

Dermatitis herpetiformis and rheumatoid arthritis

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ABSTRACT

Dermatitis herpetiformis (DH) is a rare, intensely pruritic, chronic, recurrent, papulovesicular disease. The disease can be clearly distinguished from the other subepidermal blistering eruptions by histologic, immunologic, and gastrointestinal criteria. Most patients have an associated gluten-sensitive enteropathy (GSE) that is usually asymptomatic. Both enteropathy and the dermatologic findings disappear with a gluten-free diet, therefore, DH is thought to be the specific dermatologic finding of celiac disease (CD). An association between CD and autoimmune disease has been documented in several studies. Similar associations have been reported in DH. We report a 46-year-old man with DH diagnosed more than 10 years previously who developed GSE, pernicious anemia, and rheumatoid arthritis in the following years.

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Dermatitis herpetiformis (DH) is characterized by an intensely itchy, chronic papulovesicular eruption that is usually distributed symmetrically on extensor surfaces. Most patients have an associated gluten-sensitive enteropathy (GSE) that is usually asymptomatic. In addition to GSE, DH patients have other autoimmune diseases such as rheumatoid arthritis (RA), Sjögren's syndrome, pernicious anemia (PA), thyroid disease, and insulin-dependent diabetes.¹ We present a 46-year-old male patient with a 10-year history of DH who was also diagnosed with RA 2 years previously. The patient also had GSE and PA. We discuss DH and its relation with other autoimmune diseases and the treatment of the patient.

Case Report. A 46-year-old male patient was admitted to our clinic with pain and swelling in his right elbow, both wrists and hands, and left ankle. He reported one hour of morning stiffness. Two years ago,

based on similar symptoms, he was diagnosed with RA at another hospital. Despite treatment with 2 gm sulfasalazine orally daily and 100 mg indomethacin as suppository daily for 2 years, the joint complaints continued. He had itching skin lesions that had been diagnosed as DH 10 years before. Sulfone (Dapsone[®]) had been prescribed to him irregularly and the skin manifestations were almost under control. He did not comply with instructions to implement a gluten-free diet, probably because he had no gastrointestinal system complaints. During his physical examination, his blood pressure was 120/70 mm Hg, pulse 88/min, and body temperature 36.2°C. His cardiovascular and respiratory systems and abdominal examinations were normal. Excoriated papulovesicular lesions were observed on the dorsum of elbows, back and buttocks (Figure 1). Examination of the musculoskeletal system revealed swelling and warmth of his right elbow, both wrists, left ankle, and 1st, 2nd and 3rd metacarpophalangeal joints together with Boutonniere

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Figure 1 - Itchy papulovesicular lesions.

deformity on the 5th phalanx of the left hand. Laboratory findings were as follows: hemoglobin: 8.9 g/dl (13.6-17.2), hematocrit: 25% (39.5-50.3), mean corpuscular volume: 122 fl (80.7-95), mean corpuscular hemoglobin: 42.2 pg (27.2-33.5), mean corpuscular hemoglobin concentration: 34.6 g/dl (32.7-35.6), white blood count: 9600 (4300-10300), thrombocytes: 88000 (156000-373000), erythrocyte sedimentation rate: 66 mm/hr (0-10), C-reactive protein: 15.1 mg/L (0.00-5.0), rheumatoid factor: 410 IU/ml (0-20), alanine aminotransferase: 48 U/L (0-38), aspartate aminotransferase: 32 U/L (0-40), Gamma-glutamyltransferase: 56 U/L (7-50), alkaline phosphatase: 193 U/L (98-279), and lactate dehydrogenase: 1902 U/L (91-232). All other biochemical tests were normal. HBsAg: (-), Anti HCV: (-), antinuclear antibody: (-), Anti-double stranded DNA: (-), and IgG, A, and M, C3, C4 and thyroid function tests were also observed as normal. Hypersegmented neutrophils were seen in the peripheral blood preparation. Vitamin B12 and folic acid levels were 93 pg/ml (211-911) and 4.31 (3-17) respectively. The Gastroenterology Department was consulted and gastric mucosa biopsy was performed, which revealed active chronic atrophic gastritis. Antiparietal antibody was detected as negative, whereas the anti-intrinsic factor antibody was positive. According to these findings, PA was diagnosed, and parenteral vitamin B12 treatment was started. Jejunal biopsy performed on the patient at the same time revealed villous atrophy and lymph plasmocytes in the lamina propria, together with nuclear mass in the epithelium surface. These findings were consistent with gluten enteropathy. We also found anti-gliadin IgA as 188.7 RU/ml (0.0-50.0), anti-gliadin IgG as 53.4RU/ml (0.0-50.0), and endomysium IgA: (-). To confirm the diagnosis of DH, a skin biopsy was performed and

