

Narrowband UVB-induced lichen planus pemphigoides

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Abstract

Lichen planus pemphigoides (LPP) is an autoimmune disease characterised by evolution of subepidermal blisters on normal and lichen planus affected skin. We describe a case of LPP in a 54-year-old Chinese woman. The patient presented with psoriasiform plaques and was diagnosed with guttate psoriasis. Narrowband ultraviolet B (NBUVB) therapy was commenced, and she experienced a generalised eruption of violaceous papules, bullae over the lower limbs, and Wickham's striae over the buccal mucosa. Histology from a plaque revealed interface dermatitis, while a specimen from a blister showed subepidermal bulla. Direct immunofluorescence showed linear deposition of IgG and C3 along the basement membrane. A diagnosis of LPP was made on clinicopathological grounds. This is the first case report of NBUVB alone in unmasking LPP. In this case report, we describe the pathological mechanism of NBUVB in the development of LPP and key features distinguishing LPP from bullous lupus erythematosus, bullous lichen planus, bullous pemphigoid, and psoriasis.

Introduction

Lichen Planus Pemphigoides (LPP) was first described by Kaposi¹ in 1892. It is a rare acquired autoimmune condition resulting in subepidermal blistering, where bullous eruptions occur at sites of lichen planus (LP) and normal skin. Though LPP is usually idiopathic, it has been reported to arise after treatment photochemotherapy with psoralen and ultraviolet A therapy (PUVA), cinnarizine, captopril, anti-tuberculosis therapy, ramipril and simvastatin.² Brenner *et al.*³ have described a case of NBUVB, paracetamol, and ibuprofen in triggering LPP, however the patient was also receiving hormonal therapy for infertility, therefore a definitive cause of the development of bullous eruption on LP lesions and unaffected skin could not be identified. The pathogenesis of LPP is not fully understood, though likely due to basement membrane zone damage, and consequential

development of autoantibodies to antigen exposure by a lichenoid inflammatory process.⁴ We report the first case report of NBUVB alone in unmasking LPP.

Case Report

A 54-year-old Chinese woman was referred to our clinic for evaluation of one month of generalised pruritic rash, which started from the forearms and spread to the rest of the body. She was otherwise well, with no past medical or drug history of note. Physical examination revealed papulosquamous guttate rash over limbs, trunk, confluent eczematous patches over extensor surfaces of upper arms and distal onycholysis in some nails. Based on the clinical presentation, a diagnosis of acute guttate psoriasis was made. Twice weekly NBUVB therapy was started. After undergoing four weeks of treatment, the patient developed tense blisters on bilateral lower extremities (Figure 1A). Phototherapy was stopped and our patient was re-evaluated.

Examination of our patient revealed violaceous papules and plaques, distributed symmetrically on the trunk and limbs, with tense blistering at sites of violaceous plaques and unaffected skin. Wickham's striae were noted over the buccal mucosa (Figure 1B). Based on the clinical development of subepidermal blisters and oral mucosal lesions, new differentials of bullous lupus erythematosus (BLE), bullous lichen planus, lichen planus, and lichen planus pemphigoides were suspected.

Laboratory investigations including full blood count, blood urea, creatinine, electrolytes, liver function test were within normal range. Anti-nuclear antibody was positive with speckled pattern a titre of 1/100. Anti-extractable nuclear antigen was negative and antibodies directed against bullous pemphigoid 180kDa antigen were found to be positive at 81.6 U/mL (positive >9 U/mL).

Punch biopsies were obtained from two different sites: one from a violaceous plaque on the abdomen and another from a blister on the left calf. Histology from the abdomen revealed lichenoid dermatitis (Figure 2A), hyperkeratosis, focal wedge-shaped hypergranulosis, acanthosis, saw-teething of rete ridges, colloid bodies, pigmentary incontinence and band-like infiltrate consistent with lichen planus (LP). The subepidermal bulla (Figure 2B) from the calf showed neutrophil predominant infiltration. Direct immunofluorescence (DIF) demonstrated a linear band of immunoglobulin G (IgG) and complement 3 (C3) along the dermo-epidermal junction (Figure 2C). Indirect immunofluorescence of patient's serum demonstrated circulating IgG autoantibodies with an epider-

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mal pattern of binding on human salt-split skin in a 1:160 titre. Based on the clinicopathological revelation, a diagnosis of LPP was made. Our patient subsequently responded well to oral prednisolone at 0.5 mg/kg/day.



Figure 1. (A) Violaceous lichenoid plaques and papules with blisters (arrowed) at sites of lichen planus and unaffected skin. (B) Wickham's striae over buccal mucosa.

