

Leukocytoclastic Vasculitis as the Presenting Feature of Dermatitis Herpetiformis

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Background: Dermatitis herpetiformis is an autoimmune disease typically characterized by pruritic vesicles located on the extensor surfaces. Classic disease consists of neutrophils in the dermal papillae. Additional histopathologic findings include fibrin deposition and edema within the dermal papillae. Subepidermal vesicles also may be present. Direct immunofluorescence demonstrates granular IgA in the dermal papillae.

Observations: A 58-year-old man with tender and pruritic erythematous macules and papules ranging from 2 to 6 mm in diameter had bilateral knee, elbow, forearm, scalp, and neck involvement. Petechiae also were present on the hands, thigh, knee, and ankle. A biopsy specimen initially demonstrated leukocytoclastic vasculitis. The

results of workup for systemic vasculitis were negative. Subsequent biopsy specimens and direct immunofluorescence showed histologic evidence of dermatitis herpetiformis and leukocytoclastic vasculitis in the setting of an elevated serum IgA antitissue transglutaminase level. Marked improvement of the lesions was observed with a reduction of gluten in the patient's diet.

Conclusions: Physicians should consider the possibility of dermatitis herpetiformis in patients with petechiae and leukocytoclastic vasculitis because leukocytoclastic vasculitis may be a prominent feature of dermatitis herpetiformis.

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DERMATITIS HERPETIFORMIS (DH) is a well-known autoimmune disease typically characterized by pruritic vesicles located on the extensor surfaces. Classic disease consists of neutrophils within the dermal papillae. Additional histopathologic findings include fibrin deposition and edema within the dermal papillae. Subepidermal vesicles also may be present. Direct immunofluorescence demonstrates granular deposition of IgA in the dermal papillae. Typically, patients with DH demonstrate elevated levels of serum IgA antitissue transglutaminase or IgA endomysial antibodies. Also, they may have gastrointestinal symptoms related to the disease and may show a flattened villous architecture on small bowel biopsy specimens. Treatment typically consists of a gluten-free diet or dapsone.

cluding urinalysis; erythrocyte sedimentation rate; C-reactive protein; complete blood cell count; basic metabolic panel; liver function tests; anti-DNA tests; total hemolytic complement; complement profile; partial thromboplastin time; prothrombin time; rheumatoid factor; and antineutrophil cytoplasmic, ribonucleoprotein, Smith, Ro, and La antibodies testing, were negative. The antinuclear antibody test result was positive to a dilution of 1:160. The patient subsequently developed mildly pruritic, erythematous macules, pustules, and crusted papules ranging from 2 to 6 mm in diameter on the bilateral aspect of the knees, elbows, forearms, scalp, and neck (**Figure 2**). The patient's review of systems revealed episodes of loose stool, which had occurred several times a week since adolescence.

The initial biopsy specimen of the finger demonstrated findings consistent with leukocytoclastic vasculitis (LCV), including perivascular neutrophils, extravasated red blood cells, and fibrin deposition in the vessels (**Figure 3**). Classic features of DH were not seen. Eleven months later, a biopsy specimen from the right arm demonstrated spongiosis with

REPORT OF A CASE

A 58-year-old man had a 9-month history of tender petechiae on the hands, feet, ankle, thigh, and knee (**Figure 1**). He also reported a history of psoriasis. The results of workup for systemic vasculitis, in-

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Figure 1. A petechiae on the finger.



Figure 2. Knee demonstrating erythematous macules and pustules.

a mixed inflammatory infiltrate predominantly in a perivascular distribution. Only rare neutrophils were seen in the papillary dermis. The biopsy specimens from the left arm and the right leg demonstrated prominent LCV in the superficial and middle dermis along with features of DH, including neutrophils and edema in the dermal papillae and the formation of subepidermal vesicles (**Figure 4A-C**). Of interest, acute folliculitis also was seen (**Figure 4D**). Direct immunofluorescence revealed granular deposition of IgA in the dermal papillae and the dermoepidermal junction (**Figure 5**). Deposition of IgA was not seen in the vessel walls. Intermittent granular deposits of C3 and fibrin also were noted at the dermoepidermal junction.

