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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REPORT OF A CASE

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 endomyosial 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.

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, including 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...
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 dermoeidermal 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 dermoeidermal 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 dapsone because he was responding to a gluten-free diet.

Previously reported cases of petechiae in DH have been restricted to the palmar and, more rarely, to the plantar 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.5,6 Petechial lesions of DH also may show a perivascular mixed inflammatory cell infiltrate,7 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 published8,9 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-
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 IgA, 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. 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 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 ×200). B, Perivascular inflammation with nuclear debris (arrowheads) and fibrin deposition (arrow) around a superficial vessel with extravasated erythrocytes (asterisk) (hematoxylin-eosin, original magnification ×400). C, Neutrophils (arrowheads) in the papillary dermis (hematoxylin-eosin, original magnification ×400). D, Acute perifollicular inflammation (arrowheads) (hematoxylin-eosin, original magnification ×100).

Figure 5. Direct immunofluorescence demonstrating granular deposition of IgA (arrows) (original magnification ×400).
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 hydras’s disease for the Greek mythological monster Hydras from Lerna, which had 9 heads, with the one in the middle being immortal. Gervais Uc¸ay (17th century) named the numerous symptoms and clinical features of syphilis Proteus’s 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. Almenar stated, “Venerial 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 humour, 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 venerel 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, endemic, 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 Minadio (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. Also, the quack salver Vergery de Velnos (XVI-XVII century) called the disease maladie de Cythère (or Hydrie disease) from Citera, actually Kythira, 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 (1497-1538) 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.”

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2. Luigon L, ed. De morbo gallic compost suae excit mutatione medicos cuiscumque nationis, qui vel integris libris, vel quasqualesmod huius affectus carationem methodicae aut traditurum diligentem incide conquista, sparsum inuenus, erroribus expurgata, & in unum tandem hoc corpus redacta. Venice, Italy: Giordano Ziletti; 1566-1567.