Table 1. Distinguishing features between bullous lupus erythematosus, bullous lichen planus, lichen planus pemphigoid, lichen planus, bullous pemphigoid, lichen planus pemphigoides, and psoriasis.

	Bullous lupus erythematosus	Bullous lichen planus	Bullous pemphigoid	Lichen planus	Lichen planus pemphigoides	Psoriasis
Clinical features	<ol style="list-style-type: none"> Systemic lupus erythematosus (fulfill American Rheumatism Association criteria for SLE) Symmetrical vesiculobullous eruption on trunk, proximal upper extremities, neck and face 	<ol style="list-style-type: none"> Blistering on lichen planus affected skin of life Tense bullae on skin surface with predilection on flexural areas 	<ol style="list-style-type: none"> Affects elderly in fifth to seventh decades Papules and plaques over the extremities and trunk Wickham's striae Mucosal involvement 	<ol style="list-style-type: none"> Shiny, flat-topped violaceous to erythematous papules with overlying silvery scales affecting the buttocks, elbows, lower back, scalp and knees 	<ol style="list-style-type: none"> Violaceous, planar papules and plaques Subepidermal blisters affecting lichen planus and non-affected skin 	<ol style="list-style-type: none"> Symmetrically distributed, well demarcated erythematous Nail dystrophy Arthropathy
Histology	<ol style="list-style-type: none"> Subepidermal blister with predominant neutrophilic dermal infiltrate DIF – IgG (+/- IgA and IgM at BMZ) 	<ol style="list-style-type: none"> Intense, and exaggerated basal vacuolar alteration resulting in a subepidermal cleft Other features of LP DIF – Shaggy fibrinogen along the basement membrane and IgM ovoid bodies. Negative for IgG and C3 along the BMZ. 	<ol style="list-style-type: none"> Subepidermal blisters with predominant eosinophil infiltration. DIF – linear deposition of IgG and C3 at BMZ IIF – IgG autoantibodies that bind to the epidermal (roof) of salt-split skin substrate 	<ol style="list-style-type: none"> Epidermal acanthosis with hypergranulosis Saw-toothed appearance of rete ridges Band-like infiltrate of lymphocytes in the upper dermis Colloid bodies and apoptotic keratinocytes DIF – Shaggy fibrinogen along the BMZ and IgM ovoid bodies 	<ol style="list-style-type: none"> Subepidermal blister May occur with or without features of lichen planus DIF – IgG and C3 along the BMZ IIF – IgG autoantibodies that bind to the epidermal (roof) side of salt-split skin substrate 	<ol style="list-style-type: none"> Parakeratosis Psoriasiform hyperplasia Neutrophilic and lymphocytic exocytosis +/- Munro's microabscesses
Antibodies	Type VII collagen, bullous pemphigoid antigen 1, laminin-5 and laminin -5 ¹¹	Associated with HLA-B7, DR1, DR10	IgG autoantibodies to bullous pemphigoid antigens	Associated with HLA-B7, DR1, DR10 BP230 and BP180	Anticollagen XVII (directed against BP180), BP antigens against 200kDa, and 230-kDa	Elevated levels of TNF- α HLA-Cw6
Treatment	<ol style="list-style-type: none"> Corticosteroids Dapsone Azathioprine, methotrexate, mycophenolate mofetil 	<ol style="list-style-type: none"> Corticosteroids (topical and systemic) NBUVB, Psoralen with UV-A Acitretin, sulfasalazine 	<ol style="list-style-type: none"> Corticosteroids (topical and systemic) Tetracycline, niconinamide, and erythromycin Azathioprine, methotrexate, mycophenolate mofetil, cyclophosphamide Rituximab 	<ol style="list-style-type: none"> Corticosteroids (topical and systemic) NBUVB, Psoralen with UV-A Acitretin, sulfasalazine 	<ol style="list-style-type: none"> Corticosteroids Vitamin D analogues, topical retinoids Phototherapy Methotrexate, acitretin, ciclosporin, hydroxyurea Biologics 	<ol style="list-style-type: none"> Topical corticosteroids Vitamin D analogues, topical retinoids Phototherapy Methotrexate, acitretin, ciclosporin, hydroxyurea Biologics

BMZ, basement membrane zone; DIF, direct immunofluorescence; HLA, human leukocyte antigen; IIF, indirect immunofluorescence; TNF, tumour necrosis factor.

