Granulomatous pigmented purpuric dermatoses: report of three cases and review of the literature

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ABSTRACT

Purpuric pigmented dermatoses represent a form of chronic, recurrent capillaritis characterized by petechiae and purpuric macules over the lower limbs. We report three female cases who presented with clinical features of purpuric pigmented dermatosis with unusual histopathologic features. The first patient had golden-brown pigmented purpura over bilateral knees, shins and dorsal feet. The second patient showed purpuric papules on the medial aspects of the ankles. The third patient presented with numerous petechiae on her lower legs. All three patients demonstrated granulomatous inflammation in addition to the histologic features of pigmented purpuric dermatosis. A total of 11 patients have currently been reported in the literature. A review of the clinical details of the cases revealed a high incidence of hyperlipidemia (7/11) and hypertension (4/11) among these patients.

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KEYWORDS

Granuloma
Pigmented purpuric dermatoses

Introduction

Pigmented purpuric dermatoses (PPDs) are a relatively common group of diseases characterized by clinically brown to golden-brown purpuric lesions, mainly on the lower limbs. They share the similar histopathologic finding of capillaritis. Several variants have been described. Granulomatous PPD was first reported by Saito and Matsuoka in 1996 and is a histopathologic variant characterized by granulomatous infiltrates, in addition to capillaritis. Only a few cases have been reported in the literature, and some of these had associated systemic disorders. We report three more cases and review their clinical features.

Case reports

Case 1

A 49-year-old woman presented at our department with a 2-year history of numerous, progressively extending, asymptomatic rashes over her lower legs. She had a history of hypertension. Physical examination showed many golden-brown macules, patches and papules located on her dorsal feet, shins and knees (Figure 1A). She had no varicose veins on either lower limb. The movement, pulsation and temperature of her bilateral lower limbs were normal. She denied previous traumatic injury or known allergies to drugs or food.

Histopathologic examination of a biopsy specimen from the dorsal aspect of the right foot showed capillaritis and striking dense nodular infiltration in the papillary dermis (Figure 1B). The papillary dermal nodules were composed of well-formed epithelioid granulomas, lymphocytes and extravasation of red blood cells (Figure 1C). Periodic acid-Schiff (PAS) and Grocott’s methenamine silver staining were negative for fungi, and acid-fast stain was negative for mycobacterial organisms. Iron staining revealed a large amount of hemosiderin deposition in the upper reticular dermis (Figure 1D). Medium-potency topical corticosteroids were prescribed under the diagnosis of granulomatous PPD. The patient failed to return regularly and was lost to follow-up after several visits.

Case 2

A 66-year-old woman presented with a history of a persistent rash on her lower limbs for over 10 years. She had a...
history of medically controlled hyperlipidemia and cardiac arrhythmia. There were purpuric macules, papules and patches over the medial aspects of both ankles, with no itching or tenderness (Figure 2A). She had no varicose veins and no evidence of stasis dermatitis on her lower limbs.

Laboratory examination showed elevated total cholesterol (248 mg/dL [6.42 mmol/L], normal range 130–200 mg/dL [3.36–5.18 mmol/L]) and low-density lipoprotein (163 mg/dL [4.22 mmol/L], normal range 62–130 mg/dL [1.61–3.37 mmol/L]). High-density lipoprotein, triglyceride and alanine aminotransferase levels were normal. No hepatitis B or hepatitis C antibodies were detected.

Histopathologic examination of a biopsy specimen from the medial aspect of the right ankle showed capillaritis, red blood cell extravasation, and perivascular inflammatory infiltration, mainly in the papillary dermis, containing lymphohistiocytic cells (Figure 2B). Some less well-formed epithelioid granulomas and multinucleated giant cells were seen (Figure 2C). PAS and Grocott’s methenamine silver stains were negative for fungal organisms, and acid-fast stain was negative for mycobacterial bacilli. Iron staining demonstrated large amounts of hemosiderin deposition in the upper reticular dermis (Figure 2D). No obvious improvement was noted after topical corticosteroid treatment.

