Palmar petechiae in a patient with diabetes mellitus

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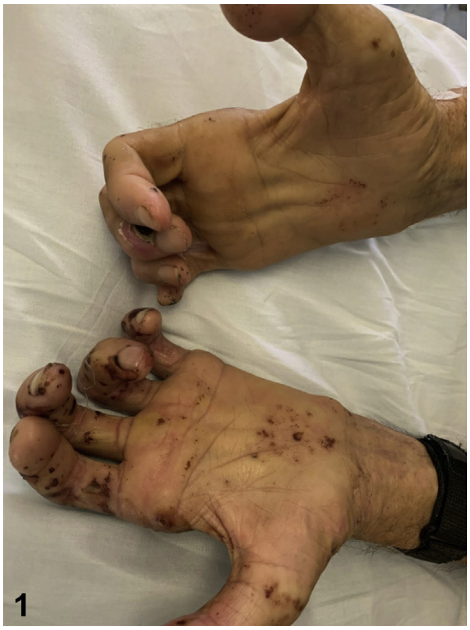

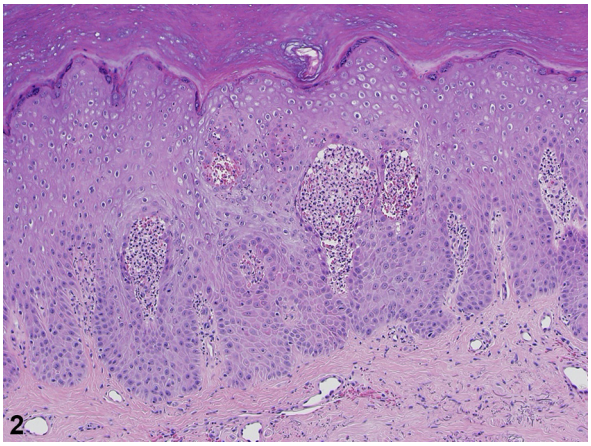

A 64-year-old man with a history of celiac disease (CD), congestive heart failure, and diabetes mellitus complicated by end-stage renal disease and peripheral neuropathy, was admitted to the hospital for non-healing ulcerations of his hands with osteomyelitis from his peripheral arterial vascular disease. He reported that his CD was under good control with a strict gluten-free diet prior to admission. Physical exam revealed prominent petechiae on his bilateral palms and fingers (Fig 1). A biopsy was performed and demonstrated collections of neutrophils in the papillary dermis (Fig 2).

Question 1: What is the most likely diagnosis?

A. Arterial vascular disease

B. Capillaritis

C. Dermatitis herpetiformis

D. Janeway lesions

E. Rheumatoid vasculitis

Answers:

A. Arterial vascular disease — Incorrect. Cutaneous findings of arterial vascular occlusive disease typically include erosions, ulcers, and ischemic changes.

B. Capillaritis — Incorrect. Capillaritis classically presents as copper-brown macules and petechiae on the lower extremities.

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C. Dermatitis herpetiformis (DH) — Correct. Palmar petechiae are a rare presentation of DH in adults and can result in delayed diagnosis when being the initial or isolated manifestation of disease. Although papules and vesicles on extensor surfaces in DH are pruritic, palmar petechiae may be pruritic, painful, or asymptomatic.[1-3]

D. Janeway lesions — Incorrect. Janeway lesions are seen in bacterial endocarditis and present as angular hemorrhage on the palms.

E. Rheumatoid vasculitis — Incorrect. Rheumatoid vasculitis develops during advanced rheumatoid arthritis and can manifest as purpura, ulcerations, digital ischemia, and nodules on the hands.[4]

Question 2: What would direct immunofluorescence (DIF) microscopy most likely show?

A. Linear deposition of IgA along the basement membrane of perilesional skin

B. Granular deposition of IgA within the dermal papillae of perilesional skin

C. Linear deposition of IgG and C3 along the basement membrane of perilesional skin

D. Linear and granular deposition of IgG along the basement membrane of perilesional skin

E. Intercellular IgG within the epidermis of perilesional skin

Answers:

A. Linear deposition of IgA along the basement membrane of perilesional skin — Incorrect. While also characterized by a neutrophilic infiltrate in the papillary dermis, DIF shows linear deposition of IgA along the basement membrane in all cases of linear IgA bullous dermatosis.[4] Uncommonly, DH may demonstrate linear deposition of IgA, but granular deposition is much more typical.

