

## Linear IgA Disease and Chronic Active Hepatitis—a Coincidence or Not?

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Linear IgA disease (granular type) associated with chronic active hepatitis in a sixteen-year-old male patient is described. The diagnosis was established by clinical and histopathological findings supported by immunofluorescence studies. The immunofluorescence pattern (granular IgA deposits along the basement membrane, more pronounced at tips of papillae) showed much transition in dermatitis herpetiformis and also to a lesser extent in pemphigoid (linear IgG and IgM deposits along the basement membrane). Chronic active hepatitis as linear IgA disease are significantly correlated with HLA B8. This is the first report of the association of linear IgA disease and chronic active hepatitis. *Key words:* Linear IgA deposits; Dermatitis herpetiformis; HLA B8; Immunofluorescence. (Received January 29, 1985.)

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Linear IgA disease is an extremely itching skin disease very similar to dermatitis herpetiformis and/or pemphigoid. The major histocompatibility antigen HLA B8 is associated with linear IgA disease, but to a lesser degree than with dermatitis herpetiformis (1). It can be difficult to decide whether a patient has dermatitis herpetiformis, linear IgA disease or pemphigoid.

This report deals with an unusual combination of linear IgA disease of the granular type and chronic active hepatitis.

### CASE REPORT

In 1983, a sixteen-year-old boy presented himself at the out-patients department of Pediatric Dermatology with complaints of pruritic and painful blisters on the legs, arms, in the mouth and on the buttocks.

He was already known with the diagnosis chronic active (autoimmune) hepatitis made in 1981. Clinically there were no spider nevi, or erythema palmare at the skin; liver and spleen were not palpable below the costal margins. The diagnosis was based on laboratory investigations, which showed elevated serum levels of bilirubin, glutamic-oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT). Serologic tests for infectious, i.e. hepatitis A and B antigen or antibody were negative. Metabolic causes were ruled out. Antinuclear antibody and smooth muscle antibodies were positive; mitochondrial antibodies were negative repeatedly. Tests for lupus erythematosus cells (LE-cell test) and antibody to deoxyribonucleic acid (DNA) were negative (LE-cell only once weakly positive). Histopathological examination of a needle biopsy of the liver showed pronounced portal inflammatory infiltration, consisting of lymphocytes, histiocytes and plasma cells with slight periportal fibrosis and bile duct proliferation. Treatment consisted of oral prednisone in doses starting from 40 mg daily and gradually reduced to 10 mg per alternate day. Serum bilirubin and transaminase level returned to normal and a follow-up liver biopsy showed no activity of inflammation.

When he presented himself the patient was taking 20 mg prednisone on alternate days orally. At dermatological examination bullae, partly disrupted and crusted, were seen in the mouth, on the buttocks, the legs and arms. Topical therapy by applications of corticosteroid ointments was initiated. In several months the skin disease healed and disappeared for the most part. Half a year later a severe exacerbation was noted with scattered lesions all over the body (Fig. 1).



Fig. 1. Typical skin lesions on the patient's back.

Fig. 2. Subepidermal blister formations at the tips of papillae filled with neutrophils and nuclear debris. (Hematoxylin-Eosin, original magnifications  $\times 185$ .)

Histopathological studies of biopsies taken from the buttocks and back showed subepidermal blister formation at the tips of the papillae. The blisters revealed abscesses filled with neutrophils and nuclear debris and other necrotic material (Fig. 2). Perivascularly an infiltrate consisting of neutrophils and lymphocytes was found, mostly in the papillary dermis.

Immunofluorescence studies (from an erythematous border of a lesion) revealed granular IgA deposits, linearly arranged along the basement membrane but most pronounced at the tips of the papillae. In a lesser degree weak linearly arranged IgG and IgM deposits along the basement membrane were noted.

There were no complaints concerning diarrhoea or other signs of coeliac disease. Jejunal biopsy revealed no abnormalities. The patient was typed for HLA-A, B and DR. This revealed HLA-type A3, Aw24, B7, B8, DR4 and DR6 (DR3 negative).

Because of the extensive skin lesions the patient was admitted to the hospital for clinical evaluation and initiation of treatment with diaminodiphenylsulfone (Dapsone®) orally and a gluten-free diet. Dosage was started with 100 mg daily. In a few weeks the lesions disappeared. After some months the dosage had been lowered to 25 mg two times daily. He is still restricted to a glutenfree diet.

## COMMENT

In this patient the diagnosis of linear IgA disease of the granular type was established by clinical and histopathological findings supported by immunofluorescence studies (1). Atypical findings were linear IgG and IgM deposits at the epidermal-dermal junction, indicating some transition into pemphigoid. The good response and prompt improvement in symptoms and signs of disease activity after oral diaminodiphenylsulfone (Dapsone®) therapy support the diagnosis of linear IgA disease; oral lesions, maybe atypical, are not uncommon in this disorder. The fact that corticosteroids did not influence the course of the skin and oral mucous membrane lesions, is an indication against pemphigoid. Granular linear arranged deposits of IgA are in favour of linear IgA disease, but these deposits were more pronounced at the tips of papillae as in classic dermatitis herpetiformis, thus showing much transition in the latter disease.

Gluten plays a dominant role in the pathogenesis of dermatitis herpetiformis. Most patients, adults and children with this disease have some degree of jejunal villous atrophy, even if they have no or few symptoms of coeliac disease (2). The incidence of enteropathy is less frequent in linear IgA disease; but in this case there is much overlap with dermatitis herpetiformis. In view of this we prescribed our patient a gluten free diet, though the jejunal biopsy showed no abnormalities.

Several skin diseases are reported in patients with chronic active hepatitis. Lichen planus (3), pyoderma gangrenosum (4, 7), systemic scleroderma (8, 9) and cutaneous vasculitis (10) are included. Linear IgA disease (such as dermatitis herpetiformis) has never been described before in a patient with chronic active hepatitis. The pathogenesis of both diseases is unknown, but hypothetically a previous damage, due to unknown stimuli, of both hepatic elements on the one hand, skin and oral mucous membranes on the other hand, might have induced alterations in cellular immunity, secondarily leading to the autoimmune phenomena in certain predisposed individuals.

Therefore the finding of HLA B8 in this patient is very interesting. The two diseases chronic active hepatitis and linear IgA disease as well as dermatitis herpetiformis are significantly correlated with HLA B8 (1, 11). Because of this correlation the combination of chronic active hepatitis and these skin diseases could be expected to occur more than sporadically.

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