

Coincidence of Bullous Pemphigoid and Pityriasis Rubra Pilaris

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Bullous pemphigoid (BP), an autoimmune blistering skin disease characterized by pruritus, urticarial plaques, blisters, and erosions, is induced by IgG-autoantibodies against the hemidesmosomal proteins BP180 and/or BP230 (1, 2). Erythrodermic BP is an unusual variant with generalized erythroderma (3). Pityriasis rubra pilaris (PRP) is a rare chronic inflammatory papulosquamous disorder of unknown etiology.

CASE REPORT

A 71-year-old Caucasian woman presented with a 6-week history of pruritic erythroderma that started on her left chest. She did not report recent infections, fever, night sweats, or weight loss. Her past medical history included breast cancer, chronic hypersensitivity pneumonitis (CHP) and diabetes. Physical examination showed generalized erythroderma and fine scaling with concomitant blisters around her mastectomy scar (Fig. 1a). Blood tests were unremarkable. A lesional biopsy showed a subepidermal blister and an inflammatory infiltrate containing lymphocytes and eosinophils. Direct immunofluorescence (IF) of a perilesional biopsy revealed linear deposition of C₃ and IgG along the basement membrane (Fig. 2a). IgG-autoantibodies bound to the roof of an artificial blister on human salt-split skin (Fig. 2b). Whereas no serum IgG against BP180 NC16A and BP230 was detected by enzyme-linked immunoassay (ELISA), IgG reactivity was observed against the

120-kDa cell-derived soluble ectodomain of BP180 (LAD-1) by immunoblotting (Fig. 2c). An initial diagnosis of erythrodermic BP was made. Treatment included oral antihistamines and topical clobetasol propionate for 2 weeks; however, the skin lesions did not improve. The patient subsequently also developed palmoplantar hyperkeratosis, scaling of the scalp, thickened nails, islands of normal-appearing skin, cervical lymphadenopathy and oedema of the lower legs (Fig. 1b and c), and a biopsy taken from lichenified erythema revealed acanthosis, parakeratosis, papillomatosis, a prominent granular layer, and a dermal perivascular lymphocytic inflammation. These findings were consistent with a diagnosis of PRP. To exclude a relapse of her breast cancer a positron emission tomography-computed tomography (PET-CT) scan was performed, which was unremarkable. Treatment was expanded to include oral acitretin 10 mg per day. However, there was an unsatisfactory improvement. Due to its best effect/side-effect profile, we administered intravenous immunoglobulin (IVIg) 2 g/kg body weight (160 g) over 4 days every 4 weeks. Within the next 2 months scaling, palmoplantar hyperkeratosis and erythroderma improved significantly and no new blisters appeared (Fig. 1d). Exacerbation of her pre-existing CHP required short-term non-invasive ventilation and administration of oral methylprednisolone 1 mg/kg body weight, which was gradually tapered to a maintenance dose of 4 mg. Subsequently, the tyrosine kinase inhibitor nintedanib was started for her interstitial lung disease.

In summary, the patient presented with coinciding PRP and BP with autoantibodies against LAD-1. After initiation of high-dose IVIg, both diseases showed a significant improvement.



Fig. 1. Clinical pictures of the patient. (a) Blisters and erosion around the mastectomy scar and nappes claires. (b) Generalized erythroderma with (c) white scaling and islands of normal skin. (d) Hyperkeratotic plaques on the palm. (e, f) Significant improvement of phenotype with intravenous immunoglobulin.

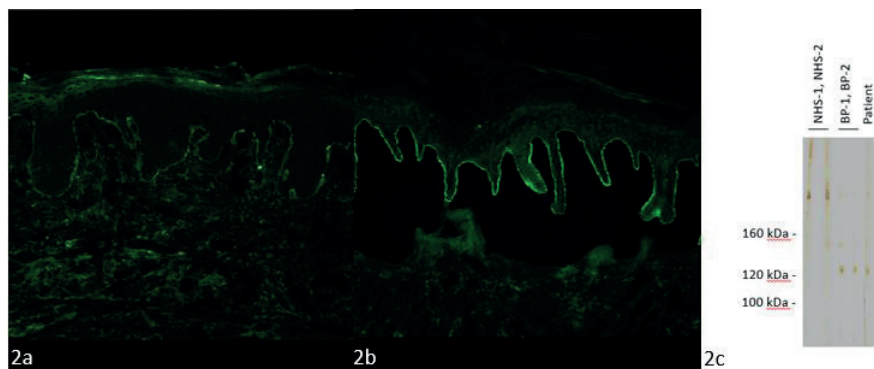


Fig. 2. Immunofluorescence (IF) and immunoblot findings. (a) Linear deposition of immunoglobulin G (IgG) along the dermal-epidermal junction by direct immunofluorescence (IF) of a perilesional biopsy. (b) Indirect IF on salt-split skin showed lineal staining of IgG at the roof of the artificial blister. (c) Immunoblotting with conditioned supernatant of cultured keratinocytes showed IgG reactivity with the 120-KDa soluble ectodomain of BP180 (LAD-1; Patient). Two patients with bullous pemphigoid (BP-1, BP-2) and 2 normal human sera (NHS-1, NHS-2) served as controls. Arrow indicates LAD-1.

DISCUSSION

The coincidence of PRP and BP is very rare; only one patient has previously been reported in the literature (4). BP can rarely present as erythroderma. However, palmoplantar keratoderma and islands of uninvolved skin and the histology were consistent with concurrent PRP. In contrast to a previous report of coinciding BP and PRP (4) with antibodies against BP180 NC16A and BP230, the current patient presented IgG-antibodies against the BP180 ectodomain (LAD-1) outside the immunodominant NC16A domain. BP with antibodies to LAD-1 is very rare; currently only 4 patients have been reported in the literature (5).

Triggers relevant for both BP and PRP remain unknown in the current patient. As both disorders may be associated with malignancies and autoimmune diseases (6), a relapse of her breast cancer or other malignant disease was excluded; a thorough medication history did not identify possible drug triggers. It is conceivable that the erythroderma exposed autoantigens in the epidermis of the current patient, since additional cases with psoriatic erythroderma and LAD-1 BP have been reported (7, 8), and PRP is known to be associated with other autoimmune disorders, including myasthenia gravis, thyroiditis, coeliac disease, and vitiligo.

The use of IVIg is known as an effective treatment of severe forms of autoimmune blistering diseases, dermatomyositis, systemic vasculitic syndromes, lupus erythematoses, toxic epidermal necrolysis or scleromyxoedema (9). It is well tolerated, but can sometimes lead to minor side-effects, such as headache, myalgia, or nausea, which are usually self-limiting (10). Because of a reported higher risk of recurrence or incidence of neoplasia, we decided against TNF α inhibitors as a treatment option (11). Although there is no increased risk for malignancy with ustekinumab, the patient declined this therapy (12).

In conclusion, clinicians should consider the coincidence of BP and PRP in patients with concurrent erythroderma and blistering skin disease. The use of high-dose IVIg is a safe and effective therapeutic option for both diseases.

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