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Acral Purpura as Leading Clinical Manifestation of Dermatitis Herpetiformis: Report of Two Adult Cases with a Review of the Literature

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Key Words
Dermatitis herpetiformis · Purpura · Petechial lesions · Adult

Abstract
Dermatitis herpetiformis (DH) is an autoimmune disease that clinically manifests as pruritic vesicles and papules. The diagnosis of DH is often challenging because of its wide spectrum of clinical presentations. We here report 2 patients with DH in whom finger petechiae represented the initial and leading manifestation of the disease, and the confirmed diagnosis critically relied on immunopathological studies. Therefore, besides the classic causes, clinicians should also consider DH in the differential diagnosis of acral purpura, even in patients only presenting with discrete acral petechial lesions. We also review the recent literature regarding the rare cases of petechiae in adult DH patients.

Introduction

Dermatitis herpetiformis (DH) is an autoimmune disease that clinically manifests as highly pruritic eruption involving the extensor surfaces of elbows, forearms, buttocks, knees and scalp. Histopathologically, it is typically associated with neutrophilic abscesses in the dermal papillae with subepidermal blister formation. The diagnosis is based on the detection of granular IgA deposits in the dermal papillae and/or along the dermoepidermal junction by direct immunofluorescence studies [1, 2]. DH is almost invariably associated with a gluten-sensitive enteropathy, in which ingestion of gluten results in a chronic inflammation in genetically predisposed individuals [3]. While tissue transglutaminase represents the major autoantigen of coeliac disease, DH is associated with an IgA and IgG autoimmune response directed primarily against another isoform of transglutaminase, the epidermal transglutaminase [4]. Evidence has recently been provided indicating that immune complexes of both IgA and epidermal transglutaminase are formed in the dermal papillae and are directly responsible for the cutaneous manifestations [3, 4].

The diagnosis of DH is often difficult because of its wide spectrum of clinical presentations with absent vesicular and bullous lesions [5]. We here report 2 patients with DH in whom finger petechiae represented the initial and leading manifestation of the disease, which raised a challenging differential diagnosis.

Case Reports

Case 1

A 32-year-old man had a 2-year history of recurrent petechial lesions involving the fingers (fig. 1a, b). Since the lesions were asymptomatic, the patient did not seek for advice. His past history was otherwise unremarkable. He had no drug intake and had no systemic symptoms. On examination, he had several petechial lesions and crusted brownish lesions located exclusively on the lateral sides of the fingers and on the fingertips. The remaining mucocutaneous examination was normal. There was no evidence of organomegaly or lymphadenopathy. Complete cardiovascular and neurological physical evaluation was normal. There was no heart murmur. Light microscopy studies of a biopsy specimen obtained from a digital lesion revealed orthohyperkeratosis, epidermal acanthosis, with formation of several subepidermal splits containing abundant neutrophils, lymphocytes and erythrocytes (fig. 2a). Direct immunofluorescence studies showed the presence of granular linear IgA deposits along the dermal-epidermal junction and dermal papillae (fig. 2b). Full blood cell count, inflammatory markers, electrolytes, hepatic and renal tests were within normal limits. Serological analyses revealed the presence

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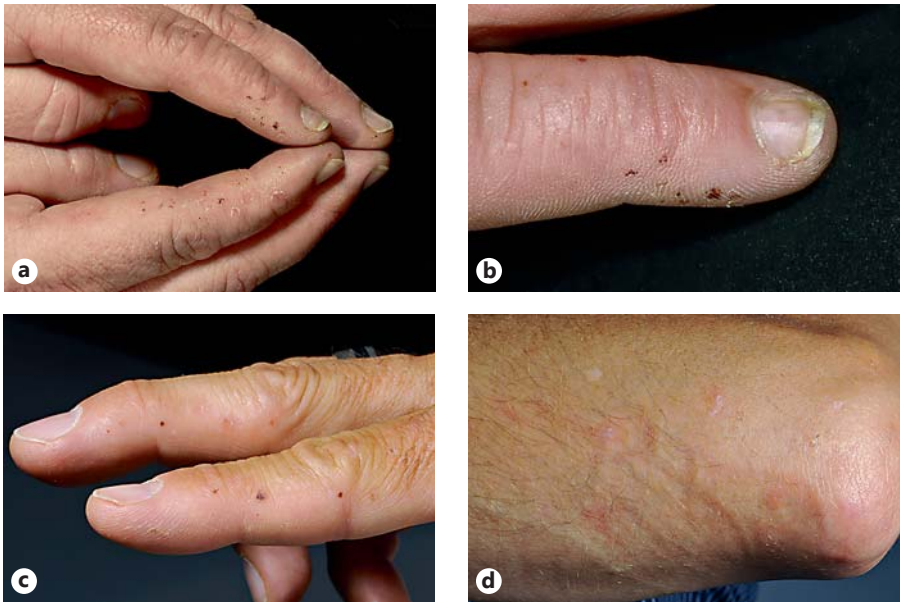

