

## Prurigo Pigmentosa in a 21-year-old Caucasian Man: A Clinicopathological Correlation

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Accepted May 30, 2017; Epub ahead of print May 31, 2017

Prurigo pigmentosa (PP) is a rare inflammatory skin disease first described in Japan and clinically typified by symmetrically distributed pruritic papules, papulovesicles and vesicles (1, 2). Lesions resolve over time, leaving post-inflammatory hyperpigmentation arranged in a reticulated pattern (2). The majority of patients diagnosed with PP are Asians, more frequently women (1), but is often misdiagnosed in Western countries.

### CASE REPORT

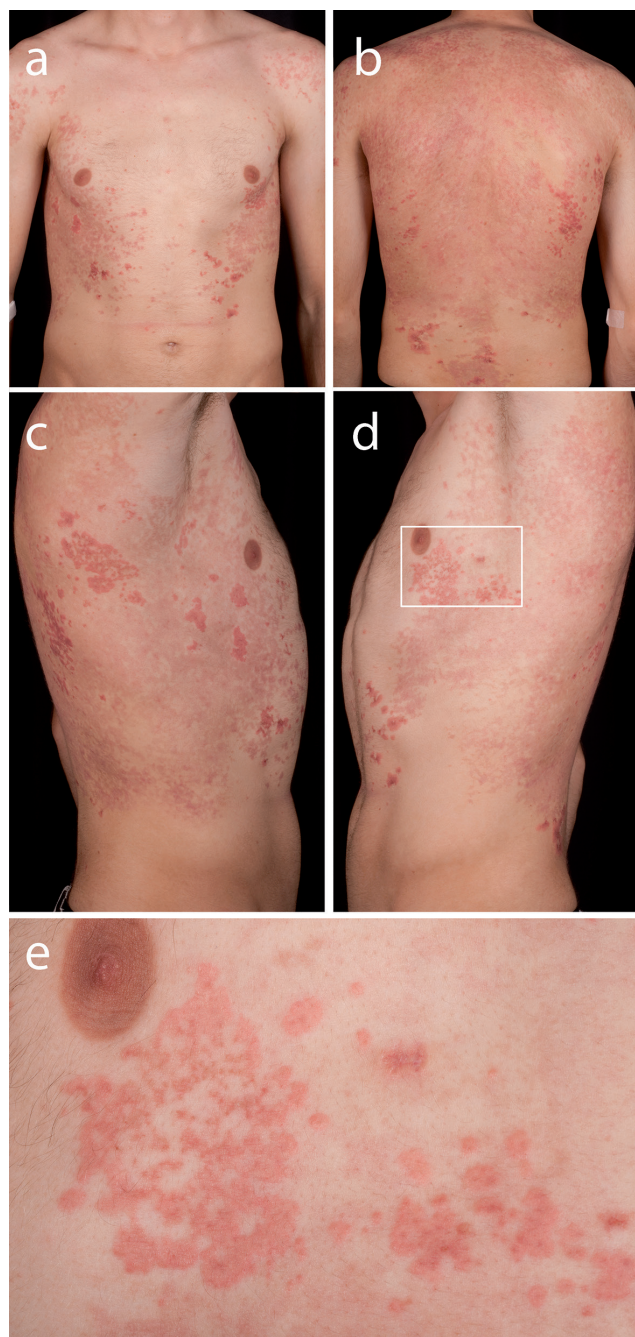
An otherwise healthy 21-year-old Caucasian man was referred to our clinic with symmetrically distributed erythematous papules and plaques covering his chest and lateral trunk. Furthermore, the patient's back was extensively involved. The lesions showed a reticulate pattern with overlying focal scaling and crusting (Fig. 1). Despite occasional and moderate pruritus the skin lesions were asymptomatic and the patient did not report any further symptoms. The remaining integument, as well as the mucosa and nails, were clinically unremarkable. Histopathology of a biopsy from an erythematous, urticarial papule revealed orthokeratosis and a moderate perivascular and interstitial infiltrate of lymphocytes and neutrophils admixed with some eosinophils. The spongiotic epidermis was focally infiltrated by neutrophils. Dyskeratotic keratinocytes were rare (Fig. S1 a, b<sup>1</sup>). One week later a follow-up biopsy was taken from a crusted papulovesicle. Histopathology showed a significant epidermal necrosis accompanied by many dyskeratotic and acantholytic keratinocytes. In addition, the infiltrate was much more intense and dominated by eosinophils (Fig. S1 c, d<sup>1</sup>). Complete blood cell count, total proteins, liver, kidney and thyroid function tests and metabolic panel were within normal limits.