Further workup revealed an elevated serum IgA antitissue transglutaminase level of 57 (moderate to strong positive >30) units. A jejunal biopsy specimen demonstrated mild chronic inflammation with preservation of the normal villous architecture. The biopsy had been performed after the patient was started on a gluten-free diet. In addition, the lack of villous blunting changes may have been due to sampling error. The patient reports partial adherence to the diet with marked improvement in his skin disease and a decrease in the frequency of loose stools. He was not treated with dapson because he was responding to a gluten-free diet.

COMMENT

Previously reported cases of petechiae in DH have been restricted to the palmar and, more rarely, to the plantar

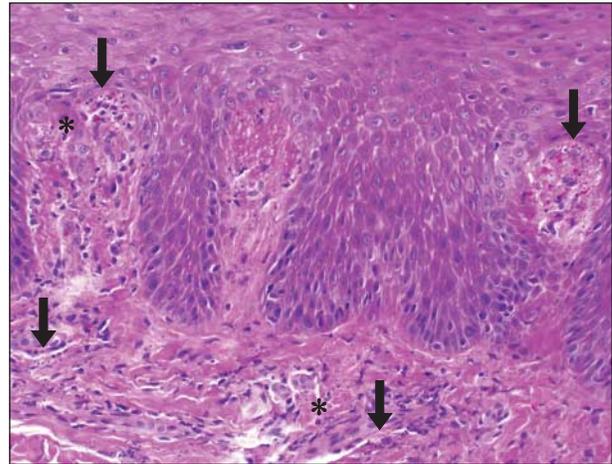


Figure 3. Biopsy of finger demonstrating sparse neutrophils (asterisks), nuclear dust (arrows), and extravasated red blood cells, predominantly in a perivascular distribution, consistent with leukocytoclastic vasculitis (hematoxylin-eosin, original magnification $\times 400$).

surfaces.¹⁻³ In the series by Karpati et al² of 47 children with DH, 30 were found to have palmar lesions and 3 to have plantar lesions. These lesions were described clinically as red-brown macules and blisters. Although distribution on the acral surfaces is a well-known clinical pattern in children, this presentation in adults only rarely has been reported.^{1,4} Our patient's petechiae involved a broader clinical distribution than the cases previously described, including the ankle, thigh, and knee.

In the English-language literature, most of the petechiae found in the setting of DH were not biopsied. Of the lesions with histopathologic findings reported, most describe classic features of DH along with extravasated red blood cells.^{4,5} Petechial lesions of DH also may show a perivascular mixed inflammatory cell infiltrate,³ as also demonstrated in our patient. However, his case is unusual in that the initial presentation was of LCV. In addition, our patient has acute folliculitis within a petechial lesion of DH. This, however, may be a separate process because folliculitis is a relatively common disease.

One case of DH has been reported with associated cutaneous vasculitis, but this was described in the clinical setting of erythema elevatum diutinum.⁶ Other authors⁷ have drawn attention to the similarity seen between upper dermal edema and the potential for vesicle formation in LCV and DH. Of importance, our case documents the presence of LCV in petechiae caused by DH. Although reports have been published^{8,9} of DH occurring within petechial lesions, it is unusual for LCV to present as petechiae, which further supports the theory that DH and LCV are part of the same process in this case. Perhaps the LCV is secondary to the recruitment of neutrophils in DH as it is in other diseases, such as Sweet syndrome and granuloma faciale.

Jones and Bhogal⁷ reported a case of LCV with clinical and histopathologic features of DH, including direct immunofluorescence of perilesional skin with granular IgA in the upper dermis. They described the similarity of superficial dermal edema and the potential for vesicle formation in LCV and DH but concluded that their case constituted LCV and not DH because no immunofluo-

