

SHORT COMMUNICATION

Evaluation of Mononuclear Cells in Lichen Planus Pemphigoides

Miho Kabuto, Noriki Fujimoto\*, Akihiko Yamaguchi and Toshihiro Tanaka

Department of Dermatology, Shiga University of Medical Science, Setatsukinowa, Otsu, Shiga 520-2192, Japan. \*E-mail: noriki@belle.shiga-med.ac.jp  
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Lichen planus pemphigoides (LPP) is a rare autoimmune blistering disease, which appears to be a combination of lichen planus (LP) and bullous pemphigoid (BP) (1). The nosological position of LPP is controversial. We report here a case of LPP and perform a comparative immunohistochemical study of biopsy specimens taken from our patient's skin lesions, and other BP and LP patients, in order to clarify the nosological position of LPP.

CASE REPORT

A 32-year-old man noticed multiple pruritic eruptions on both wrists in August 2012. The eruptions increased even though he was treated with topical steroids by a local doctor; therefore, he was referred to our hospital 2 months later. Physical examination revealed flat-topped and hyperkeratotic erythematous papulovesicular eruptions with erosions on the ankles, soles and wrists (Fig. 1A, B). The index value of anti-BP180 antibodies was 10 (normal range <9) at the first visit and 28 at the initiation of prednisolone, based on an enzyme-linked immunosorbent assay (ELISA) using BP180 NC16a domain recombinant protein. Other laboratory examinations showed almost normal values. Bacterial, mycological, and mycobacterial cultures of the vesicles were all negative. Histopathological examination of biopsy specimens taken from the LP-like sole and wrist lesions revealed hyperkeratosis with parakeratosis, acanthosis with partial hypergranulosis, necrotic keratinocytes in the epidermis, vacuolar degeneration of the basement membrane zone (BMZ), multiple small subepidermal clefts, and band-like inflammatory cell infiltration consisting mainly of lymphocytes in the upper dermis (Fig. 1C). Direct

immunofluorescence (IF) examination of his soles demonstrated linear IgG (Fig. 1D) and C3 (Fig. 1E) deposition in the BMZ. Indirect IF examination was negative. Indirect IF using 1M NaCl-split skin detected slight IgG deposition on the epidermal side. Based on these findings, we diagnosed the patient with LPP. Oral prednisolone, 15 mg/day, and topical steroids led to improvement of the lesions, and the pruritus disappeared 4 weeks later.

Although some elevated eruptions remained, the dosage of prednisolone was reduced to 12.5 mg/day. The index value of anti-BP180 antibodies was 16. Over the following 3 months the lesions gradually became pigmented and flat. When the dosage of prednisolone was gradually reduced to 7.5 mg/day, the elevated eruptions without pruritus recurred. Therefore, prednisolone was increased again to 10 mg/day. Two months later, prednisolone was gradually tapered to 7.5 mg/day, maintained for 2 months, and then discontinued. After one year, the patient visited our hospital due to the recurrence of eruption 6 months previously. Oral prednisolone, 15 mg/day, was initiated again, and the lesions improved without recurrence, regardless of the gradual tapering of the dosage of prednisolone to 7.5 mg/day.

MATERIALS AND METHODS (see Appendix S1<sup>1</sup>)

RESULTS

The mean percentages of positively-stained cells among dermal-infiltrated cells in this LPP patient and the 3 patients each with BP and LP treated in our institute are

<sup>1</sup><http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-2191>

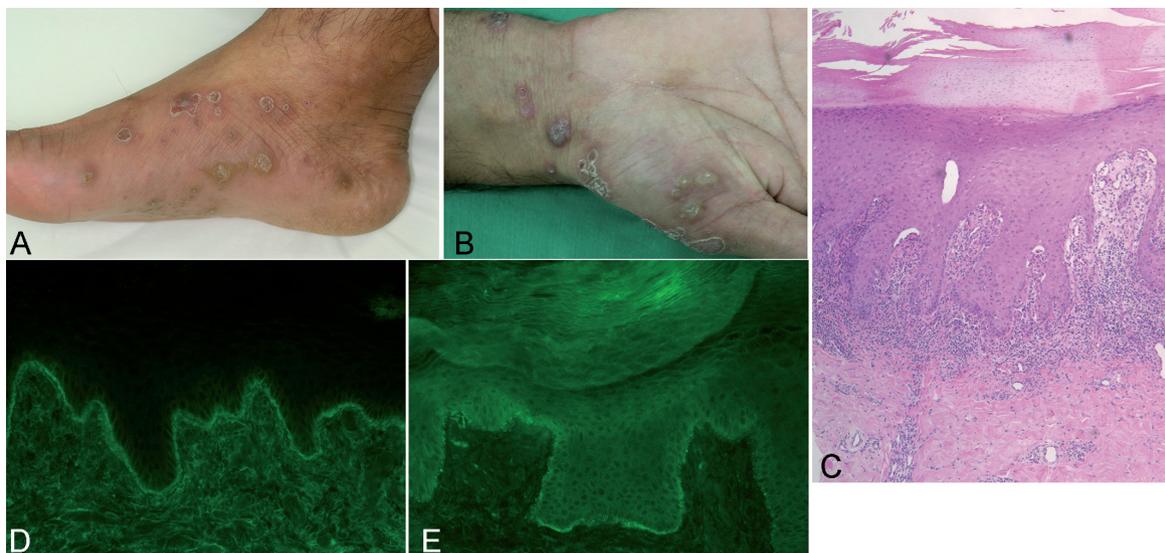


Fig. 1. (A, B) Initial clinical presentation. Flat-topped and hyperkeratotic erythematous papulovesicular eruptions with erosions on (A) ankles, soles, and (B) wrists. (C) Histopathological findings in a lichen planus-like lesion on his sole (see text) (H&E original magnification ×100). (D, E) Direct immunofluorescence examination demonstrated the linear deposition of IgG (D) and C3 (E) on the basement membrane zone (original magnification ×200).

