Urticarial dermatitis herpetiformis: A rare presentation of an uncommon disorder

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Key words: celiac disease; dermatitis herpetiformis; direct immunofluorescence; urticaria.

INTRODUCTION

Dermatitis herpetiformis (DH) is a cutaneous manifestation of gluten-sensitive enteropathy (celiac disease) that classically presents as an intensely pruritic, scaly, erythematous, papulovesicular eruption on the extensor extremities and buttocks symmetrically.[1] Histologically, DH is characterized by microabscesses with fibrin and neutrophils at the dermal papillae; direct immunofluorescent (DIF) staining demonstrates granular deposition of immunoglobulin A (IgA) at the dermoepidermal junction.[2]

Here, we report a rare case of a 37-year-old patient who presented with a diagnosis of chronic idiopathic urticaria and no systemic signs of gluten sensitivity. A review of the presentation suggested DH, and a subsequent laboratory examination revealed anti-tissue transglutaminase antibodies. The diagnosis of a rare urticarial manifestation of DH was confirmed by histology and DIF biopsy.

Abbreviations used:

DH: dermatitis herpetiformis
DIF: direct immunofluorescence
IgA: Immunoglobulin A

CASE REPORT

A 37-year-old woman presented with 3 years of recurrent and intensely pruritic hives on her elbows, sacrum, and, occasionally, her knees. The patient reported localized pruritus before the lesions emerged, with an individual lesion lasting approximately 24 hours before resolving. A review of records revealed a prior skin biopsy read as neutrophil-predominant urticaria. Laboratory studies at the time of the original biopsy demonstrated a negative antinuclear antibody and rheumatoid factor, normal thyroid-stimulating hormone levels, mildly low complement C3 (76, normal laboratory reference range 87-200 mg/dL), and complement C4 (15, normal range 18-52 mg/dL). At that time, she was diagnosed with chronic idiopathic urticaria and was started on fexofenadine 180 mg twice daily and cetirizine 10 mg 4 times daily. These medications helped reduce the intensity of the pruritus but did not resolve or prevent new hives from developing. She denied bloating, abdominal pain, or abnormal bowel movements. She had no family history of celiac disease, though her mother had ulcerative colitis.

On presentation, no skin eruption was present; however, clinical photography was reviewed, demonstrating pink edematous papules and plaques on the elbows and sacrum consistent, with urticaria (Fig 1). A celiac panel was obtained given the localization of the eruption and intensity of pruritus. Tissue transglutaminase IgA level was moderately high (22, normal reference range 0-3 U/mL); endomysial IgA titers (1:160, normal reference range <1:10) and deaminated gliadin peptide IgA level (34, normal reference rage 0-19 Units) were both elevated. Upon recurrence of the urticarial eruption, 4 mm lesional and perilesional punch biopsies of a papule on the right elbow were performed. Hematoxylin-eosin staining revealed papillary neutrophilic microabscesses accompanied by superficial perivascular and interstitial infiltrates comprised

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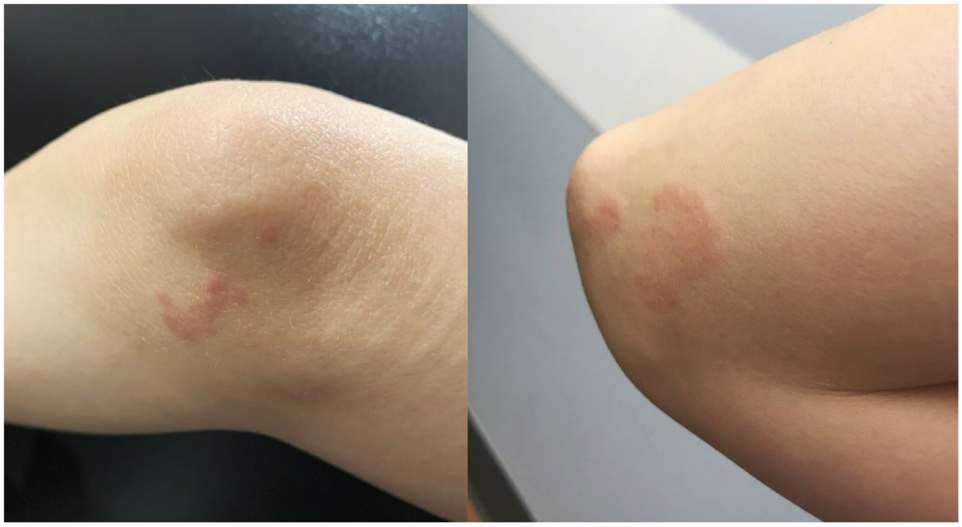

Fig 1. The patient had polymorphic, erythematous papules and plaques bilaterally on her elbows. Similar lesions were present on her buttocks and occasionally, knees.

