A persistent dermal hypersensitivity reaction associated with *Helicobacter pylori* infection

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INTRODUCTION

A dermal hypersensitivity reaction is a histopathologic entity that remains poorly understood. Although it is associated with diverse clinical presentations, common features include intractable pruritus and a recalcitrant urticarial and/or eczematous eruption. Autoimmune disease, drugs, infection, and malignancy have been reported as triggers. Often, however, the etiology is elusive. Here, we describe a unique case of persistent dermal hypersensitivity reaction associated with *Helicobacter pylori* infection, which resolved with antimicrobial therapy.

CASE REPORT

An 85-year-old Hispanic woman presented with a 10-year history of a diffuse, intensely pruritic rash that initially began on her trunk and spread to her extremities. The lesions were persistent and pruritus was intractable, interfering with sleep and daily activities. She denied any fevers, chills, weight loss, nausea, vomiting, abdominal pain, diarrhea, constipation, or other gastrointestinal complaints. Findings of detailed review of systems were negative. She had no contact with anyone who was ill, and there were no household members with similar complaints. She had no history of bullous disease or autoimmune disorder. Medical history was notable for hypertension and mitral valve replacement. Medications included losartan, atenolol, hydrochlorothiazide, and coumadin. She was afebrile, with normal blood pressure and heart rate. Full-body skin examination showed diffuse erythematous, edematous papules and plaques, most with excoriations, covering her back, chest, and extremities (Fig 1, *A*, *C*, *E*, and *G*). Results of lymph node examination were unremarkable. Prior treatment with potent topical steroids, antihistamines, and permethrin (for presumptive scabies infestation) had been ineffective.

Abbreviations used:

DHR: dermal hypersensitivity reaction
UD: urticarial dermatitis

A biopsy sample, taken 5 years earlier to rule out dermatitis herpetiformis, showed a moderately dense superficial to mid-perivascular and interstitial mixed-cell infiltrate with neutrophils and eosinophils. In the context of that biopsy, and because of the persistence of the eruption after permethrin treatment, it was hypothesized that her dermatosis may have resulted from a drug reaction. Management included clobetasol ointment, hydroxyzine, and discontinuation of losartan, also without improvement.

A repeat biopsy was performed and similarly showed a perivascular dermatitis suggestive of an eczematized dermal hypersensitivity reaction (DHR), as can be seen in the setting of a response to an arthropod or drug (Fig 2, *A* and *B*). Based on the combined histologic and clinical picture, persistent dermal hypersensitivity of unknown etiology

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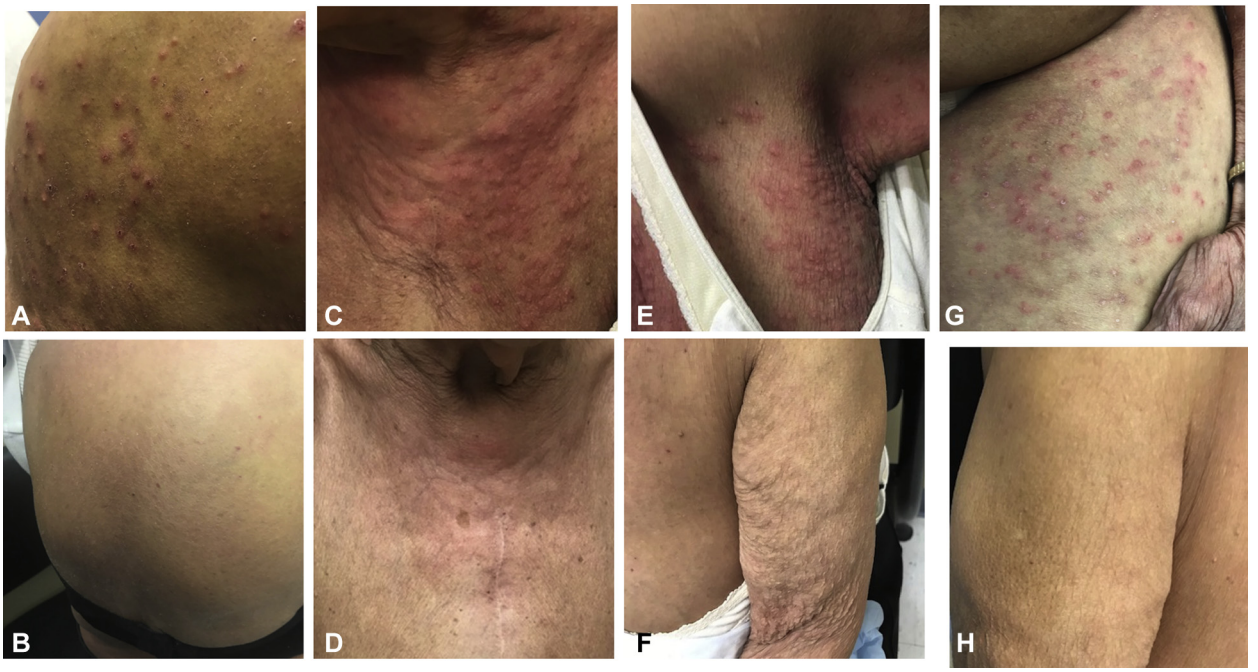

Fig 1. The (**A**) back, (**C**) chest, (**E**) axillary area, and (**G**) leg with numerous excoriated erythematous papules and plaques. The (**B**) back, (**D**) chest, (**F**) axillary area, and (**H**) arm 4 months after treatment with antimicrobial triple therapy for *Helicobacter pylori*.