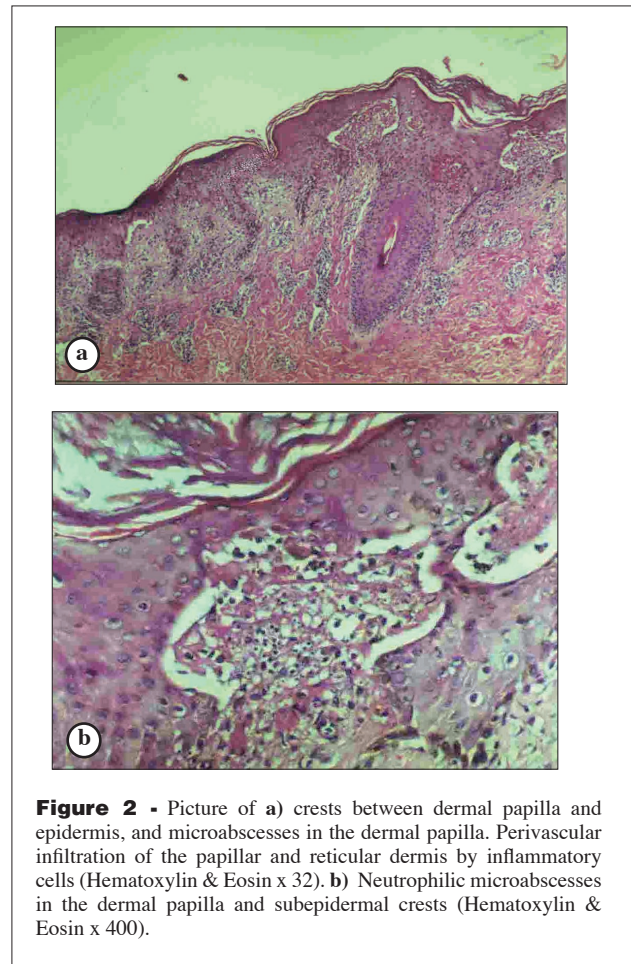


Figure 2 - Picture of **a**) crests between dermal papilla and epidermis, and microabscesses in the dermal papilla. Perivascular infiltration of the papillar and reticular dermis by inflammatory cells (Hematoxylin & Eosin x 32). **b**) Neutrophilic microabscesses in the dermal papilla and subepidermal crests (Hematoxylin & Eosin x 400).

light microscopic findings were consistent with DH (**Figures 2a & 2b**), however, immunofluorescence microscopy did not show IgA deposits. On direct radiography of the hands, periarticular osteopenia, soft tissue swelling, subchondral bone loss in the 3rd metacarpal head with slight joint space narrowing, subchondral cyst in the 2nd metacarpal head and cysts in carpal bones in the right hand were present. Ankle radiography showed prominent marginal erosion in the 1st phalangeal head. Gadolinium-enhanced magnetic resonance imaging of the hands revealed soft tissue swellings and bone edema around the joints (**Figures 3a & 3b**). Based on the patient's clinical findings and laboratory results, RA was observed to be active. Medical treatment with methotrexate 12.5 mg/week, hydroxychloroquine 200 mg/day and methylprednisolone 20 mg/day was implemented, and the steroid dosage was decreased gradually. The patient's dapsone treatment continued with 1 tablet every other day together with the gluten-free diet. On follow-up controls, skin lesions and joint complaints in his elbows, wrists, and hands had both regressed,

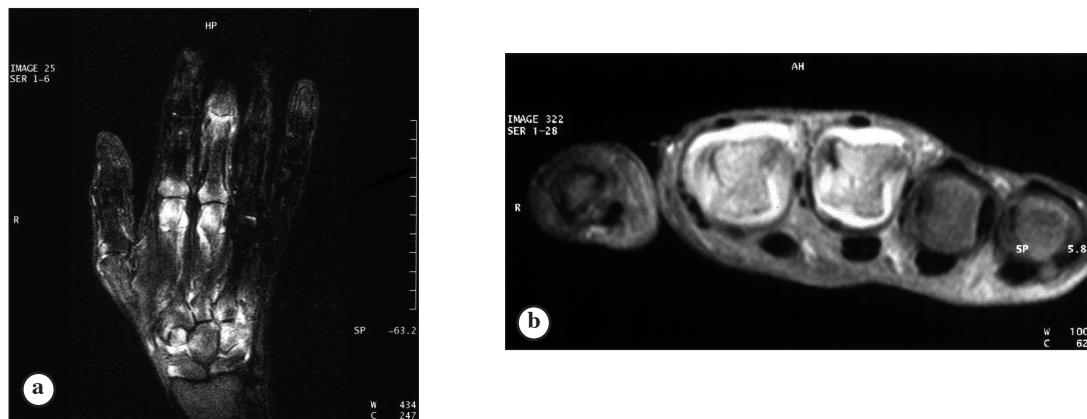


Figure 3 - Magnetic resonance imaging **a)** Synovitis/effusion and subarticular bone edema of the 2nd and 3rd metacarpophalangeal and 3rd interphalangeal joints (T2 weighted STIR sequence on coronal plane). **b)** Contrast enhancement and thickening in the synovial surfaces of the 2nd and 3rd metacarpophalangeal joints (T1 weighted STIR sequence on axial plane).

but his ankle swelling persisted. His vitamin B12 level became normal.

