Narrowband UVB-induced lichen planus pemphigoides

Wai Man Mandy Chan, Joyce Siiong See Lee, Colin Seng Thiam Theng, Sze Hon Chua, Hazel Hwee Boon Oon
National Skin Centre, Singapore

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 (BLE), bullous lichen planus, bullous pemphigoid, and psoriasis.

Introduction

Lichen Planus Pemphigoides (LPP) was first described by Kaposi 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 with phototherapy with psoralen and ultraviolet A therapy (PUVA), cinnarizine, captopril, anti-tuberculosis therapy, ramipril and simvastatin.1,2 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 generalized pururitic 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, pigmented 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 epidermal 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, bullous pemphigoid, lichen planus, lichen planus pemphigoides, and psoriasis.

| Burrus lupus erythematosus | Burullus lichen planus | Bullous pemphigoid | Lichen planus | Lichen planus pemphigoides | Psoriasis |
|----------------------------|-----------------------|-------------------|--------------|---------------------------|-----------|
| **Clinical features**      |                       |                   |              |                           |           |
| 1. Systemic lupus erythematosus (fulfill American Rheumatism Association criteria for SLE) | 1. Blistering on lichen planus affected skin of life | 1. Affects elderly in fifth to seventh decades | 1. Shiny, flat-topped violaceous to erythematous plaques and plaques over the extremities and trunk | 1. Violaceous, planar papules and plaques with overlying silvery scales affecting the buttocks, elbows, lower back, scalp and knees | 1. Symmetrically distributed, well demarcated erythematous plaques |
| 2. Symmetrical vesiculobullous eruption on trunk, proximal upper extremities, neck and face | 2. Tense bullae on skin surface with predilectioin on flexural areas | 2. Wickham’s striae | 2. Symmetrical vesiculobullous eruption on trunk, proximal upper extremities, neck and face | 2. Nail dystrophy | 2. Arthropathy |
| 3. Mucosal involvement | 3. Mucosal involvement | 3. May occur with or without features of lichen planus | 3. Arthropathy | 3. Mucosal involvement | 3. Parakeratosis |
| **Histology** | **Histology** | **Histology** | **Histology** | **Histology** | **Histology** |
| 1. Intense, and exaggerated basal vacuolar alteration resulting in a subepidermal cleft | 1. Intense, and exaggerated basal vacuolar alteration resulting in a subepidermal cleft | 1. Epidermal acanthosis with hypergranulosis | 1. Subepidermal blister with predominant eosinophil infiltration | 1. Pemphigus vulgaris | 1. Pemphigus vulgaris |
| 2. Other features of LP | 2. Other features of LP | 2. Saw-toothed appearance of rete ridges | 2. Band-like infiltrate of lymphocytes in the upper dermis | 2. Psoriasiform features | 2. Dermoepidermal junction blister |
| 3. Band-like infiltrate of lymphocytes in the upper dermis | 3. Band-like infiltrate of lymphocytes in the upper dermis | 3. Collagen and amorphous fibrillar material | 3. Band-like infiltrate of lymphocytes in the upper dermis | 3. Collagen and amorphous fibrillar material | 3. Collagen and amorphous fibrillar material |
| 4. Collagen and amorphous fibrillar material | 4. Collagen and amorphous fibrillar material | 4. Collagen and amorphous fibrillar material | 4. Collagen and amorphous fibrillar material | 4. Collagen and amorphous fibrillar material | 4. Collagen and amorphous fibrillar material |
| **Antibodies** | **Antibodies** | **Antibodies** | **Antibodies** | **Antibodies** | **Antibodies** |
| Type VII collagen, bullous pemphigoid antigen 1, laminin-5 and laminin-6 \(^a\) | Associated with HLA-B7, DR1, D10 | IgG autoantibodies to bullous pemphigoid antigens | Associated with HLA-B7, DR1, D10, BP-180 | Anticollagen XVII (directed against BP180), BP antigens against 200kDa, and 230kDa | Elevated levels of TNF-\(\alpha\) HLA-Cw6 |
| **Treatment** | **Treatment** | **Treatment** | **Treatment** | **Treatment** | **Treatment** |
| 1. Corticosteroids | 1. Corticosteroids (topical and systemic) | 1. Corticosteroids (topical and systemic) | 1. Corticosteroids (topical and systemic) | 1. Corticosteroids (topical and systemic) | 1. Corticosteroids (topical and systemic) |
| 2. Dapsone | 2. Tetraacycline, nicothiaimide, and erythromycin | 2. Tetraacycline, nicothiaimide, and erythromycin | 2. Tetraacycline, nicothiaimide, and erythromycin | 2. Tetraacycline, nicothiaimide, and erythromycin | 2. Dapsone, nicothiaimide, and erythromycin |
| 3. Azathioprine, methotrexate, mycophenolate mofetil | 3. Methotrexate, cyclophosphamide | 3. Methotrexate, cyclophosphamide | 3. Methotrexate, cyclophosphamide | 3. Methotrexate, cyclophosphamide | 3. Methotrexate, cyclophosphamide |

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

We have demonstrated the process of uncovering the diagnosis of puin by combining the findings from our patient, and aim to dissect the distinguishing features of LPP from BLE, BLP, IP, and po.
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.

References

1. Kaposi M. Lichen ruber pemphigoides. Arch dermato syph 1892;24:343-6.
2. Cohen DM, Ben-Amitai D, Feinmesser M, Zvulunov A. Childhood lichen planus pemphigoides: A case report and review of the literature. Pediatr Dermatol 2009;26:569-74.
3. Maoz KB, Brenner S. Lichen planus pemphigoides triggered by narrowband UVB, paracetamol, and ibuprofen, with autoantibodies to 130kDa antigen. Skinmed 2008;7:33-6.
4. Anand D, Bernardin R, Rubin AI. Blisters and plaques on the extremities. Int J Dermatol 2011;50:147-9.
5. Wilsteed E, Bhogal BS, Das AK, et al. Lichen planus pemphigoides: a clinico-pathologic study of nine cases. Histopathology 1991;19:147-54.
6. Swale VI, Black MM, Bhogal BS. Lichen planus pemphigoides: two case reports. Clin Exp Dermatol 1998;23:132-5.
7. Chan LS, Vanderlugt CJ, Hashimoto T, et al. Epitope spreading: lessons from autoimmune diseases. J Invest Dermatol 1998;110:103-9.
8. Barnadas MA, Roé E, Dalmau J, et al. Lichen planus pemphigoides: detection of anti-BP 180 antibodies by ELISA and immunoblotting tests. JADV 2010;24:1359-69.
9. Zillikens D, Caux F, Mascaro JM, et al. Autoantibodies in lichen planus pemphigoides react with novel epitope within the C-terminal NC16A domain of BP180. J Invest Dermatol 1999;113:117-21.
10. Pižem J, Vizjak A, Tomšič M, Luzar B. Widespread vesiculobullous eruption in a 16-year-old male. Acta Dermatoven AP A 2010;19:19-22.
11. Chan LS, Lapiere JC, Chen M, et al. Bullous systemic lupus erythematosus with autoantibodies recognizing multiple skin basement membrane components, bullous pemphigoid antigen 1, laminin-5, laminin-6, and type VII collagen. Arch of Dermatol 1999;135:569-73.