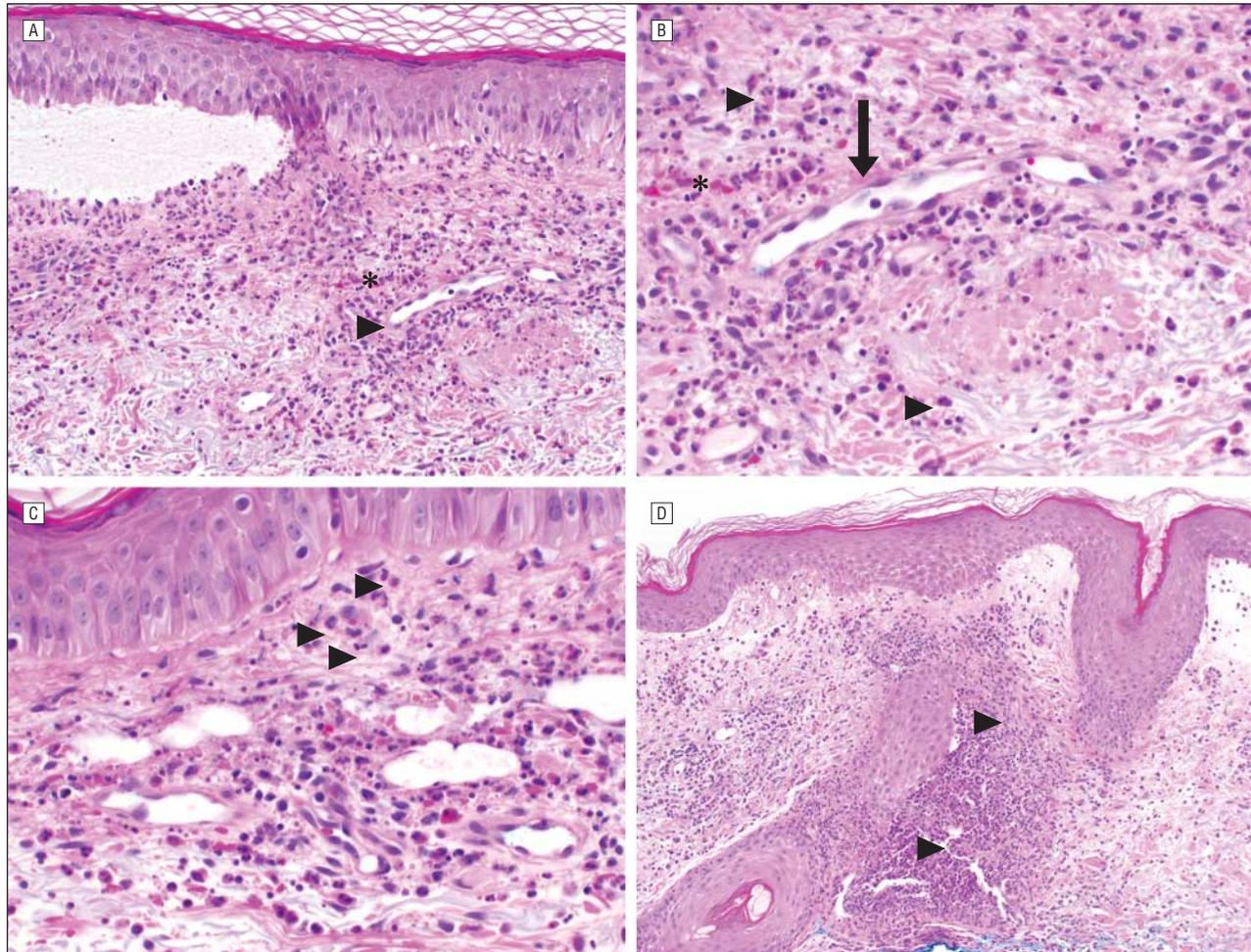


Figure 4. Biopsy specimens from the left arm and the right leg. A, Subepidermal vesicle with dermal neutrophils and nuclear dust primarily in a perivascular distribution (leukocytoclastic vasculitis, arrowhead) with interstitial involvement and extravasated erythrocytes (asterisk) (hematoxylin-eosin, original magnification $\times 200$). B, Perivascular inflammation with nuclear debris (arrowheads) and fibrin deposition (arrow) around a superficial vessel with extravasated erythrocytes (asterisk) (hematoxylin-eosin, original magnification $\times 400$). C, Neutrophils (arrowheads) in the papillary dermis (hematoxylin-eosin, original magnification $\times 400$). D, Acute perifollicular inflammation (arrowheads) (hematoxylin-eosin, original magnification $\times 100$).

rescent IgA was seen in the dermoepidermal junction in uninvolved skin. We hypothesize that this case actually may represent DH. Other authors have found that healthy skin less frequently tests positive for IgA¹⁰; therefore, some advise the use of a perilesional rather than a normal or involved skin biopsy for direct immunofluorescence as the criterion standard for diagnosing DH.^{10,11} Although we did not perform direct immunofluorescence of uninvolved skin, the response to a gluten-free diet gives further evidence that our patient has DH. We believe that the case by Jones and Bhogal, as well as that presented herein, are actually 2 unique cases of LCV found in the setting of DH. Leukocytoclastic vasculitis may be prominent in DH and can be found as the initial histologic manifestation of the disease.