The clinical presentation and histopathological findings were consistent with a diagnosis of PP.

### DISCUSSION

Since PP was first described by Nagashima in 1971 (1), more than 200 Japanese patients have been reported. Only a few non-Japanese patients have been reported to date (1, 2). The "life of lesions" in PP is extraordinarily dynamic, i.e. the histopathological features transpire rapidly, just as

do the lesions clinically. Therefore many patients have PP for weeks or months before a correct diagnosis is made (3–5). As pruritus is a prominent feature in many cases,



**Fig. 1.** Patient with symmetrically distributed erythematous papules and plaques in a reticulate pattern with overlying focal scaling and crusting. (a) Chest, (b) back, (c, d) lateral flanks, and (e) close-up.

<sup>1</sup><https://doi.org/10.2340/00015555-2713>

patients frequently scratch the lesions. The typical clinical picture may therefore be altered and concealed.

Nagashima described a female:male ratio of 6:1 (1), whereas Teraki et al. reported a ratio of 4:1 (2, 6). The mean age at time of diagnosis is approximately 25 years and PP has not been reported in prepubescent children or elderly people (2). Some cases of PP are described in association with metabolic diseases, such as diabetes mellitus and ketosis. Furthermore fasting, dieting, anorexia nervosa and pregnancy are reported as associated conditions (7). PP is characterized by frequent recurrences followed by times in remission lasting from weeks to years (2). Interestingly, there are also reports of unilateral, segmentally arranged PP (8). Among others, confluent reticulated papillomatosis (CRP) and Dowling-Degos disease (DDD) have to be considered as differential diagnoses (9). The post-inflammatory hyperpigmentation in CRP is similar to PP; however, CRP is not characterized by precedent erythematous papules. DDD may well be differentiated from PP by histopathology and the distribution of the skin lesions. DDD classically involves flexural sites that are not involved in PP (9).

The histopathological features of PP and their changes over time had been described in much detail by Böer et al. (3). Initially, a relatively sparse superficial infiltrate of perivascular and interstitial neutrophils is present. Neutrophils also show exocytosis into the spongiotic epithelium, that often contains few necrotic keratinocytes. Neutrophilic microabscesses are sometimes detectable. After some days eosinophils and lymphocytes predominate the infiltrate, which increasingly assumes a lichenoid pattern. As epidermal changes also become more intense, intraepidermal vesicles, ballooning of keratinocytes, epidermal foci of necrosis and prominent vacuolar alteration of the basement membrane zone may appear. Nuclear dust of neutrophils and extravasated erythrocytes could also be seen. After some weeks late-stage lesions are characterized by epidermal hyperplasia, parakeratosis and dermal melanophages as histopathological hallmarks (3).

The vast majority of skin biopsies in PP are taken from rather late or resolving lesions. As these lesions reflect the end stage of an inflammatory process, they are often classified histopathologically as “non-specific”. Therefore, clinico-pathological correlation is crucial, and follow-up biopsies during the course of the disease may lead the way to the correct diagnosis.

The pathogenesis of PP is not yet fully understood. Investigations on potential causative factors of PP indicate a number of correlations with various environmental and biological agents, such as contact allergens or infections with *Helicobacter pylori* (11). Chao and co-workers studied 14 patients with PP and 5 controls with regard to accompanying *Borrelia* infections. *Borrelia* spirochetes

were isolated from skin biopsies of 3 patients with PP. These findings were confirmed by elevated IgG and IgM antibodies against the major protein antigens of *Borrelia burgdorferi* in serum samples (9). Nevertheless, a potential causative role of *Borrelia* spirochetes in the context of PP needs to be studied in more detail.

Therapy for PP remains a challenge. Dapsone (diaminodiphenyl-sulfone), doxycycline and minocycline, a semi-synthetic tetracycline, have proven effective in PP (2). These drugs can inhibit the migration and function of neutrophils, which predominate the infiltrate in early PP lesions. Dapsone at doses of 25–100 mg, as well as minocycline and doxycycline at doses of 100 mg have been used with great efficacy (2, 9). Whereas the inflammatory component and pruritus respond well to these drugs, the residual hyperpigmentation of PP cannot be prevented by this approach (2).

In our patient the clinical diagnosis of “drug-induced rash” was made externally and systemic steroids (60 mg prednisolone once daily) with subsequent tapering over 14 days were not effective. After alternating remissions and relapses without further treatment we were able to confirm PP due to the clinical course and histopathology results. Finally, doxycycline 100 mg once daily for 3 weeks resulted in stable remission.

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