

# Childhood Dermatitis Herpetiformis: A Case Report and Review of the Literature

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## GOAL

To understand dermatitis herpetiformis (DH) in children to better manage patients with the condition

## OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Describe the prevalence of DH in children.
2. Discuss the clinical presentation of DH in children.
3. Explain methods of diagnosing DH.

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*Dermatitis herpetiformis (DH) is a chronic pruritic cutaneous eruption associated with gluten-sensitive enteropathy (celiac disease [CD]) and immunoglobulin A (IgA) deposition in the skin. While the disease is not uncommon among adolescents, DH is rarely seen in prepubertal patients. Children with DH present similarly to adults; however, uncommon skin findings have been reported. Because of an increased risk for*

*autoimmune diseases and lymphoma, accurate diagnosis and treatment are imperative.*

*We present a case of DH in a 6-year-old Latino boy previously diagnosed with atopic dermatitis and recurrent urticaria. Our aim is to highlight the various cutaneous presentations of DH and encourage clinicians to consider this diagnosis in young patients with recalcitrant atypical skin disease.*

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## Case Report

A 6-year-old Latino boy presented with a history of pruritic skin lesions (beginning at the age of 9 months) previously diagnosed as atopic dermatitis and recurrent urticaria. His pediatrician prescribed

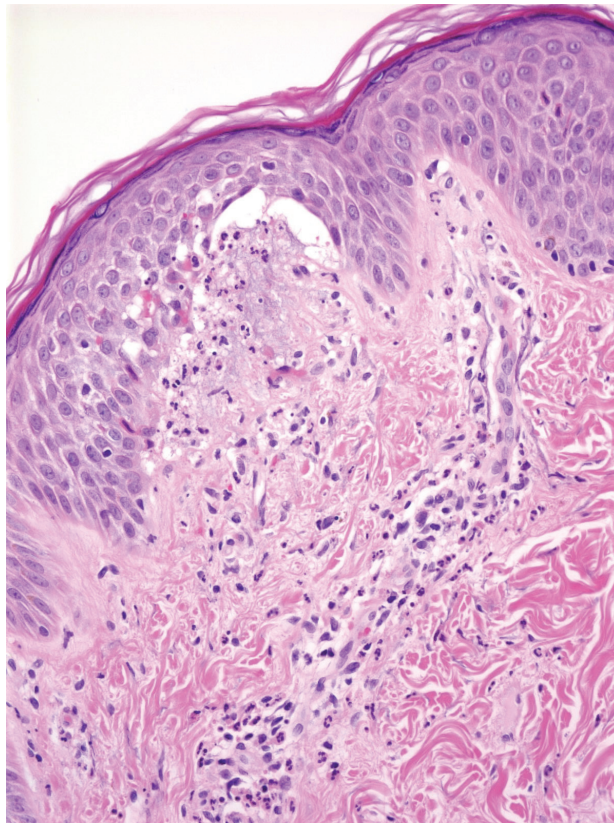


**Figure 1.** Patient at presentation, with excoriated edematous papules on the buttocks.

topical steroids and oral diphenhydramine hydrochloride, without improvement. On examination, the patient had few excoriated edematous papules on his buttocks (Figure 1) and urticarial plaques on his upper extremity. His skin was xerotic but lacked any lichenified plaques or papules in the antecubital and popliteal fossae. The patient denied any associated nausea or diarrhea. Family history was negative for atopy and autoimmune disease. The mother reported that the patient was, at one time, “small for his age” but is now closer in size to his peers.

A punch biopsy was obtained from an urticarial plaque on his arm and treatment was initiated with desonide cream 0.05% twice daily to the affected areas. The biopsy revealed collections of neutrophils in the papillary dermis as well as clefting at the dermoepidermal junction (Figure 2). A second biopsy for direct immunofluorescence (DIF) was performed from perilesional gluteal skin. This specimen exhibited granular immunoglobulin A (IgA) deposits in the papillary dermis, thus confirming the diagnosis of dermatitis herpetiformis (DH).

Evaluation by a gastroenterologist who performed serologic testing and endoscopic biopsy of the small intestine further substantiated the diagnosis. In the serum, the presence of immunoglobulin G antigliadin (42.3 U/mL; reference, <10), IgA anti-tissue transglutaminase (anti-tTGase) (>100 U/mL; reference, <4), and IgA antiendomysial (positive; reference, negative) antibodies were detected. The intestinal biopsy revealed villous atrophy accompanied by duodenitis consistent with celiac



**Figure 2.** Neutrophils in the papillary dermis with clefting at the dermoepidermal junction (H&E, original magnification  $\times 40$ ).

disease (CD). HLA typing was not performed. A complete blood count with differential blood count, comprehensive metabolic panel, thyroxine, thyroid stimulating hormone, and thyroglobulin antibodies were all within reference range. The patient was initiated on a gluten-free diet and subsequently developed fewer lesions and reduced pruritus.

### Comment

DH is a cutaneous manifestation of CD, which is an immune-mediated enteropathy caused by gluten sensitivity. The symptoms of childhood CD include persistent diarrhea, failure to thrive, abdominal pain, and vomiting. Iron deficiency anemia also may be present as well as other sequelae of malabsorption. Although patients with DH usually do not have gastrointestinal symptoms, virtually all patients with DH show evidence of the same gluten-sensitive enteropathy of the small bowel.

