titer of 1:160, which bound to the epidermal side of the split. A Western immunoblot analysis disclosed that the antibodies recognized both BP180 and 230 kDa (BP230) antigens (Fig. 1). Prednisolone, 10 mg daily, was started and cyprohepatidine hydrochloride and tetracycline were added 1 week later. One month of therapy improved his skin lesions, but cessation of prednisolone resulted in the recurrence of blisters. At present his condition is being well controlled by daily administration of 5 mg prednisolone.

DISCUSSION

As summarized in Table I, 10 scabetic patients presenting with bullous eruptions as determined by histopathological or immunofluorescence analyses have been reported (7–15). Subepidermal blister formation was a common finding in 8 cases, while one case displayed eosinophilic spongiosis. BP is thought to be an autoimmune disease mediated by auto-antibodies against the two hemidesmosomal antigens BP230 and BP180 (17). Our 2 patients had circulating antibodies against BP180 and/or BP230. This is the first report demonstrating that at least some of the bullous eruptions occurring in scabetic patients are BP as determined by Western blotting analysis.

Several studies have demonstrated deposits of immunoglobulins or complement at the BMZ or vessel wall in scabetic patients, even when bullous eruptions were not apparent (18–20). Frenzt et al. (18) have reported that 2 of 11 scabetic patients showed deposits of both IgM and C3 or C3 alone at the BMZ. According to Salo et al. (19), 3 of 18 patients with scabies had deposition of C3 at the BMZ. Moreover, Hoefing & Schroeter (20) found C3 or IgM deposition at the BMZ in 3 of 4 scabetics. In addition, their cases also exhibited IgM or C3 deposits at the vessel wall, IgG or IgA in the cornified

Table I. Reported scabetic patients with bullous eruptions

Sex/age (years)	Duration of disease (months)	Histology	DIF	IIF	Scabies mite ^a	Reference
F/34	5	SB	Negative	Negative	Positive	7
M/67	4	SB	Granular IgG (BMZ)	ND	Negative	8
M/76	3	ES	Linear IgG, C3 (BMZ)	IgG anti-BMZ 1:10	Negative	8
F/36	1.5	SB	Linear C3 (BMZ) IgM, C3 (VW)	Negative	Negative	9
M/73	4	SB	Granular C3 (BMZ)	Negative	Positive	10
M/69	6	SB	Granular IgM, C3 (BMZ)	Negative	Positive	11
M/74	2	SB	Negative	Negative	Negative	12
F/66	2	SB	Granular C3 (BMZ, VW)	Negative	Negative	13
M/76	6	SB	Linear IgG, C3 (BMZ)	Negative	Positive	14
F/76	3	ND	ND	ND	Positive	15
M/75	4	ND	ND	IgG anti-BMZ ^b 1:160	Negative	Case 1
M/72	4	SB	Linear C3 (BMZ)	IgG anti-BMZ ^b 1:160	Negative	Case 2

^aScabies mites were found positively from bullous lesions; ^bantibodies reacted with BP180 (cases 1 and 2) and/or BP230 (case2)

DIF=direct immunofluorescence; IIF = indirect immunofluorescence; BMZ=basement membrane zone;

ND=not done; ES=eosinophilic spongiosis; SB=subepidermal blister; VW=vessel wall.

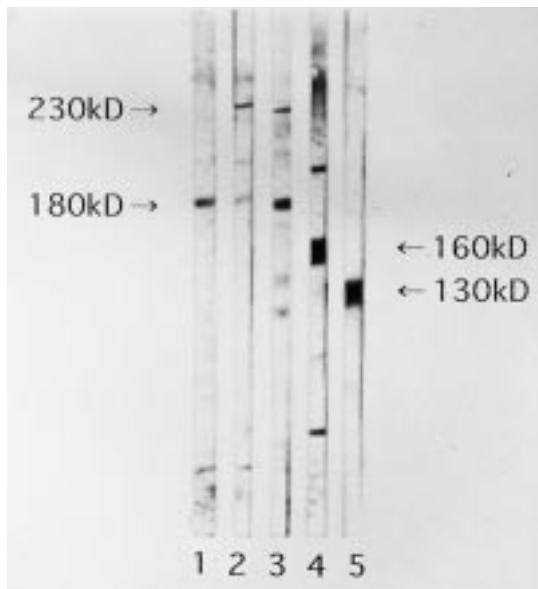


Fig. 1. Western blotting study of sera from cases 1 and 2. Lane 1, case 1; lane 2, case 2; lane 3, control of BP; lane 4, control of pemphigus foliaceus; lane 5, control of pemphigus vulgaris.

layer and C3 on the surface of a mite in a burrow. However, neither clinical symptoms of BP nor positive IIF was noted in any of these cases. These findings suggest that the mite more or less induces immunological abnormalities mediated by immunoglobulins and complement. It is possible that BP results from this dysregulated immunity.

Ostlere et al. (9) suggested two hypotheses concerning the mechanism of production of BP autoantibodies in scabetic patients. First, scabies mite penetration or its lytic secretions could injure the BMZ and cause alterations in, or release of, BP antigens, leading to the production of antibodies against the BMZ. These antibodies could activate the complement cascade and recall inflammatory cells including eosinophils, which would cause dermo-epidermal separation by the release of proteolytic enzymes. Second, a component of the mite could act as an antigen that may cross-react with the BP antigens, resulting in the production of antibodies (9). More

generally, parasites may elicit antibodies that mimic those present in genuine autoimmune diseases (21). In our Western blotting study, either BP180 or BP230 and BP180 were found in the patients' sera. This agrees with the BMZ injury hypothesis rather than the cross-reactivity one. Under some circumstances, scabies may induce a systemic immunologic disorder such as BP.

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