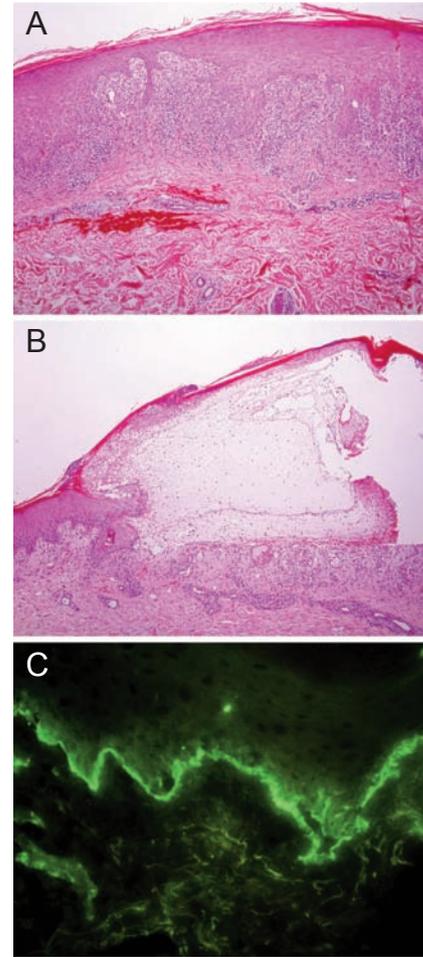


Figure 2. (A) Lichenoid dermatitis and saw-toothing of the rete ridges consistent with lichen planus (40x). (B) Subepidermal blister (40x). (C) Linear complement 3 (C3) deposits along the basement membrane zone.

Discussion

We have demonstrated the process of uncovering the diagnosis of LPP through NBUVB in our patient, and aim to dissect the distinguishing features of LPP from BLE, BLP, BP, and psoriasis.

Kaposi discovered lichen ruber pemphigoides in 1892, describing a case of typical LP with widespread bullous eruption. LPP affects all races, typically in the fourth to fifth decade of life.⁵ In most of the published case reports of LPP, LP precedes the development of bulla.⁶ The specific pathogenesis of drug and phototherapy induced LPP is unclear though the epitope spreading⁷ phenomenon has been implicated. Damage from an inflammatory process causes the release of an antigen leading to an autoimmune response against the released antigen. In our case, NBUVB is thought to have caused autoantibody forma-

tion due to damage to basal keratinocytes, leading to the exposure of previously unexposed basement membrane zone antigens to autoantibodies, resulting in the formation of subepithelial blisters. Circulating antibodies against BP 180 antigen have been detected in most cases of LPP⁸ and it was also found positive in our patient.

In LPP, there are concurrent lesions of LP and BP with the lichenoid lesions and blisters on both involved and apparently normal skin. It is differentiated clinically from bullous pemphigoid by its earlier age of presentation, less severe course, and affinity to lower extremities. Zillikens *et al.*⁹ have further demonstrated that antibody reactivity in LPP against novel epitope of region 4 of the NC16A domain of BP 180 antigen besides regions 2 and 3, were shown uniquely in LPP patients, indicating that the immunological pattern in LPP is different than BP.

Bullous lupus erythematosus is a subepidermal blistering disease which occur in patients with systemic lupus erythematosus. Vesicobullae eruptions usually distribute symmetrically on the trunk and upper arms. Blisters may develop as a result of extensive damage to the epidermal layer due to interface dermatitis caused by cutaneous lupus erythematosus leading to the exposure of epitopes and development of antibodies targeting the BMZ.¹⁰

Lichen planus is an idiopathic chronic inflammatory skin condition which is classically characterized as shiny, flat-topped violaceous to erythematous papules and plaques over the extremities and trunk, often crossed by white lines known as Wickham's striae. Bullous lichen planus is a variant LP where blisters develop on lichen planus affected skin, due to intense and exaggerated basal vacuolar alteration resulting in a subepidermal cleft, in association with a lichenoid infiltrate, and other accompanying features of LP. Histology

of the bullous lesions do not show the distinctive immunofluorescent findings of BP, linear IgG and C3 in the basement membrane zone. An important distinction from LPP is that bullae occur on sites of LP, sparing normal skin whereas in LPP, blisters are seen on sites of both lichen planus-affected and normal skin.

We should use this opportunity to highlight the key differences that allow us to distinguish lichen planus from psoriasis clinically. In retrospect, it would be the violaceous coloured papules and Wickham's striae our patient developed after phototherapy. Table 1 highlights the clinical presenting features of BLE, BP, LP, LPP, and psoriasis, the histology findings, and treatment options. When there is doubt regarding the diagnosis of the patient, a biopsy should be obtained to confirm the diagnosis.

Conclusions

Based on the case report, we conclude that NBUVB alone was the cause of development of LPP in our patient. Our patient was initially misdiagnosed with guttate psoriasis, therefore clinicians need to be aware of the presenting features of LPP, the distinguishing points between its differentials, to allow for prompt discontinuation of the inducing agents and initiating effective treatment.

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