Gluten is a grain protein found in wheat, barley, and rye, but not in oats. Gliadin, the alcohol-soluble fraction of gluten, is believed to be the inciting stimulus.<sup>1</sup> In addition to antigliadin antibodies, patients with DH have circulating antiendomysial and antitransglutaminase antibodies with uncertain

roles in pathogenesis. The prevailing theory suggests that gluten sensitivity leads to the formation of IgA antibodies to gluten-transglutaminase complexes. These antibodies cross-react with other transglutaminases, specifically epidermal transglutaminase, which is highly homologous. Deposition of IgA-transglutaminase 3 complexes within the papillary dermis cause skin lesions of DH.<sup>2,3</sup>

Childhood DH is rare, with an uncertain incidence and prevalence. Cases have been reported in children as young as 8 months,<sup>4</sup> but most children receive the diagnosis between the ages of 2 and 7 years.<sup>5</sup> DH is most prevalent in individuals of Northern European descent. In adults, men with DH outnumber women by a ratio of nearly 2:1<sup>6</sup>; however, among childhood cases, there is a female predominance.<sup>5,7</sup> A genetic predisposition for gluten sensitivity is supported by the high prevalence of DH and CD among first-degree relatives of known patients with DH and CD as well as a documented HLA association. The DQ2 and DQ8 alleles are most closely linked with DH and CD.<sup>8</sup>

The clinical presentation of DH is characterized by symmetrically distributed papulovesicular lesions and urticarial plaques, often favoring the back, buttocks, and extensor surfaces of the extremities. Because the lesions are intensely pruritic, intact vesicles are rarely observed by the clinician. Children, by most accounts, present similarly to adults; however, uncommon skin findings may be present and include isolated involvement of the palms,<sup>9</sup> hemorrhagic lesions of the palms and soles,<sup>10</sup> deep dermal papules and nodules,<sup>11</sup> and facial lesions.<sup>5,11</sup> Powell et al<sup>12</sup> described a case with a predominance of urticarial lesions. Thus, childhood DH often is misdiagnosed as atopic dermatitis, papular urticaria, scabies, linear IgA dermatosis, or chronic urticaria. Recalcitrant cases of these diseases or patients who present with atypical findings of common diseases like atopic dermatitis should prompt the clinician to consider DH in the differential diagnosis.

The gold standard for diagnosing DH is DIF of a biopsy from perilesional skin, which shows granular IgA deposits most often localized to the papillary dermis. For routine histology, a biopsy of an intact vesicle is preferred where neutrophils in the papillary dermis and clefting at the dermoepidermal junction are seen. Although granular IgA deposits seen on DIF are highly specific for DH, up to 10% of cases may have a negative DIF.<sup>13,14</sup> To confirm the diagnosis, serologic testing for anti-tTGase antibodies is useful. Using an enzyme-linked immunosorbent assay, tTGase antibodies can be detected in serum with specificity and sensitivity above 90% for patients on normal diets.<sup>15,16</sup> Desai et al<sup>17</sup> documented the

cost-effectiveness of enzyme-linked immunosorbent assay tTGase testing and proposed that serologic testing be used primarily in the diagnosis of DH. Once patients remove gluten from their diet, the skin lesions and enteropathy resolve. Furthermore, tTGase antibodies decrease to levels within reference range in the absence of gluten; thus, serologic testing can be used to monitor dietary compliance.

Patients with DH are at higher risk for autoimmune diseases, particularly Hashimoto thyroiditis, pernicious anemia, and type 1 diabetes mellitus, among others.<sup>18-20</sup> The association between DH and lymphoma, mostly T-cell lymphoma, is well-documented, with 78% of lymphomas arising from the small bowel, thus warranting vigilant surveillance and regular follow-up with a gastroenterologist.<sup>21</sup> Lewis et al,<sup>22</sup> in a retrospective study of 487 patients with DH, found that lymphoma only occurred in patients not on gluten-free diets or in patients who had followed the gluten-free diet for less than 5 years. Moreover, patients in this study who did adhere to the gluten-free diet had no increased risk for developing lymphoma over the general population.<sup>22</sup>

The primary treatment of DH is a gluten-free diet that is protective against the development of lymphoma. Dietary compliance is challenging, especially for children; therefore, referral to a dietician familiar with this area is helpful. Because months of dietary restriction are needed before a response is noted, many patients require pharmacologic treatment with dapsone. The recommended starting dose for children is 2 mg/kg daily with titration based on clinical response.<sup>23</sup> Most patients will have a rapid response to dapsone within 48 to 72 hours. However, the enteropathy is unaffected by dapsone therapy and patients should be encouraged to maintain dietary compliance.

## Conclusion

Childhood DH is rare and can present with atypical lesions involving the palms and soles, urticarial lesions, deep dermal papules and nodules, and facial lesions. If aware of these unusual presentations, clinicians may consider the diagnosis of DH and act to further evaluate cases of suspected common diseases not responding to treatment.

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