B. Granular deposition of IgA within the dermal papillae of perilesional skin — Correct. DIF microscopy of DH classically demonstrates granular deposition of IgA within the dermal papillae of perilesional skin.[4] Granular deposits may also be detected at the basement membrane, and C3 often co-migrates with IgA. Granular IgA deposition at the basement membrane can overlap with findings of linear IgA bullous dermatosis, but serologic testing can be utilized to confirm the correct diagnosis. Granular deposition of IgA in the dermal papillae, however, is pathognomonic for DH. While pharmacologic treatment does not clear the deposition of granular IgA deposits in the dermal papillae, a gluten-free diet results in resolution of these deposits.[5] In this patient, DIF demonstrated granular deposition of IgA at the basement membrane zone and within the dermal papillae.

C. Linear deposition of IgG and C3 along the basement membrane of perilesional skin — Incorrect. This pattern describes bullous pemphigoid. In bullous pemphigoid, the predominant inflammatory infiltrate is made up by eosinophils, which can be seen in the papillary dermis, in subepidermal blisters, and as eosinophilic spongiosis. DIF reveals linear IgG and C3 deposition along the basement membrane.[4]

D. Linear and granular deposition of IgG along the basement membrane of perilesional skin — Incorrect. This pattern may be observed in bullous systemic lupus erythematosus. While bullous systemic lupus erythematosus also has neutrophilic infiltrate, DIF shows deposition of IgG, sometimes along with IgA and/or IgM, in a linear and granular pattern along the basement membrane.[4]

E. Intercellular IgG within the epidermis of perilesional skin — Incorrect. This pattern describes the most common pemphigus subtypes, pemphigus vulgaris and pemphigus foliaceus.[4] Pemphigus vulgaris typically has intercellular deposition of IgG and C3, predominantly in the lower layers of the epidermis, whereas pemphigus foliaceus more commonly exhibits intercellular deposition of IgG and C3 in the upper layers of the epidermis.

Question 3: What is the most specific serologic test for dermatitis herpetiformis?

A. Anti-epidermal transglutaminase (eTG) antibodies

B. Anti-gliadin antibodies

C. Anti-tissue transglutaminase 2 (TTG2) antibodies

D. IgA endomysial antibodies

E. Indirect immunofluorescence on skin substrate

Answers:

A. Anti-epidermal transglutaminase (eTG) antibodies — Correct. High affinity and specific IgA class anti-eTG antibodies are found in patients with DH and are thought to develop through epitope spreading. While circulating anti-eTG antibodies are found in both CD and DH, deposition of these antibody-antigen complexes in the papillary dermis

leads to neutrophilic infiltration and distinguishes DH from CD.[4,6] Additionally, anti-eTG autoantibodies correlate with disease activity in DH. The sensitivity of anti-eTG antibodies for DH ranges from 60% to just over 80% depending on the study, and specificity ranges from nearly 93% to 100%.[5] While serologic studies were not performed for the patient presented here, he was reinitiated on a strict gluten-free diet in the hospital.

B. Anti-gliadin antibodies — Incorrect. IgA antibodies to gliadin, the soluble antigenic component of gluten, are formed in the gut and contribute to small-bowel involvement in both CD and DH.[4,6]

C. Anti-tissue transglutaminase 2 (TTG2) antibodies — Incorrect. IgA anti-TTG2 antibodies are seen in both CD and DH, and these antibodies correlate with small-bowel disease and gluten ingestion. A strict gluten-free diet is the treatment of choice for DH, with a reduction in the risk of small-bowel lymphoma, as well as clearance of skin lesions within 1-6 months. Dapsone can accelerate resolution of DH, with improvement within days upon initiating therapy.[4,6]

D. IgA endomysial antibodies — Incorrect. IgA endomysial antibodies are formed in the gut, and these antibodies can be found in both patients with CD without cutaneous involvement, and in DH.[4,6]

E. Indirect immunofluorescence on skin substrate — Incorrect. Indirect immunofluorescence on skin substrate is always negative in DH. Only in diseased skin do serum IgA antibodies against eTG antigen form complexes and subsequently deposit in the papillary dermis.[4,6]

Abbreviations used:

CD: celiac disease
DH: dermatitis herpetiformis
DIF: direct immunofluorescence
eTG: epidermal transglutaminase

Conflicts of interest

None disclosed.

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