shown in Table SI<sup>1</sup>. In a biopsy specimen taken from a sole in our LPP case, the percentages of CD3, CD4, CD8, CD20 and Foxp3<sup>+</sup> cells were 31.9%, 8.0%, 22.4%, 30.3% and 6.8%, respectively. In a biopsy specimen taken from a wrist in our LPP case, the percentages of CD3, CD4, CD8, CD20, and Foxp3<sup>+</sup> cells were 35.8%, 7.7%, 16.2%, 27.0% and 10.2%, respectively. The percentage of CD3<sup>+</sup> cells was significantly lower in LPP than in LP ( $p=0.0056$ ). The percentage of CD8<sup>+</sup> cells was significantly higher in LPP than in BP ( $p=0.025$ ) and lower in LPP than in LP ( $p=0.019$ ). The percentage of CD20<sup>+</sup> cells was significantly higher in LPP compared with BP ( $p=0.012$ ) and LP ( $p=0.0013$ ). There was no significant difference in the percentage of Foxp3<sup>+</sup> cells between LPP and BP ( $p=0.15$ ) or between LPP and LP ( $p=0.71$ ).

## DISCUSSION

Clinically, LPP is characterized by tense bullae arising both on lichenoid lesions, such as LP, and on uninvolved skin with a more acral distribution of bullous lesions (1, 2). Histopathologically, LPP is characterized by subepidermal bullae and linear deposits of IgG and C3 along the BMZ on IF of peribullous skin (3). The diagnosis of LPP is made based on these characteristic clinical, histopathological, and immunological features (1). In our case, the clinical features of BP and LP were coincident, the histopathological findings were compatible with LP except for the partial presence of hypergranulosis, and the results of IF examination were compatible with BP. Therefore, we diagnosed our patient with LPP.

Whether LPP is an independent disorder is controversial. Some authors consider LPP as a combination of LP and BP (2), while others consider it as a rare clinical variant of BP (4), an entity in itself (5), or a heterogeneous disease (3). All previous reports evaluated the nosological position of LPP only with regard to the profiles of circulating autoantibodies for bullous formation, which may result in confusion. Other aspects, such as immunological profiles of inflammation, should be considered. However, there has been no study in which the difference between LPP and BP or LP has been evaluated using immunohistochemical staining. Therefore, we performed an immunohistochemical study comparing our patient and 3 patients each with BP and LP treated in our institute (Table SI<sup>1</sup>). The CD20<sup>+</sup> cells in our LPP patient were significantly increased compared with those in LP and BP patients. The Foxp3/CD3 ratio in our LPP patient was 0.21 and 0.28, being higher than in the BP patients at 0.05, and LP patients at 0.12. However, there was no significant difference in the percentage of Foxp3<sup>+</sup> cells ( $p=0.15$  and 0.71, respectively). The CD4/CD8 ratio was 0.36 and 0.48, which was much lower than in BP patients, at 2.56, but slightly lower than in LP patients, at 0.71. Based on the above results, the specific finding in our

LPP patient was the predominant infiltration of B cells.

In order to confirm that the frequency of B cells is low both in BP and LP, we searched for previous reports on BP and LP. Since there has been no immunohistochemical study directly comparing BP and LP, we show data on BP and LP from some separate reports. One report on BP showed that the frequencies of T cells, CD4 T cells, CD8 T cells, and B cells among infiltrating lymphocytes were 76%, 59%, 25% and 6%, respectively, and the CD4/CD8 ratio was 2.36 (6). Another report on LP showed that the frequencies of expression of CD3, CD4, CD8 and CD20 among dermal-infiltrating cells in LP were 78.8%, 41.5%, 33.9% and 2.1%, respectively, and the CD4/CD8 ratio was 1.22 (7). Our results in Table SI<sup>1</sup> and the above reported data show the same tendency, whereby T cells are predominant and B cells are sparse both in BP and LP, as well as similar CD4/CD8 ratios in BP and LP. The Foxp3/CD3 ratio was lower in BP, at 0.10, compared with in LP, at approximately 0.25 (8, 9).

The profile of dermal-infiltrated cells of LPP was not similar to BP or LP. Although the exact aetiological significance of the increase in B cells in LPP is not clear, we speculate the following. The frequency of dermal-infiltrating CD20<sup>+</sup> cells is higher in interface dermatitis than in chronic dermatitis (10, 11), which, in part, explains the difference between LPP and BP. In interface dermatitis, dermal-infiltrating CD20<sup>+</sup> cell numbers in discoid lupus erythematosus (DLE) are higher compared with those in LP. The reason for the difference is suggested to be that humoral immunity plays more important roles in DLE than in LP (11). This may also explain the difference between LPP and LP. The frequency of dermal-infiltrating CD8<sup>+</sup> cells in LPP was expected to be similar to that in LP because of the common histopathological feature of interface dermatitis, which was significantly different from both LP and BP. These results demonstrate that the immunohistochemical profile of LPP is different from that of both BP and LP.

In summary, we present here the first case of LPP with immunohistochemical staining of infiltrating cells. Although the results of our study revealed that LPP differs from LP and BP with regard to the immunological aspect of infiltrating cells, further investigation is needed to clarify the nosological position of LPP.

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