

## SHORT REPORTS

### **IgA Class Reticulin Antibodies in Dermatitis herpetiformis: A Good Indicator of Jejunal Damage**

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Hällström O, Reunala T. IgA class reticulin antibodies in dermatitis herpetiformis: a good indicator of jejunal damage. *Acta Derm Venereol (Stockh) 1985; 65: 330-332.*

Fifty patients with dermatitis herpetiformis (DH) were examined. Reticulin antibodies (RA) were found in 34 (68%) patients; 25 (73%) of them had IgA class RA, seven (21%) had IgA and IgG class RA, and two (6%) had IgG class RA. A good correlation was found between the occurrence of RA and the presence of jejunal villous atrophy. Twenty-four (96%) of the patients with subtotal villous atrophy and nine (82%) with partial villous atrophy had RA as compared to only one (7%) of the 14 patients with normal jejunal mucosa. Gluten-free diet treatment caused disappearance of RA in every patient, suggesting that RA measurements can also be used in DH for monitoring adherence to the diet treatment. *Key words: Reticulin antibodies; Jejunal villous atrophy; Gluten-free diet.* (Received October 29, 1984.)

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Performing jejunal biopsies on patients with dermatitis herpetiformis (DH) has revealed villous atrophy in about 3/4 of the patients, although only a few show gastro-intestinal symptoms (1). The search for serological methods to detect mucosal damage has included the measurement of reticulin antibodies (RA) using immunofluorescence techniques. However, before Ljunghall et al. (2) demonstrated that RA can be exclusively of IgA class, these antibodies did not seem to be of any particular diagnostic importance either in coeliac disease or DH (3-6). The purpose of the present study was to correlate the occurrence of RA in relation to mucosal damage and to study the effect of gluten-free diet (GFD) on these antibodies in patients with DH.

## PATIENTS AND METHODS

Fifty consecutive DH patients (30 males, 20 females; age range 12-61 years) were examined. The diagnosis was confirmed by showing granular IgA deposits in the skin. A jejunal biopsy was performed and the mucosal changes were graded as subtotal villous atrophy (SVA), partial villous atrophy (PVA) or normal mucosa as previously described (7). Serum samples were collected at the time of the jejunal biopsy and thereafter during the follow-up of the diet treatment (range 3 to 36 months). Thirty-one patients were followed on a GFD and two on a normal diet. The serum samples were stored at -20°C and were examined with indirect immunofluorescence for R<sub>1</sub> type RA by using unfixed cryostat sections of rat kidney and liver as antigen (4). The sera were screened at a dilution of 1/50 and 1/100 with polyvalent FITC-conjugated goat antihuman antiserum (Kallestad, Austin, Tx, USA). The positive sera were further examined with monospecific FITC-conjugated rabbit antihuman IgA and IgG antiserum (Dakopatts a/s, Copenhagen, Denmark) as previously described by Mäki et al. (8).

## RESULTS

RA were found in 34 (68%) patients. Twenty-four (96%) of the patients with SVA, nine (82%) of the patients with PVA and one (7%) with normal mucosa had RA (Fig. 1). RA

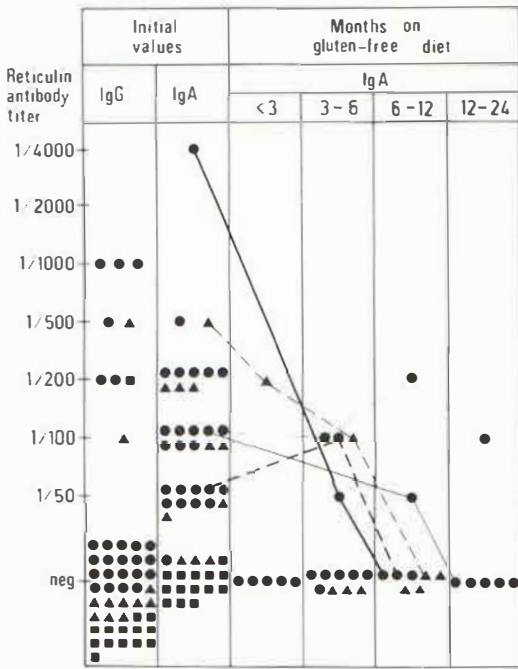


Fig. 1. Serum IgG and IgA class reticulin antibody titres in dermatitis herpetiformis patients with subtotal villous atrophy (●), with partial villous atrophy (▲) and with normal jejunal mucosa (■), and IgA class reticulin antibody titres after introduction of gluten-free diet in 27 patients with initially positive titres.

were mainly of IgA class and the titres ranged from 1/50 to 1/4000. Of the patients with positive RA, 73% had IgA class RA, 21% had IgA and IgG class RA and 6% had IgG class RA. The only patient with RA and normal mucosa had IgG RA but no IgA class antibodies.

During the follow-up period of two years, GFD treatment led to the disappearance of RA in all but one patient (Fig. 1). In this case the disease was very active and a decrease in the daily dapsone medication was not possible until three years on a GFD. After this period the first negative IgA RA samples were found. One patient whose IgA class RA became negative during a GFD returned to a normal diet, and after three months demonstrated RA again. The patient reverted to a GFD and RA fell to normal levels within two months. Two patients with normal mucosa and with negative RA continued on a normal diet but did not later demonstrate RA.

