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Dermatitis Herpetiformis (DH) in Association with H. pylori Infection: Description of a Case Report

A. H. H. Bashir[1&2*], M. A. El Tahir[2] and A. M. El Hassan[2]

[1]Department of Dermatology and Venereology, Al Jawda Hospital, University of Juba, P. O. Box 11587, Khartoum, Sudan.
[2]Khartoum College of Medical Science, Jabir AbuEliz Diabetic Centre, Sudan.

Case Study

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ABSTRACT

Dermatitis herpetiformis (DH) is an autoimmune blistering disorder associated with a gluten-sensitive enteropathy (GSE), and is generally accepted as a cutaneous manifestation of celiac disease and is characterized by grouped excoriations; erythematous, urticarial plaques; and papules with vesicles. We reported an interesting case of adult DH occurred in a 30 year old Sudanese young adult with chronic inflammatory bowel disease, presented with typical string of pearls in the face, trunk and extremities for 2 months duration. The case is diagnosed and confirmed as DH where histopathologically shows a sub-epidermal bulla with microabscess formation, sigmoidoscopy and H. pylori ELISA test were positive IgA.

Our case had an adult onset of presentation. Clinical features and histopathology are typical. It is associated of H. Pylori, although poorly responding to triple therapy (Doxycyclin 100 mg bid for 8 days, Cefixime 400 mg for 5 days and Rabeprazole as proton pump inhibitor (PPI) 20 mg for 28 days), but focusing as possible antigen was of paramount concern as possible causative antigen; as in this case all serological specific tests for Coeliac disease were negative.

The case was considered to be the second case of DH with CIBD due to H. Pylori been reported in Sudan.

Keywords: Dermatitis Herpetiformis; Helicobacter pylori; Celiac disease;

**Corresponding author: Email: derma55@yahoo.com;*

1. INTRODUCTION

Dermatitis herpetiformis (DH) is an autoimmune blistering disorder associated with a gluten-sensitive enteropathy (GSE). The disease was described and named in 1884 by Dr. Louis Duhring at the University of Pennsylvania (Duhring et al., 1884). Dermatitis herpetiformis is the result of an immunologic response to chronic stimulation of the gut mucosa by dietary gluten. Dermatitis herpetiformis is generally accepted as a cutaneous manifestation of celiac disease and is characterized by grouped excoriations; erythematous, urticarial plaques; and papules with vesicles. The only United States (US) study showed a dermatitis herpetiformis prevalence of 11.2 cases per 100,000 populations. Dermatitis herpetiformis occurs more frequently in individuals of Northern European ancestry and is rare in Asians and persons of African descent. US studies show a male-to-female ratio of 1.44:1, but international studies have demonstrated a male-to-female ratio up to 2:1. Typically, the onset of dermatitis herpetiformis is in the second to fourth decade; however, persons of any age may be affected (Duhring et al., 2007). Dermatitis herpetiformis is rare in children.

The classic location for dermatitis herpetiformis lesions is on the extensor surfaces of the elbows, knees, buttocks, and back. Dermatitis herpetiformis is exquisitely pruritic, and the vesicles are often excoriated to erosions by the time of physical examination. Diagnosis requires direct immunofluorescence of a skin biopsy specimen showing deposition of immunoglobulin A (IgA) in a granular pattern in the upper papillary dermis (Zone et al., 1996), which triggers an immunologic cascade, resulting in neutrophil recruitment and complement activation. Although most patients are asymptomatic, greater than 90% have an associated gluten-sensitive enteropathy upon endoscopic examination. Among patients with celiac disease, 15-25% develops dermatitis herpetiformis (Zone et al., 2005). The mainstays of treatment are dapsone (Coleman et al., 1993) and a gluten-free diet.

Both dermatitis herpetiformis and celiac disease (CD) are associated with an increased expression of HLA-A1, HLA-B8, HLA-DR3, and HLA-DQ2 haplotypes. In patients with dermatitis herpetiformis, 10-15% of their first-degree relatives have dermatitis herpetiformis or celiac disease (Gaspari et al., 1990).