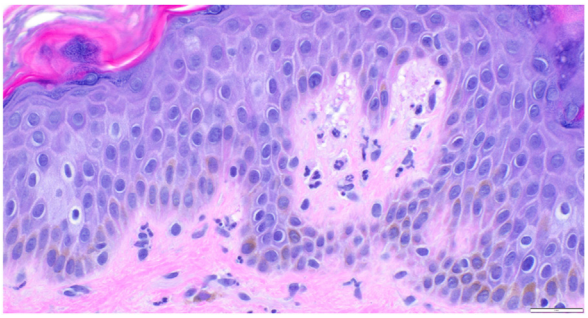

Fig 2. Histopathological examination of right elbow 4 mm punch biopsy reveals neutrophils concentrated within dermal papillae where there is also papillary dermal edema.

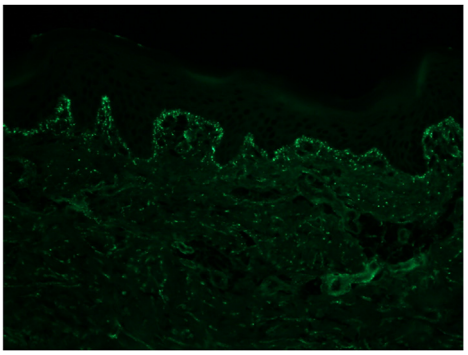

Fig 3. Direct immunofluorescence staining of right elbow 4 mm punch biopsy showing deposition of focal granular C3 and strong granular immunoglobulin A along the dermoepidermal junction and within dermal papillae.

of lymphocytes, histiocytes, eosinophils, and neutrophils (Fig 2). DIF revealed granular deposition of IgA and C3 along the dermoepidermal junction and within dermal papillae, diagnostic of DH (Fig 3).

The patient was subsequently referred to gastroenterology, where a small-bowel biopsy was obtained, which showed patchy intraepithelial lymphocytosis with preserved villous architecture. Her skin eruption improved with a gluten-free diet alone and she no longer takes antihistamines. She experienced a flare without prodromal itching after receiving the COVID-19 vaccination and reports intermittent eruptions coinciding with accidental gluten ingestion.

DISCUSSION

The classic symptoms of gluten-sensitive enteropathy include chronic diarrhea, malabsorption, and weight loss. However, not all patients present with this classic manifestation. Some patients may have minor gastrointestinal disease or only extraintestinal symptoms, while others may present with anemia, osteoporosis, failure to thrive, and other signs of malabsorption.[3] While DH is associated with an enteropathy in over 90% of cases, the enteropathy may not be symptomatic, as in our patient.[4]

Lesions in DH vary widely, thus predisposing to misdiagnosis and leading to delayed definitive diagnosis and treatment. Furthermore, the histopathology of DH is nonspecific in as many as 40% of skin biopsies—even, rarely, upon repeat biopsy.[5,6] For this reason, DIF studies, which are far more sensitive and specific, are concomitantly performed when a diagnosis of DH is under consideration. However, though DIF with granular dermoepidermal IgA deposition is considered pathognomonic, there are

reports of alternative immunofluorescence patterns, in particular, fibrillar IgA deposition.[7]

Serologies considered a confirmatory test for DH due to their high sensitivity (50%-95%) and specificity (>90%), can additionally be used to monitor response to a gluten-free diet.[2] As DH is considered a cutaneous expression of CD, duodenal biopsy in cases of proven DH is not strictly necessary, though it is the gold standard for celiac diagnosis.[6] Duodenal biopsies performed in patients with DH are variable, with mild to moderate villous atrophy present in approximately 75% of patients.[4] In the remaining 25%, including our patient, intraepithelial lymphocytosis is present with no evidence of villous atrophy.[3] Such findings are nonspecific for celiac disease and may have several other etiologies.

With the broad range of possible presentations and clinical and histopathological findings that may be uniformly nonspecific or misleading, DH can prove an elusive diagnosis. One case of DH presenting as chronic urticaria in a child—notably nonpruritic and asymptomatic—has previously been reported.[8] Other cases in the literature have highlighted unusual presentations, including palmoplantar keratosis and prurigo pigmentosa-like lesions.[9,10] Our case report emphasizes that patients with chronic pruritus and skin eruption in typical anatomic sites for DH, even in the absence of gastrointestinal or systemic symptoms, should undergo workup for celiac disease to avoid diagnostic delay. Furthermore, as has also been demonstrated elsewhere in the literature, continued follow-up with repeat biopsies may be required as initial histopathologic studies may fail to demonstrate classic features.

Conflicts of interest

None disclosed.

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