Discussion. Diagnosis of DH is determined by both skin biopsy and the clinical findings. In skin examination, there are excoriated papulovesicles and eczematous changes that are lichenified on the shoulders, trunk and buttocks. The microscopic findings include neutrophil accumulation (microabscesses) in the dermal papilla, and lymphocytes and histiocytes in the dermis and around the vessels. As a result, vesicles appear in the dermal-epidermal junction. Immunofluorescence examination shows granular IgA deposits in the dermal papilla, which are present both in the lesions and the normal appearing skin in DH patients. Erythema multiforme, neurotic excoriations, scabies, eczema, pemphigoid, and other dermatoses can be easily differentiated on the basis of histologic and immunologic criteria.² In our patient, IgA deposits could not be shown. A high index of suspicion is very helpful, even in the absence of IgA deposits in the dermal papillary tips. Marks³ was also unable to show the IgA deposits in his rare number of DH patients. We diagnosed DH based on the morphology and distribution of the skin lesions, light microscopic findings, and regression of the lesions with dapsone. The diagnosis was confirmed by the presence of several autoimmune diseases in this patient. Many autoimmune disorders can be seen together. Dermatitis herpetiformis can also be seen with other autoimmune diseases, among them RA. The first study in the literature regarding such an association was in 1978 by Davies et al.⁴ They

found 2 cases of RA in 42 DH patients. Rothwell et al⁵ presented 3 cases of RA and DH and emphasized that the relation between these diseases is not by chance. Like in celiac disease (CD), gluten sensitivity is seen in the gut mucosa of DH patients. However, the lesions in the jejunum are not as severe as in CD, and gastrointestinal symptoms are not present in most of the patients. In our patient, gluten enteropathy was also observed histopathologically, but he did not have gastrointestinal symptoms. Parke et al⁶ presented 3 patients with CD and RA, 2 of whom also had DH. They noticed that in CD, circulating immune complexes may be responsible for the lesions other than in the gastrointestinal system. Reunala et al,⁷ reviewed 305 patients with DH for other autoimmune diseases, and found that endocrinological diseases were the most frequently observed (5.2%). Connective tissue diseases were found at a rate of 4.3%. In 2 patients (0.7%), RA was diagnosed. There were also cases in that study with more than 2 autoimmune diseases present. In our search of the literature, we found no report of an association of RA, DH, PA and GSE. Some studies have shown that PA may be seen with DH.^{7,8} Our case also had a low vitamin B12 level and chronic atrophic gastritis. More recent studies have shown that although CD affects the proximal intestine, there might be vitamin B12 deficiency without autoimmune gastritis.⁹ Although in our patient the problem was atrophic gastritis, the intestinal pathology may also contribute to the vitamin B12 deficiency. Wang et al presented a case with both PA and RA, and noted that it is a rare condition.¹⁰ A strict gluten-free diet may

lower the incidence of autoimmune pathologies.¹¹ Our patient did not adhere to the gluten-free diet, which may explain the coexistence of so many autoimmune pathologies.

In conclusion, we present a case report with DH, RA, PA and GSE. Dermatologists should be alerted to other autoimmune pathologies in a DH patient.

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References

1. Katz SI. Dermatitis Herpetiformis. In: Freedberg IM, Eisen AZ, Wolff K, Austen KF, Goldsmith LA, Irwin M, et al editors. Fitzpatrick's Dermatology in General Medicine. New York: McGraw-Hill; 2003. p. 616-621.
2. McKee PH, Calonje E, Granter SR. Pathology of the Skin with Clinical Correlations. China: Elsevier Mosby; 2005. p. 131-134.
3. Marks JM. Dogma and dermatitis herpetiformis. *Clin Exp Dermatol* 1977; 2: 189-207.
4. Davies MG, Marks R, Nuki G. Dermatitis herpetiformis - a skin manifestation of a generalized disturbance in immunity. *Q J Med* 1978; 47: 221-248.
5. Rothwell RS, Percy JS, Davis P. Dermatitis herpetiformis and rheumatoid arthritis. *Ann Rheum Dis* 1979; 38: 399.
6. Parke AL, Fagan EA, Chadwick US. Coeliac disease and rheumatoid arthritis. *Ann Rheum Dis* 1984; 43: 378-380.
7. Reunala T, Collin P. Diseases associated with dermatitis herpetiformis. *Br J Dermatol* 1997; 136: 315-318.
8. Kaplan RP, Callen JP. Dermatitis herpetiformis: autoimmune disease association. *Clin Dermatol* 1992; 9: 347-360.
9. Dickey W. Low serum vitamin B-12 is common in coeliac disease and is not due to autoimmune gastritis. *Eur J Gastroenterol Hepatol* 2002; 14: 425-427.
10. Wang PL, Liou LB, Dunn P. Development of rheumatoid arthritis in a patient with pernicious anemia: case report. *Chang Gung Med J* 2001; 24: 125-129.
11. Lewis HM, Renaula TL, Garioch JJ, Leonard JL, Fry JS, Collin P, et al. Protective effect of gluten free diet against development of lymphoma in dermatitis herpetiformis. *Br J Dermatol* 1996; 135: 363-367.