Case 3

A 54-year-old woman had a medical history of hypertension, hyperlipidemia, and thyroid goiter. She had a 10-year history of purpuric skin lesions on her lower legs and dorsal feet. Her father had hypertension and her mother had diabetes mellitus, but neither her parents nor her siblings had similar skin lesions. Laboratory examination showed an elevated total cholesterol level of 253 mg/dL (6.55 mmol/L).

Histopathologic examination showed well-defined granulomas composed of histiocytes and perivascular lymphocytes in the upper dermis just beneath the epidermis (Figures 3A and 3B). The capillaritis and red blood cell extravasation were interpreted as features of PPD. Hemosiderin deposition in the upper dermis was revealed by iron staining. Granulomatous PPD was diagnosed. No specific treatment was prescribed after the skin biopsy.

Discussion

The granulomatous variant is a rare form of PPD, mostly reported in East Asians.1–3 A total of 11 cases (2 Japanese and 9 Taiwanese), including the three patients reported in this
article, have been described in the literature and the pooled data are summarized in Table 1. Among these patients, only two had no medical history of systemic disorders. Interestingly, hyperlipidemia was present in 7 of the 11 cases; 4 of these 7 cases had hypertension, while 2 had hepatitis C or cryoglobulin.

There were slight differences in the clinical features between patients with the granulomatous variant and those with other types of PPD. Patients with granulomatous PPD were mainly middle aged to elderly, ranging from 22 to 71 years old (mean age, 53 years), and were generally older than patients with the Majocchi or lichen aureus variants. Moreover, most variants of PPD were more common in males, while 60% of the patients with the granulomatous variant were female.

Granulomatous PPD showed similar clinical characteristics to the most common variant of PPD, Schamberg’s disease. Most cases involved the lower legs and dorsal feet;

Figure 2 (A) Scattered purpuric macules, papules on the medial aspects of the ankles. (B) Mild lymphohistiocytic perivascular infiltration, capillaritis and erythrocyte extravasation without leukocytoclasis. Ill-defined granulomas in the superficial dermis with multinucleated giant cells (H&E, 100×). (C) Perivascular granuloma (H&E, 400×). (D) Hemosiderin deposition demonstrated by iron staining (H&E, 100×).

Figure 3 (A) Well-defined granuloma in the superficial dermis and lymphohistiocytic perivascular infiltration, capillaritis and erythrocyte extravasation (H&E, 100×). (B) Close view of the granuloma (H&E, 400×).
changes, such as pseudocarcinomatous hyperplasia. The infiltrate in the infectious process is usually denser, with a mixed cell population. PAS stain and acid-fast stain are helpful for identifying the organism. Granulomatous PPD shows typical features of capillaritis, in addition to granulomas. Iron staining is therefore useful for detecting the large amounts of hemosiderin deposition in the superficial dermis in PPD, as shown in our cases.

The true pathogenesis of PPD is still unclear. Many mechanisms have been proposed including infection, capillary fragility, venous hypertension, gravitational dependency, drugs and chemicals. An association with some medical disorders has been described: Some have suggested relationships between PPD and mycosis fungoides, and hepatitis B or hepatitis C. Leukocytoclastic vasculitis and cutaneous necrotizing vasculitis are frequently reported in hepatitis C, presenting as lymphocytic vasculitis in the late resolving stage. Thus, some authors have hypothesized that patients may have chronic and recurrent cutaneous necrotizing vasculitis, resulting clinically as PPD and histologically as lymphocytic vasculitis. However, the case numbers in these reports were small and no definite association can be established.