Fig. 1. a, **b** Petechiae on the fingertips in case 1. **c** Petechiae and crusted lesions on the finger edges in case 2. **d** Papular lesions and hyperpigmented macules on the elbows in case 2.

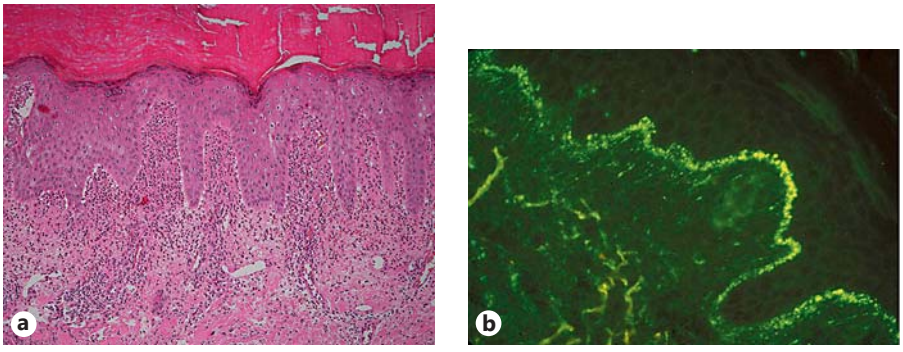

Fig. 2. a Light microscopy studies of a biopsy skin specimen obtained from patient 1 show several subepidermal splits with abundant neutrophils, lymphocytes and erythrocytes. HE. ×200. **b** Direct immunofluorescence studies demonstrate intense granular IgA deposits along the dermoepidermal junction. ×400.

of IgA (71 IU; normal <20) and IgG antigliadin antibodies (66 IU; normal <20), IgA anti-endomysium antibodies (at a titer of 1:80), IgA anti-tissue transglutaminase (77 IU; normal <20). Small bowel biopsies showed total villous atrophy and hyperplasia of crypts with goblet cells with findings consistent with coeliac disease. Based on the mild activity of the cutaneous disease, the patient was first given a strict gluten-free diet. The latter resulted in a progressive remission of the skin lesions within 3 months.

Case 2

A 54-year-old man had a 2-year history of itchy skin lesions predominantly involving the hands and elbows. On examination, the patient showed excoriated lesions on the dorsal aspect of the hands, petechiae and crusted lesions on the lateral aspects of the fingers and on fingertips (fig. 1c) as well as some papular lesions and postinflammatory hyperpigmented macules on the elbows (fig. 1d). The rest of the examination revealed isolated excoriated lesions of the knees and back. Complete cardiovascular and neurological physical examination was normal. There was no evidence of either organomegaly or lymphadenopathy.

A skin biopsy obtained from a lesion on the left elbow showed subepidermal cleft formation with many neutrophils and some eosinophils in the dermal papillae and upper dermis. Direct immunofluorescence studies revealed strong granular deposits of IgA in the papillary dermis. Full blood cell count, inflammatory markers, electrolytes, hepatic and renal tests were within normal limits. Serological analyses demonstrated the presence of circulating IgA (31.0 IU; normal <20) and IgG (123.0 IU, normal <20) autoantibodies against gliadin by enzyme-linked immunosorbent assay, whereas the search for IgA antibodies against tissue TG and indirect immunofluorescence with anti-endomysium IgA remained negative. The patient was initiated on a strict gluten-free diet and was given topical corticosteroids resulting in a progressive improvement of the lesions. The patient was offered a gastroduodenoscopy examination, which he refused. He was subsequently lost to follow-up.