Evidence is mounting that epidermal transglutaminase 3 (eTG) is the dominant autoantigen of dermatitis herpetiformis (Sardy et al., 2002).

In addition, serum from dermatitis herpetiformis patients contains high-affinity anti-eTG IgA autoantibodies. Co-localized IgA and eTG deposits have been demonstrated in the papillary dermis in patients with dermatitis herpetiformis and, to lesser extent, in healthy skin of gluten-sensitive enteropathy patients (Cannistraci et al., 2007).

DH may develop in patients with partial IgA deficiency, indicating that pathogenically directed IgA antibodies are likely sufficient for cutaneous IgA deposition in this disease. IgA deposits can disappear after long-term (up to 10 years) avoidance of dietary gluten (Samolitis et al., 2006).

Gluten is a protein present in grasses of the species *Triticeae,* which includes barley, rye, and wheat. Rice and oats belong to different species and are generally well tolerated. Strict compliance with a gluten-free diet results in normalization of the small bowel mucosal changes and control of the cutaneous manifestations of dermatitis herpetiformis in most patients. Levels of circulating antibodies also tend to normalize (Garsed et al., 2007).

The gluten-sensitive enteropathy does not cause symptoms in most dermatitis herpetiformis patients. Less than 10% exhibit symptoms of bloating, diarrhea, or malabsorption. However, greater than 90% show abnormalities upon endoscopic examination. Two thirds have villous atrophy detected on intestinal biopsy specimens. The other third shows elevated intraepithelial lymphocyte counts, increased T-cell receptor gamma/delta intraepithelial lymphocyte counts, or both (Rodrigo et al., 2006).

DH is associated autoimmune diseases include dermatomyositis, type 1 diabetes mellitus, myasthenia gravis, rheumatoid arthritis, Sjögren's syndrome, systemic lupus erythematosus, and thyroid abnormalities. Thyroid abnormalities are present in as many as 50% of dermatitis herpetiformis patients and include hypothyroidism, hyperthyroidism, thyroid nodules, and thyroid cancer (Gaspari et al., 1990).

Neurologic manifestations such as ataxia have been rarely described (Helsing et al., 2007).
Associated neoplastic conditions include GI lymphomas and non-Hodgkin lymphoma; patients are at increased risk of developing these cancers (Sigurgeirsson et al., 1994).
A gluten-free diet may reduce the incidence of dermatitis herpetiformis–associated lymphomas (Swerdlow et al., 1993).

Celiac disease usually involves more severe and widespread intestinal involvement. Celiac disease has been associated with genetic abnormalities, including Down syndrome, Turner syndrome, and William syndrome. Liver disease, neurologic disorders, and other skin diseases are also increased in celiac disease, possibly due to common HLA regions on chromosome 6 or immune molecule cross-reactivity (Rodrigo et al., 2006).

Gastric manipulation (surgery) may induce dermatitis herpetiformis.In a recent study, authors concluded that gastritis in coeliac disease and dermatitis herpetiformis is largely caused by H pylori infection (Crabtree et al., 1992).

2. THE CASE

A female patient, single, 30 years old, civil employee, descent from second degree relativeparents, resident in Taief and Gaalei tribe (Mixed Arab race) was complaining from generalized blistering for 2 months.

The condition started 2 months ago with insidious onset and progressive course, presented with severely itchy, small blisters, mainly at face and upper trunk. Patient was seen by dermatologist and put on Prednisolone oral therapy with initial good response where severe relapse after cessation of treatment was noticed. The patient was under supervision by gastroenterologist as suffering from abdominal discomfort and difficulty in defecation. Sigmoidoscopy done to show Ulcerative colitis, then blisters start to appear and to disseminate, where a dermatological opinion asked by GI specialist. No related family history was detected.

3. GENERAL EXAMINATION

The general condition is well, pale, not icteric, as well no palpable spleen, and liver. No palpable lymph nodes.

