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Simultaneous Occurrence of Diabetes Mellitus and Coeliac Disease

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Subtotal villous atrophy in the proximal jejunum was observed in six patients affected by juvenile diabetes. Introduction of gluten free diet invariably led to clinical improvement, in the four patients in whom also rebiopsy was performed the jejunal mucosa exhibited improvement. In all cases gluten sensitive enteropathy was diagnosed after the onset of diabetes. Marked stunting in growth, strikingly labile carbohydrate tolerance, pronounced proneness to hypoglycaemia or development of Mauriac's syndrome were the symptoms pointing to coeliac disease. Protracted diarrhoea was seen only in two patients, pronounced deceleration in weight development occurred in none of the six children. In four patients out of six the presence of both HLA B8 and DR3 antigens was demonstrated, in a fifth patient only DR3 was present; this suggests a common genetic background of the simultaneous occurrence of the two disorders. Untreated coeliac disease aggravates preexisting diabetes. The importance of early recognition of latent coeliac disease is stressed.

A close relationship between coeliac disease and diabetes is supported by the fact that certain HLA antigens show a much higher frequency in both disorders than in the general population. The simultaneous occurrence of the antigens B8 and DR3 is characteristic of both disorders while a high incidence of B15 and DR4 has been only observed in diabetes and these latter antigens exhibit no increased frequency in coeliac disease [9]. In a previous study we demonstrated a 32.8% occurrence of B8 in juvenile diabetes [1], while in coeliac disease B8 was demonstrated in 66.7, and DR3 in 77.8% of the cases [5].

This study has been performed to analyse the clinical features and establish the incidence of HLA antigens in six patients affected by both diabetes mellitus and coeliac disease.

Material and Methods

Of the patients two were boys and four were girls. Their age varied between 0.5 and 7 years at the onset of diabetes the diagnosis of which was based on the characteristic history, clinical and laboratory findings. At the time of the first jejunal biopsy their age ranged between 2.5 and 11.5 years. Coeliac disease was diagnosed on the basis of subtotal villous atrophy of the jejunal mucosa and clinical and mucosal improvement after introduction of a gluten-free diet. No rebiopsy has yet been performed in patients 5 and 6 because of shortness of time having elapsed since the first biopsy. In the morphometric clas-

TABLE I

Clinical data and HLA antigens of patients

Serial number of patient	Sex	Age in years at onset of diabetes	Age in years at time of 1st jejunal biopsy	Duration of treatment with gluten-free diet (years)	Height deficit in SD		Height corrected weight in SD deviating from the mean	
					before introduction of gluten-free diet	after	before introduction of gluten-free diet	after
1	girl	2.25	9.5	1.0	−1.9	−1.5	+0.1	+2.0
2	girl	1.5	2.5	7.75	−2.4	−4.0	−0.6	+3.5
3	boy	0.75	9.75	2.25	−2.75	−4.0	−0.6	+2.7
4	girl	7.0	11.5	1.0	−1.8	−1.6	+0.4	+0.9
5	boy	0.5	3.75	0.5	−6.0	−5.6	+0.6	+1.8
6	girl	5.5	5.75	0.5	−1.8	−2.3	−1.0	+1.8

sification of the jejunal mucosa the principles of Kuitunen et al [7] were applied. The antigens HLA A, B and C were determined by the standard NIH method, the DR antigens by the lymphocyte cytotoxicity micromethod of prolonged incubation time.

RESULTS

The findings are summed up in Table I. The onset of diabetes preceded the first manifestation of coeliac disease in all six patients. At that time the deficit in height of these patients ranged between −1.8 and −6.0 SD for age while their height corrected weight was normal. There was no improvement in age related height during the gluten-free diet; in fact, in two patients there was a further aggravation of the deficit. Weight gain ensued in all patients during the diet. The first symptom pointing to coeliac disease were diarrhoea and hypoglycaemia in one patient, only diarrhoea in one patient, appearance of Mauriac's syndrome in three patients and herpetiform dermatitis in one patient. In patient 3 diabetes and coeliac disease were accompanied by autoimmune haemolytic anaemia and chronic persistent hepatitis.

B8 was found in four and DR3 in the same four and in one additional patient. None of these five patients possessed B7. The presence of antigens B7 and DR2 is not characteristic of either diabetes or coeliac disease [1, 5]; these two antigens, quite conspicuously, were present in the patient affected by additional autoimmune haemolytic anaemia and chronic persistent hepatitis, but this patient had no B8 or DR3.

