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ISLET CELL ANTIBODIES AND ANTITHYROID ANTIBODIES IN TYPE 1 DIABETICS

(islet cell antibodies/thyroid microsomal antibodies/type 1 diabetics)

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Islet cell antibodies (ICA) and thyroid microsomal antibodies (MCHA) were studied in many type 1 diabetics. The incidence of ICA and MCHA was 28.8% and 14.4%, respectively. It was significantly higher than in controls ($p<0.01$). The highest percentage (63.6%) of ICA-positive cases was found during the first year. This incidence gradually decreased as the clinical course proceeded. With regard to the incidence of MCHA, it was also high during the first year but did not decline significantly at 6-10 years after diagnosis. On the other hand, six cases had both ICA and MCHA. Three of these were of short duration and two were of long duration following the onset.

Since the first reporting of islet cell antibodies (ICA) in 1974 (1), (2), it has been suspected that type 1 diabetes mellitus might be an organ-specific autoimmune disorder (3). ICA were detected in 33-74% of recently diagnosed patients with type 1 diabetes and it was shown that the incidence of ICA decreased with the duration of the disease (4-8).

On the other hand, there are several reports (9-11) which show that the incidence of antithyroid antibodies (MCHA) in type 1 diabetes is high; however, few reports show the relationship between ICA and MCHA in type 1 diabetes. Therefore, the present study was done to define the incidence of ICA and MCHA in type 1 diabetes and to investigate the relationship between these

endocrine organ-specific autoantibodies and the duration of the disease.

SUBJECTS AND METHODS

Subjects; As table I shows, one hundred and forty-six diabetics participated in a childhood diabetes camp in the Kinki District. Serum samples were collected from these participants, who had insulin-dependent diabetes mellitus. As controls, four hundred and seventy-three non-diabetics were studied. These were normal elementary school children and junior and senior high school children. In these two groups, ICA and MCHA were studied.

Table I. NUMBER OF TYPE I DIABETICS AND NORMAL CONTROLS

	Men	Women	Total
Type 1 D.M.	65	81	146
Controls	240	233	473

Methods; Standard indirect immunofluorescence methods(1), (2) were used to detect ICA. As antigen, fresh human pancreas of blood group O were utilized. MCHA were measured by the tanned red cell hemagglutination method, using commercially available kit, Microsome Test.

RESULTS

Table II shows the incidence of ICA and MCHA in type 1 diabetics and in controls. Forty-two out of 146 diabetics, or 28.8%, and 2 out of 473 controls, or 0.4%, were positive for ICA. The incidence of ICA in type 1 diabetics was significantly higher ($p < 0.01$). On the other hand, the incidence of MCHA in patients and in controls was 14.4% and 0.8%, respectively. There was a significant difference between them ($p < 0.01$).

Fig. 1 shows the prevalence of ICA and MCHA based on duration from the onset of the diabetes. The prevalence of ICA during a period of less than one year was 63.6% and was the highest. This value decreased with duration, 28.2% at 1-5 years, 16.7% at 6-10 years and 0% at more than 10 years. On the other hand, the prevalence of MCHA was 22.7% at less than one year,

Table II. INCIDENCE OF ICA AND MCHA IN TYPE 1 DIABETICS AND NORMAL CONTROLS

	Type 1 D.M.	Controls
ICA (%)	42/146 (28.8)	2/473 (0.4)
MCHA (%)	21/146 (14.4)	4/473 (0.8)

