Lighting up an uncommon diagnosis

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Abstract

Immunofluorescence is an essential technique for the accurate diagnosis and classification of immune-mediated inflammatory dermatoses. We report a case of lichen planus pemphigoides, a very rare entity within this group of dermatoses, which shows overlapping features of lichen planus and bullous pemphigoid. We discuss the value of pattern-based morphologic assessment and clinical correlation, along with the vital role of immunofluorescence in arriving at the correct diagnosis.

Keywords immunofluorescence; inflammatory skin disorders; tissue reaction patterns

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Case report

A male patient in his early twenties presented with a four-week history of a pruritic violaceous maculopapular eruption affecting the trunk and extremities. More recently, the patient noticed tense blisters arising both on the involved and uninvolved skin of the arms and legs (Figure 1a). He had no significant prior medical history and was not on any medications. An incisional skin biopsy from the forearm showed a subepidermal blister associated with an eosinophil-rich lymphocytic infiltrate in the superficial dermis (Figure 1b, c). Peripheral to the blister, there was a band-like lymphocytic infiltrate associated with numerous eosinophils and apoptotic keratinocytes with early dermo-epidermal separation (Figure 1d). Direct immunofluorescence (IF) showed linear deposition of IgG and C3 at the basement membrane zone (BMZ) (Figure 1e). Circulating antibodies against basement membrane zone (BMZ) material were detected in the patient's serum on indirect IF using monkey oesophagus as the tissue substrate (Figure 1f).

A diagnosis of lichen planus pemphigoides (LPP) was made. The patient responded well to oral prednisolone which was gradually tapered and withdrawn after 8 weeks. There was no recurrence of bullous lesions during a follow-up period of 6 years.

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Discussion

Inflammatory dermatoses are a challenging area of dermatopathology. Rendering an accurate diagnosis is dependent upon the integration of (1) a pattern-based assessment of histological morphology, (2) clinical correlation, and (3) adjunct techniques particularly IF.[1]

Pattern-based morphologic evaluation is the first step in the assessment of an inflammatory skin biopsy.[1] We find the following list of tissue reaction patterns useful in our day-to-day practice: spongiotic, psoriasiform, interface, vesiculobullous, perivascular with no epidermal changes, nodular/diffuse, folliculitis, fibrosing, vasculitis, and panniculitis.[1] This case shows a combination of lichenoid interface and eosinophil-rich subepidermal vesiculobullous dermatitides. Lichen planus (LP) is a prototypic example of lichenoid interface pattern but eosinophils are never seen in such large numbers in idiopathic LP. Bullous pemphigoid (BP) is the prototype disorder for eosinophil rich subepidermal vesiculobullous pattern but the lichenoid interface changes at the periphery and young age would be most unusual. Such "mixed" patterns pose diagnostic dilemmas.[1]

Clinically, the presentation with pruritic, violaceous, flat-topped papules and plaques is typical of LP. There are two scenarios where LP may be accompanied by blisters. Firstly, in bullous LP, blisters arise due to an exaggeration of the subepidermal clefts formed as a result of severe basal layer damage. Such blisters are limited to the LP lesions. Secondly, LPP represents a rare subset of LP where patients develop blisters both within the lichenoid lesions and also normal skin.[2] The pathogenesis of blister formation in LPP is closely related to BP and IF studies are essential to establish the diagnosis.[2]

IF is a vital diagnostic adjunct for immune-mediated inflammatory dermatoses e.g. immunobullous disorders, autoimmune connective tissue disorders and vasculitides.[1] It involves two principle techniques: direct IF (detection, localization and characterization of fluorescein-conjugated antibodies against immunoglobulins and complement fractions in tissue biopsies) and indirect IF (detection of circulating antibodies in patients' serum using fluorescein conjugated anti-IgG and a mucosal substrate e.g. monkey oesophagus).[3]

LPP is a rare immune-mediated dermatosis with less than 100 reported cases. It is a heterogeneous entity best conceptualized as a combination of LP and BP presenting with two distinct forms of primary lesions: lichenoid papules/plaques and tense blisters. Blisters generally appear after the lichenoid eruption but can be concomitant and rarely antedate the rash.[4] The pathogenesis is