Discussion

DH may closely mimic a variety of dermatological conditions such as atopic dermatitis, contact dermatitis, scabies, chron-

Table 1. Survey of reported adult DH patients with petechial acral lesions

Reference (first author)	Year	Age/sex	History	Clinical features	Associated diseases	Therapy
McCleskey [17]	2002	46/M	burning sensation of the palmar surfaces with petechial lesions	petechiae on palms and volar aspect of fingers	–	GFD, dapsone
Hofmann [10]	2009	33/M	recurrent painful petechiae on fingertips of 6-month duration	grouped petechiae on volar and lateral aspects of fingertips	coeliac disease	GFD
Flann [9]	2010	34/F	18-year history of itchy lesions on fingertips and toes	multiple petechial lesions on fingertips and toes with small tense blister on the right hand	coeliac disease	GFD
Flann [9]	2010	36/F	4-year history of brown macules and papules, peeling of hands	multiple petechiae scattered over the hands	coeliac disease	GFD
Naylor [11]	2011	58/M	9-month history of tender petechiae on hands, feet, ankle, thigh and knee	pruritic erythematous macules, pustules, and crusted papules on the knees, elbows, forearms, scalp and neck	leukocytoclastic vasculitis	GFD
Heinlin [12]	2012	15/F	recurrent digital petechiae on hands and feet over 6 months	reddish brown hemorrhagic maculae on the volar aspect of fingers, on fingertips, toes and heels	tonsillitis	GFD, dapsone
Present case 1		32/M	2-year history of recurrent petechial lesions on fingers	petechial lesions and crusted brownish lesions on the lateral sides of fingers and fingertips	coeliac disease	GFD
Present case 2		54/M	2-year history of petechial lesions on fingers, itchy lesions on hands and elbows	petechiae and crusted lesions on fingertips, excoriated lesions on hands and elbows	–	GFD

GFD = Gluten-free diet.

ic prurigo, as well as other autoimmune blistering diseases of the skin, such as bullous pemphigoid [2]. Our 2 cases were unusual, since the petechial lesions on the fingers and fingertips represented the initial and leading manifestation of the disease. Differential diagnosis of petechial lesions involving the fingertips and hands is wide and challenging. In addition to subacute bacterial endocarditis and other infectious conditions, vasculitis, trauma-induced hemorrhages, and thrombocytopenic purpura should be considered and excluded [2, 6].

The potential development of digital petechial lesions has been emphasized in childhood DH. For example, Karpati et al. [6] described palmoplantar involvement in the majority of their 47 children with DH. Lesions varied from discrete red-brown macules to more extensive exudative, bullous palmoplantar lesions [6]. Importantly, these authors noted the presence of discrete petechial spots and small blisters on the flexor surface of fingers and on the palms in 30 cases (64%) at least once in the course of the disease. In contrast, in adults the presence of petechiae has received little attention so far. In 1971, Marks and Jones [7] first reported a case of DH presenting as purpuric, hemorrhagic palmar-plantar lesions. Moulin et al. [8] subsequently described palmar petechiae in 4 patients with DH. Six additional cases of DH associated with recurrent petechial lesions involving the fingers have been reported in the last decade (table 1). In affected patients, these lesions were either asymptomatic or associated with mild discomfort, pruritus, a sensation of burning, stinging or pain. In the majority of cases, palmar-plantar petechiae developed in combination with widespread pruritic lesions, while in other patients petechial lesions occurred in the presence of obvious abdominal manifestations of coeliac disease [9, 10]. In 1 case, extensive petechial lesions on hands, thighs, knee and ankle with a leukocytoclastic vasculitis were the presenting features of DH [11]. Two DH patients with digital petechiae had a previous history of psoriasis [11, 12]. Our cases were thus peculiar and unusual in our experience, since the petechial lesions represented the first manifestations of DH, which finally led to the diagnosis. Therefore, besides the classic causes, clinicians should also consider DH in the differential diagnosis of acral purpura. While in some cases light microscopy studies are of little help by showing a perivascular mixed inflammatory cell infiltrate and hemorrhages, the diagnosis of DH critically relies on the detection of IgA deposits in the dermal papillae and/or the dermoepidermal junction. Serological analyses may be very useful to corroborate the diagnosis. However, IgA autoantibodies to endomysium and tissue transglutaminase may be absent in up to 15% of patients with a gluten-sensitive enteropathy, as observed in our second case [13]. Recent studies indicate that the combined use of deamidated gliadin or gliadin peptides in enzyme-linked immunosorbent assays increased diagnostic accuracy for search of coeliac disease-associated antibodies [14, 15]. Duodenoscopy with small bowel biopsies remains critical

to confirm the diagnosis of coeliac disease and proper patient management and follow-up [16].

Our two observations remind us of the wide clinical spectrum of DH and should prompt clinicians to consider the diagnosis of DH even in patients presenting with discrete acral petechial lesions with or without associated pruritic skin lesions and systemic symptoms.

Disclosure Statement

The authors have no conflict of interest to disclose.

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