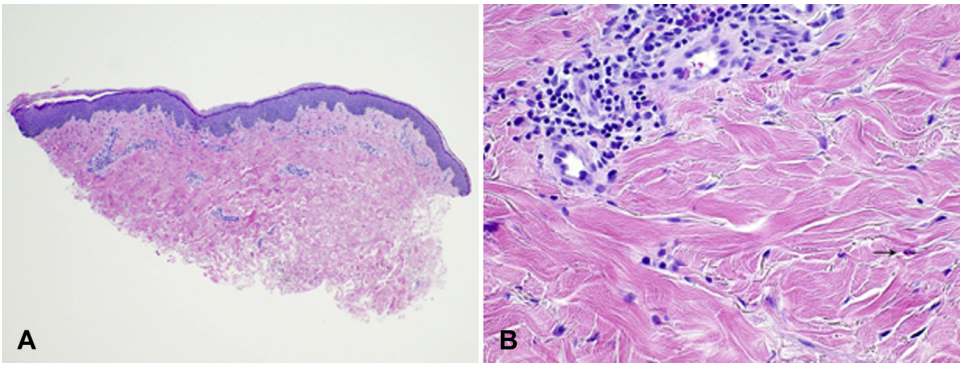

Fig 2. Histopathologic examination (hematoxylin-eosin stain; original magnifications: **A**, ×4; **B**, ×40) shows a superficial to mid-perivascular and interstitial lymphohistiocytic infiltrate with occasional eosinophils. The arrow points to an eosinophil.

was ultimately diagnosed. The patient was then started on 15 mg of oral prednisone for better control while awaiting the results of further testing. Within weeks, she reported diminished pruritus and a significant improvement in the appearance of the rash. However, when the prednisone was tapered or stopped because of noncompliance, the eruption would abruptly recur.

Results of a thorough laboratory workup, including complete blood count, basic metabolic panel, lipid panel, liver function test, hepatitis panel, thyroid function test, rapid plasma reagin, antinuclear antibody screening, DNase-B antibody test, QuantiFERON Gold (Qiagen, Germantown, MD), and HIV testing, were unremarkable. Patch testing was negative. *H pylori* IgG antibody test result was positive, and an *H pylori* stool antigen test was indicative of active infection. Although the patient had no symptoms of gastritis, we elected to investigate *H pylori* as a possible trigger of her eruption due to the many reported associations of *H pylori* with urticaria and inflammatory skin disease in the dermatologic literature.[1,2]

The patient was then referred to the gastroenterology department for treatment in the hope that this infection was the trigger for her intractable

dermatosis. She was successfully treated with pantoprazole, amoxicillin, and clarithromycin, the so-called *triple therapy*. Repeat *H pylori* stool antigen testing results were negative, suggestive of a cure. Although the plan was for a slow prednisone taper and monitoring for a flare, the patient stopped taking prednisone shortly after finishing her antibiotic treatment. She returned to the clinic a few months later with no evidence of cutaneous pathology and completely diminished pruritus (Fig 1, *B, D, F, H*).

DISCUSSION

A dermal hypersensitivity reaction is considered a largely histologic diagnosis without uniform or consistent accompanying clinical characteristics.[3] The term *urticarial dermatitis* (UD) has been proposed by some as a subset of DHRs with shared features.[4] In the strict definition outlined by Kossard et al[5] in 2006, UD was described as pruritic, erythematous papules and plaques resembling urticaria but lasting longer than 24 hours and sometimes accompanied by eczematous lesions. Although the dermatopathologic correlate to UD is a dermal-predominate hypersensitivity reaction, the precise histologic criteria delineating UD from a DHR continue to be somewhat controversial in the dermatologic literature.[4-6] As a result, the term *UD* may not be a universally accepted diagnostic entity at this time. Thus, we chose to classify the eruption as a DHR despite the fact that presentation may largely fit within the category of UD by Kossard et al's definition.[5]

Despite the relative frequency in which dermal hypersensitivity reactions are encountered, the process remains poorly understood and often presents a diagnostic and treatment dilemma. Although many cases are idiopathic, reported causes include infection, atopy, systemic malignancy, and autoimmune disorders, to name a few.[3,6,7] Patients with this dermatosis are often extremely uncomfortable and experience a severely diminished quality of life due to intractable pruritus. The recalcitrance of this dermatosis and its resistance to topical therapies renders treatment difficult. A retrospective cohort study by Banan et al[8] showed that 13 of the 19 patients initially treated with topical corticosteroids with or without antihistamines required a course of oral corticosteroids, phototherapy, or treatment with immunosuppressive agents at some stage. Some success has been reported with the use of dapsone, hydroxyurea, azathioprine, cyclosporin, and mycophenolate mofetil.[8-10]

In our case, after multiple courses of topical steroids, antihistamines, and permethrin had failed, we were able to control the eruption with oral prednisone while awaiting the results of further laboratory tests. Uncovering the etiologic trigger of a DHR is even more critical in light of the fact that many of the patients presenting with this eruption are elderly and often frail. Our patient was osteopenic, was taking blood thinners for a metallic valve, and was at risk for falls. Therefore, she was a poor candidate for long-term control with prednisone. Although triple therapy for *H pylori* with antimicrobials resulted in a complete and sustained remission, there remains the remote possibility of a concurrent occult bacterial infection, which may have been the actual culprit of the eruption and was simultaneously treated with the antibiotic cocktail. In the absence of reinfection with *H pylori* and recurrence of the rash, this cannot be conclusively ruled out.

At present, there are no definitive guidelines for the diagnosis, prognosis, or management of DHRs. Nonetheless, it is essential that a systematic investigation be undertaken to identify the cause of the eruption. As such, it is prudent to perform a thorough history and consider direct immunofluorescence, patch testing, and screening for occult malignancy and infectious agents.[6,8]

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