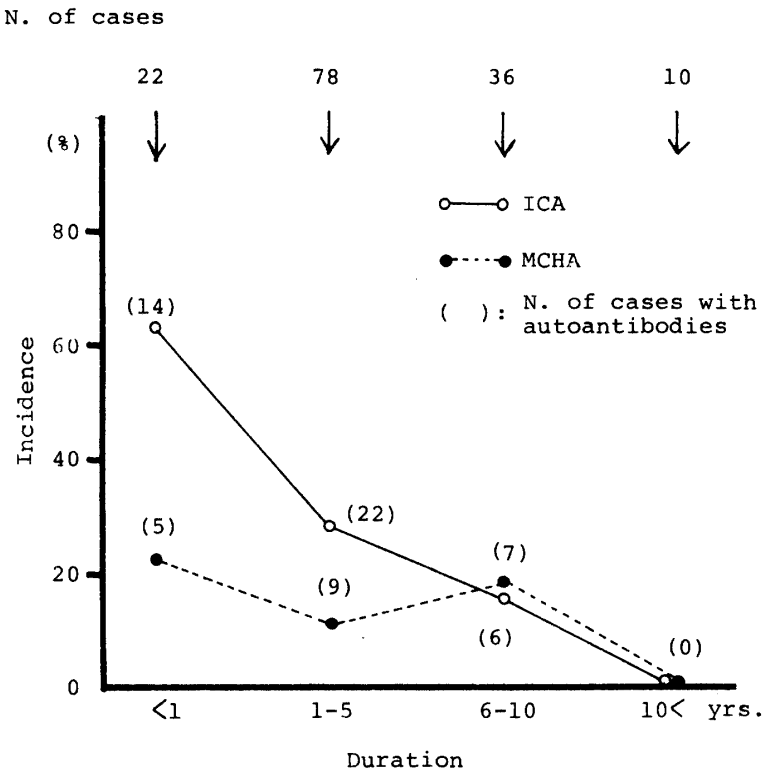

Fig. 1. Incidence of ICA and MCHA based on duration in type 1 diabetes

Table III. RELATIONSHIP BETWEEN INCIDENCE AND DURATION IN CASES WITH BOTH AUTOANTIBODIES

	<1	1-5	6-10
Number	3/14	1/22	2/6
Incidence(%)	21.4	4.5	33.3

11.5% at 1-5 years, 19.4% at 6-10 years and 0% at more than 10 years.

The relationship between incidence and duration of cases with both autoantibodies is shown in table III. It was 21.4% at

less than one year, 4.5% at 1-5 years and 33.3% during 6-10 years.

DISCUSSION

It is well known that the incidence of ICA in type 1 diabetics is significantly high. The incidence of ICA in Japanese type 1 diabetics was about the same as for those surveyed of Mexican-American origin (7); however, in a Caucasian survey (8), the incidence was higher than in our survey. The reason for this difference is unclear; however, it may be due to a difference in genetic factors or in race. It is now accepted that ICA is most common in newly diagnosed type 1 diabetes, the prevalence of the antibodies declining with the increasing duration of the diabetes. The present study was also consistent with some previous reports (4-8). Until now it was unknown why ICA should be highest in recent onsets of type 1 diabetes and why it should gradually decline with duration; however, an analogy may be noticed with the transient appearance of smooth muscle autoantibodies in viral infection (12), and this may give indirect support to the viral hypothesis in the pathogenesis of type 1 diabetes (13). Viral agents may induce acute beta-cell damage with acute type 1 diabetes, and an increased amount of beta-cell autoantigens may activate lymphocyte to a transient production of specific autoantibodies (5).

On the other hand, in MCHA, the number of positive cases in this study was higher than in the control subjects. There are few reports that demonstrate the relationship between the incidence of MCHA and the duration in type 1 diabetics. The transient presence of ICA in majority type 1 diabetics is in contrast to the time course of adrenal antibodies in idiopathic Addison's disease or of gastric parietal cell antibodies in pernicious anemia or of thyroid antibodies in Hashimoto's thyroiditis or in primary atrophic hypothyroidism, where the antibodies generally persist for many years (6). In most ICA positive cases with type 1 diabetes, the antibodies are transient over a period of months to a few years, while in the minority the antibodies persist for many years and these are the ones who have a particularly strong association with organ-specific autoimmune diseases and HLA-B8 (6). In this survey, it was found that the incidence of MCHA in patients with less than one year from the

onset was high but this value did not decline significantly at 6-10 years different from that in ICA in type 1 diabetics.

Six cases had both ICA and MCHA. Three out of them had a short duration and two had a long duration from the onset. The duration of the latter two cases was nine and ten years, respectively. Thus further study of the latter two cases, in which persist organ-specific autoantibodies, such as ICA and MCHA, for many years, will probably yield more information about the pathogenesis of typ 1 diabetes mellitus, namely "primary autoimmune" diabetes (14).

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