Dermatitis herpetiformis

Part I. Epidemiology, pathogenesis, and clinical presentation

Diana Bolotin, MD, PhD, and Vesna Petronic-Rosic, MD, MSc
Chicago, Illinois

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Learning Objectives
After completing this learning activity, participants should be able to use the recent advances in epidemiologic studies on dermatitis herpetiformis to counsel patients and their families, to describe the relationship between the pathophysiology of dermatitis herpetiformis and its clinical manifestations, and to recognize the clinical features of dermatitis herpetiformis and its associated disorders.

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Dermatitis herpetiformis (DH) is an autoimmune disease that is linked to gluten sensitivity and has a clear relationship to celiac disease. Both conditions are mediated by the IgA class of autoantibodies and the diagnosis of DH is dependent on detection of granular deposits of IgA in the skin. There is an underlying genetic predisposition to the development of DH but environmental factors are also important. Typically, young adults present with excoriations only, as the severe pruritus effectively destroys any primary lesions. Based upon our experience with DH and a comprehensive literature review, we provide an update of DH epidemiology, pathophysiology, and clinical presentation. (J Am Acad Dermatol 2011;64:1017-24.)

Key words: autoimmune bullous disease; blister; celiac disease; dermatitis herpetiformis; gliadin; gluten-sensitive enteropathy; human leukocyte antigen—DQ2; human leukocyte antigen—DQ8; transglutaminase.

Dermatitis herpetiformis (DH) was initially described by Louis Duhring in 1884.[1] Recent progress in understanding the pathogenesis of this disease has led to improved treatment. Linking gluten sensitivity to DH led to the adoption of the gluten-free diet as a key component of treatment. DH is an autoimmune disease, a finding that is strongly supported by landmark studies revealing the granular deposition of immunoglobulin in the skin.[2,3] The immunologic basis of DH shows a clear relationship to celiac disease (CD). Both conditions are mediated by the immunoglobulin A (IgA) class of autoantibodies. Tissue transglutaminase (tTG) is the major autoantigen targeted in CD, and epidermal transglutaminase (eTG) is the autoantigen most closely linked to DH. IgA anti-eTG is the most sensitive serologic marker for DH. Many details about the immunologic basis and pathogenesis of DH are still emerging in the literature. Part I of this series will focus on the epidemiology, pathophysiology, and presentation of DH.

CAPSULE SUMMARY

- Dermatitis herpetiformis is a multifactorial disease with strong genetic and autoimmune influences
- All patients with dermatitis herpetiformis have gluten intolerance
- Hypothyroidism is the most common autoimmune condition associated with dermatitis herpetiformis

EPIDEMIOLOGY

Key points

- **Dermatitis herpetiformis is most prevalent in patients of Northern European descent**
- **Men have a higher prevalence of dermatitis herpetiformis than women**

A number of epidemiologic studies have elucidated the incidence and prevalence of DH. Most of these studies focus on individuals of Northern European heritage, both in Europe and the United States, in whom this disorder is most common. Studies in these populations performed in the late 1970s to early 1980s report a prevalence range from 1.2 to 39.2 per 100,000 people and an incidence range of 0.4 to 2.6 per 100,000 people per year.[4-8] In addition, a population-based study performed in Utah in 1992 documented a prevalence of 11.2 per 100,000 people and an incidence of 0.98 per 100,000 people per year, and both rates are comparable to studies performed in Europe.[8] Because the population of Utah has a high proportion of people with Northern European ancestry, the concordance of this finding with previous studies is not surprising. The reported incidence of DH is also comparable to that reported for other immunobullous diseases, such as bullous pemphigoid and pemphigus vulgaris.[9]

A few studies in Asian populations have shown that DH is very rare among this group and even rarer among African Americans. In fact, so few cases have been described that no larger population-based studies have been reported in these ethnic groups.[10,11] Although DH was not considered a familial condition for many years, that view is now changing because a number of genetic studies and epidemiologic reports have recorded familial cases of DH.[12-14] The prevalence and presentation of DH varies geographically. Northern Europe appears to have the largest number of cases overall, but DH with onset in childhood tends to be more common in Mediterranean countries.[15] This may be related to differences in diet or to a genetic predisposition within these populations.

Males have a higher prevalence of DH.[8] In fact, most population-based studies to date have found male to female ratios ranging from 1.5:1 to 2:1.[8] Interestingly, the opposite is true of the prevalence of CD, with female to male ratios ranging from 2:1 to 4:1.[16,17]

Most patients report the onset of symptoms during the warmer months of the year, any time from spring to late summer.[8] Whether this finding is related to the pathophysiology of the condition is unclear. The time of onset of DH is variable, with the most common age range at presentation being 30 to 40 years old; however, the age at diagnosis varies widely from infancy to the geriatric population.[8,15] Childhood DH is rare, and for many years it was grouped with the diagnosis of linear IgA bullous dermatosis of childhood. Therefore, the true prevalence of childhood DH is not well characterized.

PATHOGENESIS

Key points

- **A strong genetic predisposition to dermatitis herpetiformis exists among affected families**
- **Human leukocyte antigen–DQ2 and human leukocyte antigen–DQ8 are associated with**

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Reprint requests: Vesna Petronic-Rosic, MD, MSc, Section of Dermatology, The University of Chicago, 5841 S Maryland Ave, MC5067, Chicago, IL 60637. E-mail: vrosic@medicine.bsd.uchicago.edu.
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