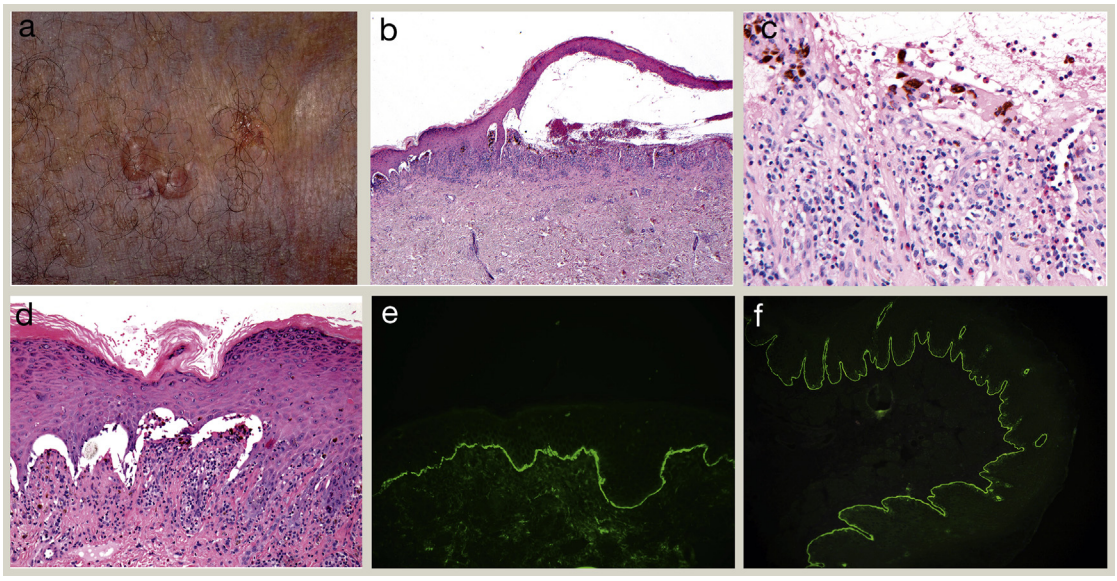

Figure 1 (**a**) Scattered tense blisters arising on hyperpigmented violaceous papules and plaques and also intervening normal skin. (**b**) Subepidermal blister with a superficial dermal inflammatory cell infiltrate. Note the areas of early epidermal separation towards the left. (**c**) High power view of the blister base showing numerous eosinophils along with lymphocytes and melanophages. (**d**) Close up of the areas of early dermo-epidermal separation showing apoptotic keratinocytes, lymphocytes and eosinophils in the papillary dermis. (**e**) Direct immunofluorescence of perilesional skin showing linear deposition of IgG at the basement membrane zone. (**f**) Indirect immunofluorescence using monkey oesophagus shows circulating antibodies binding to the basement membrane zone. (**a**) and (**b**) are adapted from Biswas A., Pearls and Pitfalls in Inflammatory Dermatopathology, Cambridge University Press, 2017. © Cambridge University Press.

believed to involve inflammation-mediated exposure of sequestered BMZ epitopes which are then targeted by auto-antibodies. Although different subdomains are involved, both LPP and BP feature autoantibodies directed against type XVII collagen (COLXVII, BPAG2), a hemidesmosomal protein.[5] The prognosis is good, many patients display an excellent response to oral or topical corticosteroids, and the recurrence rate is lower than BP.[5]

Conclusion

We present a case of LPP, a rare immune-mediated inflammatory dermatosis which shows overlapping features of LP and BP, and highlight the importance of integrating pattern-based morphologic evaluation, clinico–pathological correlation, and immunofluorescence. ◆

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Practice points

- Skin biopsies from inflammatory dermatoses should be assessed using a pattern-based approach.
- IF has a crucial role in the diagnosis of immune-mediated inflammatory dermatoses.
- LPP is a rare inflammatory dermatosis which shows clinical, histological and immunopathological overlap between LP and BP.
- Despite the similarities with BP, the prognosis and response to therapy are favourable in LPP compared with BP.

Multiple choice questions

(1) Which of the following molecules is the target of auto-antibodies in lichen planus pemphigoides?

a. COLIII
b. COLIV
c. COLVII
d. COLXII
e. COLXVII

Correct answer (e)

(2) Which of the following is the major site of immunoglobulin deposition in lichen planus pemphigoides?

a. Intercellular spaces
b. Nuclei of epidermal keratinocytes
c. Basement membrane zone
d. Papillary dermis
e. Vascular walls

Correct answer (c)

(3) Which of the following is the appropriate site to sample for direct immunofluorescence in suspected lichen planus pemphigoides?

a. Lichenoid plaque
b. Tense blister
c. Distant non-lesional skin
d. Perilesional skin
e. Buccal mucosa

Correct answer (d)