## DISCUSSION

RA have been found in increased frequency in coeliac disease and DH. Previous studies on DH have detected frequencies from 12% to 42% (2-6, 9). In the present study we found RA in 68% of our DH patients and confirmed the finding of Ljunghall et al. (2) that these antibodies can be exclusively of IgA class. That the overall frequency of RA was much higher than in previous studies is difficult to explain, especially when we used a rather high screening titre (1/50) and included only  $R_1$  type RA in the final analysis. Previously our method proved very sensitive and also specific in childhood coeliac disease suggesting that the lower figures found in other studies could be due to different antisera used in the RA determinations (8).

In the present study we showed that RA were especially evident in DH patients with villous atrophy; 96% of patients with SVA had RA and the frequency was as high as 82% in patients with PVA. In accordance with this, Lancaster-Smith et al. (5) and Ljunghall et

al. (9) also found RA often in DH patients with SVA, but in their series the frequency was only 40% as compared with 93% in our study. Most of our DH patients had IgA class RA and it seems evident that these antibodies are good markers for jejunal damage in DH but, as is also shown in the present study, a negative IgA RA titre does not exclusively rule out the presence of SVA.

The antigen to RA is not known, and the hypotheses of immune response to dietary reticulin, altered small bowel mucosal reticulin or cross-reactivity between reticulin and gliadin has been presented (5, 10). It is evident that RA are not specific for DH because these antibodies also occur in coeliac disease (5, 6, 8). However, the fact that the antibody class is mainly IgA suggests the gastro-intestinal origin of RA. In the present study GFD treatment caused a rapid disappearance of RA from the serum of DH patients, suggesting a relationship to mucosal recovery similar to that which has been found in coeliac disease by Mäki et al. (8). Control jejunal biopsies were not performed on DH patients, but indicating diminished disease activity all but two of the thirty-one patients on a GFD had decreased daily dapsone dose at the time of negative RA titres. One patient was an exception. In this case the patient had positive IgA RA titres after two years on a GFD and he could not decrease the dapsone dose. He insisted failures on adherence to GFD, and negative RA titres were not found until after three years on a GFD. In one patient we demonstrated fluctuating RA titres according to her adherence to GFD but the two patients with normal mucosa and negative RA who continued on a normal diet did not show positive RA titres. However, more patients and longer follow-up periods are necessary to confirm that changes from negative to positive RA do not occur in DH patients adhering to normal diets.

In conclusion, we found a high frequency of RA in DH patients with jejunal villous atrophy, showed that RA were mainly of IgA class and demonstrated that RA disappears rapidly during GFD treatment.

#### ACKNOWLEDGEMENTS

We are greatly indebted to Mrs Riitta Huttunen and Mrs Seija Kurjenlahti for skilful technical assistance. This study was supported by a grant from the Yrjö Jahnsson Foundation.

#### REFERENCES

1. Katz SI, Hall RP, Lawley TS, Strober W. Dermatitis herpetiformis: The skin and gut. *Ann Intern Med* 1980; 93: 857-874.
2. Ljunghall K, Scheynius A, Forsum U. Circulating reticulin antibodies of IgA class in dermatitis herpetiformis. *Br J Dermatol* 1979; 100: 173-176.
3. Seah PP, Fry L, Holborow EJ, Rossiter MA, Doe WF, Magalhaes AF, Hoffbrand AV. Antireticulin antibody; incidence and diagnostic significance. *Gut* 1973; 14: 311-315.
4. Rizzetto M, Doniach D. Types of "reticulin" antibodies detected in human sera by immunofluorescence. *J Clin Pathol* 1973; 26: 841-851.
5. Lancaster-Smith M, Kumar P, Clark ML, Marks R, Johnson GD. Antireticulin antibodies in dermatitis herpetiformis and coeliac disease. *Br J Dermatol* 1975; 92: 37-42.
6. Eterman KP, Feltkamp TEW. Antibodies to gluten and reticulin in gastrointestinal diseases. *Clin Exp Immunol* 1978; 31: 92-99.
7. Reunala T, Blomqvist K, Tarpila S, Halme H, Kangas K. Gluten-free diet in dermatitis herpetiformis. I. Clinical response of skin lesions in 81 patients. *Br J Dermatol* 1977; 97: 473-480.
8. Mäki M, Hällström O, Vesikari T, Visakorpi JK. Evaluation of a serum IgA-class reticulin antibody test for the detection of childhood celiac disease. *J Pediatrics* 1984; 105: 901-905.
9. Ljunghall K, Löf L, Grimelius L, Forsum U, Jonsson J, Scheynius A, Schilling W. Dermatitis herpetiformis: relation between circulating antibodies against reticulin and gluten, small-intestinal mucosal status and absorptive capacity. *Acta Derm Venereol (Stockh)* 1983; 63: 27-34.
10. Unsworth DJ, Johnson GD, Haffenden G, Fry L, Holborow EJ. Binding of wheat gliadin in vitro to reticulin in normal and dermatitis herpetiformis skin. *J Invest Dermatol* 1981; 76: 88-93.