

Dapsone-responsive inflammatory dermatitis with features of subcorneal pustular dermatosis and bullous pemphigoid



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INTRODUCTION

Autoimmune bullous diseases (AIBD) are complex and may overlap. It is important to find simplified, successful treatments for these patients. Here we present a case of dapsone-responsive inflammatory dermatitis with features of subcorneal pustular dermatosis (SPD) and bullous pemphigoid (BP). SPD, or Sneddon-Wilkinson disease, is a rare chronic, pustular eruption consisting of symmetric sterile flaccid pustules on the trunk, flexor limbs, and intertriginous areas, which easily rupture, resulting in scaling, crusting, and hyperpigmentation.¹⁻³ Histologically, SPD is characterized by a subcorneal neutrophil accumulation with minimal acantholysis.⁴ Dapsone is the preferred first-line treatment.³ BP is the most common AIBD. Patients develop tense bullae on an erythematous base commonly affecting the axillae, abdomen, inguinal folds, and inner aspects of the thighs.⁵ Histologically, BP exhibits spongiosis, eosinophils, and superficial dermal inflammatory infiltrate. Direct immunofluorescence highlights linear IgG and/or linear C3 staining along the basement membrane.⁶ First-line treatment is topical and/or systemic glucocorticoids, steroid-sparing agents, and anti-inflammatory antibiotics.⁶

CASE REPORT

A 66-year-old Caucasian man with a history of arthritis and chronic dermatosis presented to the clinic with a new rash. The patient reported a history of 'psoriasis' primarily affecting his palms and soles, although he had not been biopsied prior to this rash. He believed his new rash was distinct from his

Abbreviations used:

AIBD: autoimmune bullous diseases
 BP: bullous pemphigoid
 Ig: immunoglobulin
 SPD: subcorneal pustular dermatosis

previous dermatosis. Over the past decade, he had been prescribed multiple systemic medications for his arthritis (carrying the diagnosis of rheumatoid or psoriatic arthritis), including adalimumab, etanercept, apremilast, methotrexate, and, in recent months, secukinumab and tofacitinib. Upon presentation to our clinic, the patient had a 2-month history of a pruritic, tingling vesiculopustular eruption that began on the chest and spread to the abdomen, back, axillae, groin, scalp, and extremities (Fig 1, A and B). The new pustules consisted of gravity-dependent purulent material with clear fluid atop. Pustules coalesced into annular, serpiginous plaques with peripheral pustules and superficial crust and scale. His eruption was not relieved by antifungal creams, topical corticosteroids, or mupirocin.

Initial and repeat biopsies submitted to hematoxylin-eosin staining demonstrated a pustule formed by primarily neutrophils and eosinophils in the subcorneal space with limited focal acantholysis, suggesting a subcorneal inflammatory dermatitis (Fig 2, A). Direct immunofluorescence microscopy studies of intact, perilesional skin were negative; direct immunofluorescence studies of the biopsy after treatment with 1 M NaCl revealed *in-situ* deposits of IgG localized to the epidermal side of the patient's

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Fig 1. Clinical photos of subcorneal pustular dermatosis. **A**, Initial clinical presentation 2 months after onset of rash. **B**, Seven months after initial presentation while on dapsone and occasional topical steroids.

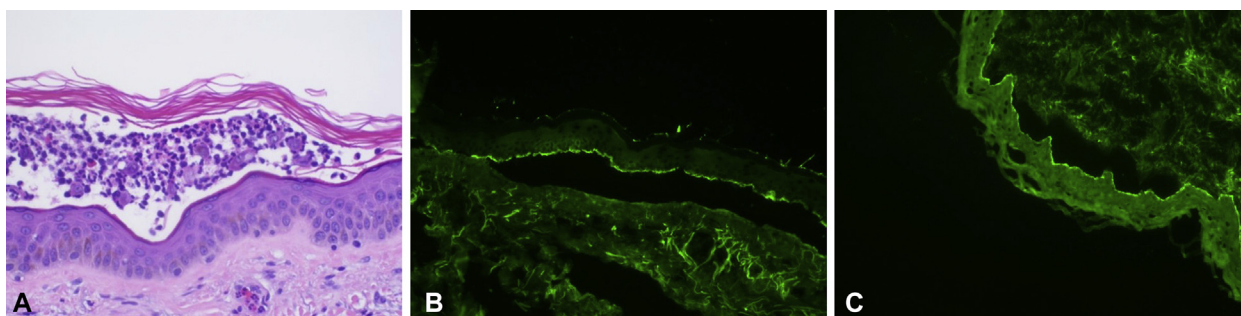


Fig 2. Light microscopy and immunofluorescence microscopy. **A**, Subcorneal pustule formed by infiltrates of neutrophils and eosinophils, along with focal acantholytic keratinocytes (Hematoxylin-eosin stain; Original magnification: $\times 400$). **B**, Continuous deposits of IgG immunoreactant to the epidermal side of salt split skin (Direct Immunofluorescence Microscopy Study of Patient 1 Molar NaCl Split Skin; Original magnification: $\times 400$). **C**, Positive IgG immunoreactant (Indirect immunofluorescence Microscopy Study of 1M NaCl Split Skin; Original magnification: $\times 400$).