An increasing number of recent reports suggest that inflammatory cell infiltrates play an important role in PPD. Some authors consider PPD to be a chronic lymphoid dyscrasia; this is supported by the fact that many patients with typical presentations of PPD were devoid of true venous insufficiency or other traumatic causes. The typical

### Table 1: Eleven cases of the granulomatous variant of pigmented purpuric dermatoses.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Age/sex</th>
<th>Duration</th>
<th>Location</th>
<th>Clinical features</th>
<th>Laboratory data</th>
<th>Associated diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saito &amp; Matsuoka¹</td>
<td>61/F</td>
<td>2 mo</td>
<td>Dorsum of feet</td>
<td>Brown pigmentation with hemorrhagic papules</td>
<td>ANA 1:80</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>53/F</td>
<td>1 yr</td>
<td>Dorsum of feet</td>
<td>Brown pigmentation with hemorrhagic papules</td>
<td>RF</td>
<td>Hepatitis C</td>
</tr>
<tr>
<td>Wong et al²</td>
<td>67/F</td>
<td>20 yr</td>
<td>Dorsum of feet</td>
<td>Erythematous to brown macules</td>
<td>ANA, RF</td>
<td>Hyperlipidemia, COPD</td>
</tr>
<tr>
<td>Lin et al³</td>
<td>57/M</td>
<td>8 mo</td>
<td>Dorsum of feet</td>
<td>Brown papules and plaques</td>
<td>ANA, RF</td>
<td>Hyperlipidemia, hypertension NA</td>
</tr>
<tr>
<td></td>
<td>37/M</td>
<td>1 yr</td>
<td>Right wrist</td>
<td>Brown macules and papules</td>
<td>NA</td>
<td>Hyperlipidemia, hypertension</td>
</tr>
<tr>
<td></td>
<td>22/M</td>
<td>6 mo</td>
<td>Legs</td>
<td>Purpuric papules</td>
<td>Cryoglobulin IgG+, IgA+, IgM+, ANA</td>
<td>Hyperlipidemia, hepatitis C, hyperuricemia</td>
</tr>
<tr>
<td></td>
<td>71/F</td>
<td>5 yr</td>
<td>Legs and feet</td>
<td>Brown to purpuric papules</td>
<td>ANA 1:320</td>
<td>Hyperlipidemia, hypertension diabetes mellitus, thrombocytopenia</td>
</tr>
<tr>
<td>Case 1</td>
<td>47/M</td>
<td>3 yr</td>
<td>Legs, feet, dorsum of hands</td>
<td>Erythematous to brown papules and plaques</td>
<td>Cryoglobulin IgG+, IgA+, IgM+</td>
<td>Hyperlipidemia, hepatitis C, hyperuricemia</td>
</tr>
<tr>
<td>Case 2</td>
<td>49/F</td>
<td>2 yr</td>
<td>Legs, dorsum of feet, knee</td>
<td>Brownish tiny macules, patches, papules</td>
<td>NA</td>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Case 3</td>
<td>66/F</td>
<td>10 yr</td>
<td>Medial aspects of ankles</td>
<td>Purpuric macules and patches</td>
<td>NA</td>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Case 4</td>
<td>54/F</td>
<td>10 yr</td>
<td>Legs, dorsum of feet</td>
<td>Purpura</td>
<td>ANA 1:80, RF</td>
<td>Hypertension, hyperlipidemia</td>
</tr>
</tbody>
</table>

ANA = antinuclear antibody; NA = not available; RF = rheumatoid factor; COPD = chronic obstructive pulmonary disease.
histopathologic findings of PPD showed superficial perivascular lymphocytic infiltrate with features of lymphocytic vasculitis and erythrocytic extravasation. The process of PPD may be categorized into the complex reactions between perivascular infiltrates of CD3+, CD4+ lymphocytes and CD1a+ dendritic cells. On this basis, the granulomatous reaction in PPD may represent an incompetent Th1 response, as in the pathogenesis of granulomas in leprosy. The response, induced by unknown factors possibly associated with systemic disorders, such as hyperlipidemia, hypertension or hepatitis C, could cause the granulomatous reaction seen in PPD. Further studies with large case numbers are required to confirm if this is a true causal relationship, or merely an incidental association.

In summary, we described three new patients with granulomatous PPD. This unusual variant appears to occur exclusively in middle-aged Eastern Asians. It is important for pathologists to recognize the histopathologic pattern of this disease and thus differentiate it from other granulomatous disorders. The clinical significance of the high incidence of systemic disorders, such as hyperlipidemia and hypertension, among patients with granulomatous PPD requires further study.

References