4. DERMATOLOGICAL EXAMINATION

widespread symmetrically clustered, string of pearls lesions; tense, clear, variable sized bullae, arranged at periphery of central crusted lesions and erythematous base involving mainly convex of face, upper back, upper arms, upper chest, upper thighs and elbow. Few scattered similar lesions were noticed at abdomen, forearms and legs, no erosions and ulcers were seen.

The blisters are small, tense, clear; some are eroded and crusted on erythematous base. Palms and soles: No similar lesions at both soles and palms.

Nails: No nails dystrophy has been noticed.
Ears: No Abnormality was detected. .
Hair: No Abnormality was detected.
Oral cavity: **No** oral blisters or erosions were seen.

5. INVESTIGATIONS DONE

Skin biopsy:
Date: 08/02/2010.
Slide: # 326/Z/10.
Sections show a sub-epidermal bulla with microabscess formation. The dermis contains a mild peri- vascular lymphocytic infiltration.
Diagnosis: Dermatitis Herpetiformis.

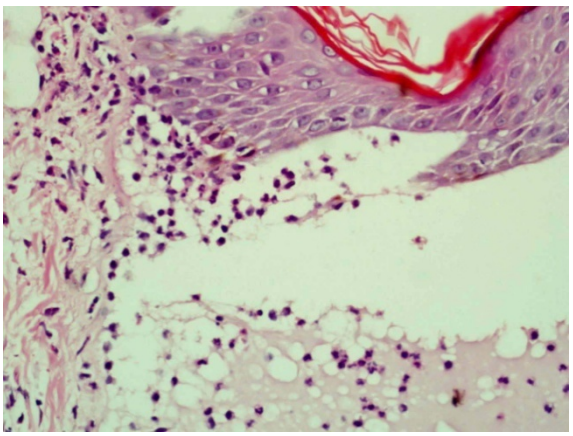

Fig. 1. Old sub epidermal bulla containing neutrophils

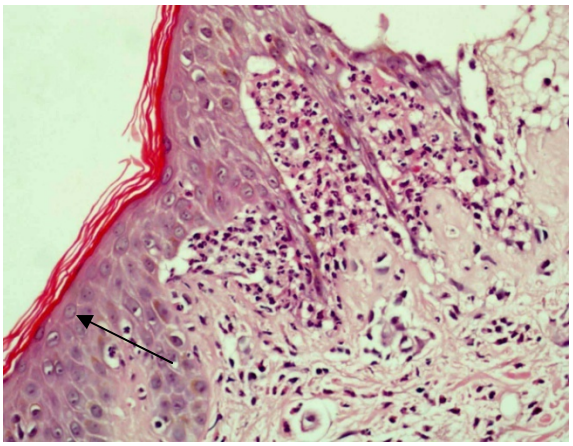

Fig 2. Early bulla showing neutrophils in the tips of the dermal papillae a characteristic feature of dermatitis herpetiformis (Arrows). (H&Ex40)