split skin (negative IgA, IgM, C3c, and fibrin). Indirect immunofluorescence analysis of human salt-split skin identified IgG (but not IgA) that bound the epidermal side (titer, ≥ 40). Indirect immunofluorescence studies of monkey esophagus found no evidence of IgA autoantibodies against epithelial cell plasma membranes; IgG against epithelial basement membrane (titer >40), however, was identified. BP, or a variant thereof, was most consistent with these findings. Enzyme-linked immunosorbent assay analysis identified IgG autoantibodies against BP230 (28 U/mL), but not BP180, desmoglein 1, or desmoglein

3, which is uncommonly pathogenic in isolation in BP (Fig 2, B and C).

After the preliminary workup, the patient's differential diagnosis included SPD, annular pustular psoriasis, BP and variants, other autoimmune bullous dermatosis, or an inflammatory dermatosis triggered by previous therapies. Immunopathologic findings suggested BP; yet, histology was less favorable for this diagnosis. The patient was started on doxycycline, antihistamines, and topical corticosteroids, which did not prevent new vesicle formation. We recommended discontinuation of other therapies prescribed

elsewhere (secukinumab, tofacitinib) as they were ineffective in improving cutaneous and arthritic symptoms. Dapsone 50 mg daily was initiated. Further workup included serum and urine protein electrophoresis. He was diagnosed with IgG K monoclonal gammopathy of undetermined significance by a hematologist. Within 3 weeks of starting dapsone, the patient's rash and pruritus improved enormously, and he no longer developed new vesicles. Dapsone was increased to 100 mg daily, and he continued doxycycline and topical corticosteroids. He was seen 1 month later and reported that he had experienced a flare after missing 5 days of dapsone. Three months after starting dapsone, doxycycline was discontinued. He did not experience a flare after discontinuing doxycycline and has remained free of skin disease with dapsone 100 mg daily for over 9 months (Fig 1, B).

DISCUSSION

This patient presented with an extensive vesiculopustular eruption, a complicated history that included uncharacterized arthritis and treatment with numerous systemic therapies, and incongruent histologic and immunopathologic findings. Occasionally, immunobullous disorders with mixed-pattern results are identified. Accurate classification may require repeat testing or exclusion of noncontributory findings. His differential diagnosis included many bullous dermatoses such as SPD, pustular psoriasis, atypical BP, or medication-induced dermatosis.⁷ Repeated light microscopy studies, demonstration of an underlying hematologic disorder, and a dramatic response to dapsone favored a diagnosis of SPD, although many AIBD may have overlapping or similar features and respond to dapsone. Most patients with SPD respond to dapsone, which can assist in differentiating pustular psoriasis from SPD. An additional consideration was whether the various biologics and immunosuppressants this patient had tried for his arthritis (now diagnosed as osteoarthritis) may have triggered this presentation, as tumor necrosis factor- α inhibitors have been suggested to trigger AIBD.^{7,8}

Although our patient's clinical and histologic features were suggestive of SPD, the preliminary immunopathology studies met the minimal criteria for BP.⁹ Interestingly, a case of BP mimicking SPD has been reported.¹⁰ BP may have a propensity to develop in patients with SPD, as for instance in patients with psoriasis. Alternatively, this patient's immunopathology findings may have developed secondary to his chronic, treatment-resistant skin disease, representing an atypical response to prior therapies, or signifying subclinical BP.

This case emphasizes the importance of simplification, when patients present with a complex

history, unique clinical features, and mixed laboratory results. By comprehensively assessing medical history, eliminating medications, obtaining further workup, and attempting disease-directed treatment, this patient was able to experience clearance of his cutaneous eruption. Further, this case reinforces the notion that repeated testing and/or elimination of noncontributory findings should be considered in complex cases, when diagnosis is not clear and, instead, to focus on treatment options and clinical status. Although this patient's diagnosis was not straightforward, narrowing his treatments, repeating light microscopy studies of lesional skin, and placing his immunopathologic findings into context allowed for a clearer clinical picture to declare itself and for successful treatment to be found.

Conflicts of interest

None disclosed.

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