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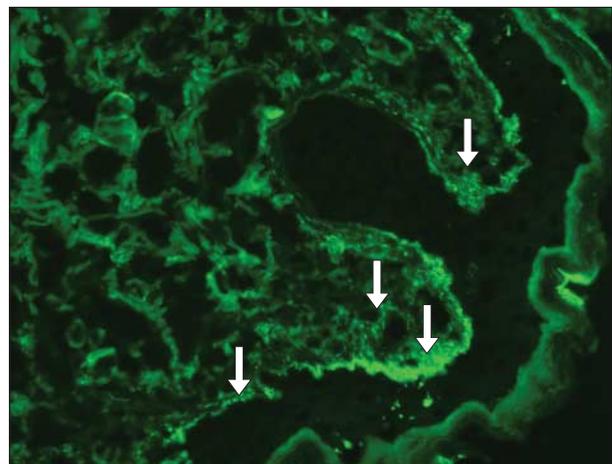


Figure 5. Direct immunofluorescence demonstrating granular deposition of IgA (arrows) (original magnification $\times 400$).

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Notable Notes

Greek and Roman Myths Recognized in Naming Syphilis

In early times, some physicians named syphilis for Greek and Roman myths as a way to explain the difficulty in overcoming the disease. Guillaume Rondelet (1507-1566) called syphilis *Hydra's disease* for the Greek mythological monster *Hydra from Lerna*, which had 9 heads, with the one in the middle being immortal. Gervais Uçay (17th century) named the numerous symptoms and clinical features of syphilis *Proteus' disease* after the Greek divinity, who was able to change his appearance according to circumstance.

People believed that the outcome of syphilis was God's severe punishment for lascivious men. Juan Almenar (15th-16th century) named the disease *passio turpis saturnina* in remembrance of the filthy passion of Saturn, a Roman divinity, known as *Kronos* in Greek mythology, who killed his own sons by eating them.¹ Almenar stated, "Venereal disease is a diathesis which is owed to the sexual trade . . . at the beginning it shows some ulcers . . . on the genital organs . . . subsequently it affects the humours, especially . . . the seminal fluids." Shortly after syphilis was introduced in Europe, physicians began to realize that the disease was sexually transmitted, leading Jacques de Béthencourt (16th century) to use the synonym *Gallic disease* and the adjective *venereal* from Venus, the love goddess in Roman mythology, and Bernardino Tomitano (1517-1576) to call it *bad Venus*. Hermann Boerhaave (1668-1738) called syphilis *aphrodisiaca lue*, from the Latin word *lues*, meaning *disease, contagious, endemy, or plague*, and *Aphrodite*, the love goddess in Greek mythology. This last appellation

did not last long, but the term *venereal lues*, which was introduced by Giulio Cesare Vanini (1585-1619), was used in Italy until the first half of the 19th century.

The seriousness of syphilis was recognized by Aurelio Minadoi (1548-1615), who believed that the disease represented a venereal epidemic and called it *venereal virulence*, while other physicians called it *venereal plague*. Antonio Nunes Ribeiro Sanchez (1699-1783) said that when a patient recovered from syphilis and the symptoms disappeared, the poison of the disease was still in the patient's body and that it could be passed from mother to child as *chronic venereal disease*.² Also, the quacksalver Vergery de Velnos (XVI-XVII century) called the disease *maladie de Cythère* (or *Cythère disease*) from Citera, actually Kytira, a Greek island, from whose seas Venus was born. The name *Cupido disease* came from Cupid, who was Venus' son and was said to be a lover of his mother by Bronzino (1503-1572). Finally, Jean Fernel (1497-1558) described the tragedy by which syphilis afflicts men as follows: "Unless God who is gentle will destroy this ruin, or unless the men mitigate their unbridled lasciviousness, the venereal disease will not end, and I believe that it will be forever the friend of the human people."³

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