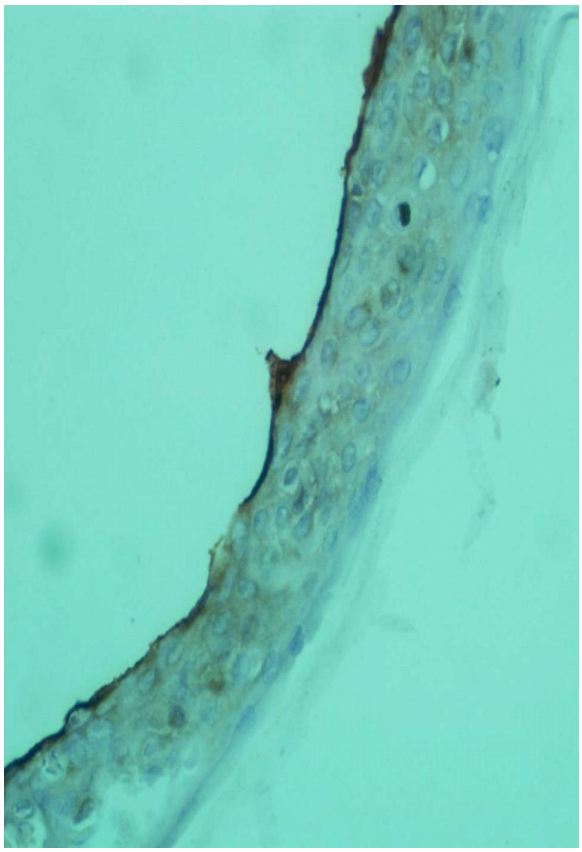

Fig. 3. Basement membrane at the epidermodermal junction is positive for IgA (Immunoperoxidase stain x40)

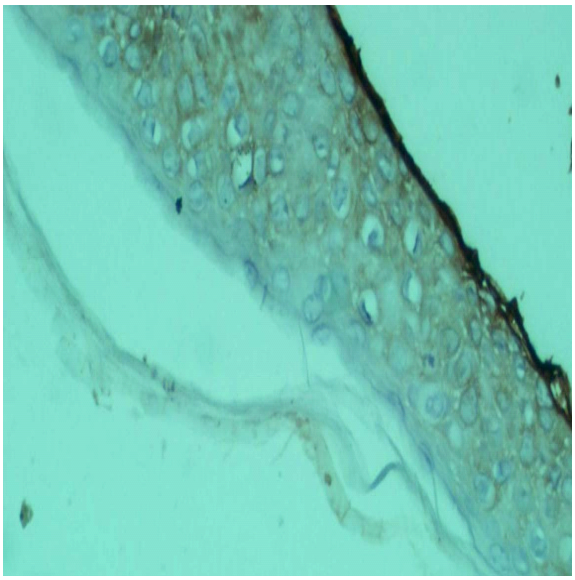

Fig. 4. Basement membrane at the epidermodermal junction is positive for IgA (Immunoperoxidase stain x40)

Anti- Reticulin: Negative
Anti- Endomyciel IgA: Negative 1/20 normal less than1/40
Anti-Gliadin (IgA): Negative 10.48 U/ml normal less than12
Immunoglobulin A (IgA): 257.4 mg/dl Negative (70-400)
Helicobacter pylori ELISA test:
IgG 4.4 Positive (= or more than 1.1 Positive)
IgA 3.8 Positive (= or more than 1.1 Positive)

6. DISCUSSION

This case was a classical one of typical DH with Coeliac disease, in a female patient, 30 years old, What was of significance in this case was the association of H. Pylori in high IgA titer (3.8) which suggested to be considered as a possible antigen as DH is of known antibody, but of unknown antigen, as well as H. Pylori has a definite relation with autoimmune diseases; thyroiditis, Diabetes Mellitus, Sjögren's Rheumatoid Arthritis, and neoplastic conditions include GI lymphomas (MALT) and non-Hodgkin lymphoma, as well as all above mentioned are known to be also associated with DH (Gaspari et al., 1990). Detection of Helicobacter pylori antibodies with dyspeptic manifestations in this case could be related to possible underlying cause as has been observed. The case was received triple therapy with some response in the form of, Doxycyclin 100 mg bid for 8 days, Cefixime 400 mg for 5 days and Rabeprazole as proton pump inhibitor (PPI) 20 mg for 28 days, then H. Pylori – stool antigen (Ag) test was done to show that antigen is not detected.

Our case had an adult onset of presentation. Clinical features and histopathology were typical, it was associated with H. Pylori, although poorly responding to triple therapy but focusing for possible antigen was of paramount concern as possible causative antigen as in this case as all serological specific tests for coeliac disease were negative.

7. CONCLUSION

DH is of known antibody IgA and unknown antigen as well as known association with coeliac disease and Glutten enteropathy. H. pylori is also of known association with autoimmune disease through specific antibody IgA , so the associated of DH , and Coeliac disease with H. Pylori, focusing for possible antigen was of paramount concern as possible causative antigen as in this case as all serological specific tests for coeliac disease were negative.

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