DISCUSSION

In the majority of our cases coeliac disease was suspected because of the appearance of non-enteral symptoms, impaired growth, labile carbohydrate metabolism and unexpected hypo-

having both diabetes and coeliac disease

Symptoms raising the possibility of malabsorption	Associated disorders	HLA antigens
Diarrhoea, Hypoglycaemia		A3, 29, B12, Bw35, Cw4, DR3, 5
Mauriac syndrome		A1, 3, B8, 12, DR, 4
Diarrhoea Mauriac syndrome	Autoimmune haemolytic anaemia, chronic persistent hepatitis	A3, 31, B7, Bw35, DR2, 5
None	Dermatitis herpetiformis	A1, 2, B8, 39, DR2, 3
Mauriac syndrome		A1, 2, B8, DR2, 3
Mauriac syndrome		A2, Aw24, B8, Bw50, DR3

glycaemia. In 13 patients out of 14 reported by Walsh et al [11] coeliac disease developed 5—15 years after the onset of diabetes.

Both coeliac disease and diabetes may be associated with autoimmune disorders, e.g. thyroiditis, rheumatoid arthritis, chronic persistent hepatitis, bronchial asthma or vitiligo [9, 10]. In one of our patients gluten sensitive enteropathy was accompanied by dermatitis herpetiformis. In all four similar cases of Holt and Blockweil [6] herpetiform dermatitis appeared after the onset of diabetes. In another patient of our material, diabetes was accompanied by chronic persistent hepatitis and autoimmune haemolytic anaemia.

The question emerges of the relationship between diabetes and coeliac disease. The significantly higher incidence of the same HLA antigens points to a close genetic relationship and may explain the association of the two disorders. Lecornu et al [8] observed decreased somatomedin levels in gluten sensitive enteropathy. This may partly explain the retarded growth of our patients. It is still obscure why the onset of diabetes precedes by so much time the recognition of coeliac disease. It may be anticipated that the onset of coeliac disease precedes the appearance of diabetes but it is not recognized because of the paucity of symptoms. Visacorpi [10] has made the interesting observation that diabetes develops in 4% of all patients affected by coeliac disease but in 10% of those in whom gluten sensitive enteropathy is diagnosed after completion of the second year of life. Among 24 diabetic patients simultaneously affected by coeliac disease the latter was diagnosed before the end of the second year of life in only two patients [2]. This is a curious finding since isolated coeliac disease is diagnosed during the first two years in the overwhelming majority of cases. From this it

may be anticipated that unrecognised, and therefore untreated, coeliac disease may predispose to a pathological carbohydrate metabolism. It is known that the gastric inhibitory peptide (GIP) released from the jejunum influences insulin secretion. Besterman et al [2] have shown in untreated coeliac patients that a test meal resulted in a significantly lower and flatter curve of plasma GIP resp. insulin than in healthy controls. Similar findings were obtained by Desjeux et al [4] in patients affected by villous atrophy of the jejunal mucosa, and Nutramigen administered directly into the duodenal lumen elicited a smaller increase in insulin levels than in control subjects with normal jejunal mucosa. Carson et al [3] found that gluten loading of coeliac patients provokes an increase in plasma glucagon. All these findings indicate that in coeliac disease, if untreated, the diabetic condition may be aggravated.

References

1. Barta L, Simon Z: Role of HLA and Bw15 in diabetic children. N Engl J Med 296;397, 1977
2. Besterman HS, Sarson DL, Johnston DI, Stewart JS, Guerin S, Bloom SR, Blackburn AM, Patel HR, Modigliani R, Mallinson CN: Gut-hormone profile in coeliac disease. Lancet 1:785, 1978
3. Carson DJ, Glasgow JFT, Buchanan KD, Sloan JM: Changes in N-terminal glucagon like immunocreativity and insulin during short term gluten childhood coeliac disease. Gut 22:554, 1981
4. Desjeux JF, Amar J, Dechamps I, Matthieu Ph, Lestradet H; Stimulation duodenale de la sécretion d'insuline. Arch Fr Pediatr 36 Suppl. 1:19, 1979
5. Gyódi É, Alföldy P, Kósnai I, Simon Z, Petrányi GG: HLA antigens and specific cell-mediated immunity in patient with coeliac disease. In: Joint report from "HLA-DR Intertransplant Workshop 79". eds Petrányi GG, Hollán RS. Tissue Antigens 16:18, 1980
6. Holt S, Blockweil J; Dermatitis herpetiformis and diabetes mellitus. Postgrad Med J 56:15, 1980
7. Kuitunen P, Kósnai I, Savilahti E: Morphometric study of the jejunal mucosa in various childhood enteropathies with special reference to intraepithelial lymphocytes. J Pediatr Gastroenterol Nutr 1:525, 1982
8. Lecornu M, David L, François R: Low serum somatomedin activity in coeliac disease. Helv Paediatr Acta 33:509, 1978
9. Shanahan F, McKenna R, McCarthy CF, Drury MI: Coeliac disease and diabetes mellitus: a study of 24 patients with HLA typing. Q J Med 51: 329, 1982
10. Visacorpi JK: Diabetes and coeliac disease. Lancet 2:1192, 1969
11. Walsh CH, Cooper BT, Wright AD, Malins JM, Cooke WT; Diabetes mellitus and coeliac disease: a clinical study. Q J Med 47:89, 1978

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