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RHEUMATOID FACTOR IN CHILDHOOD DIABETICS

(rheumatoid factor/childhood diabetics/autoantibodies)

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Several autoantibodies were detected in childhood diabetics who were type 1 diabetics. Rheumatoid factor (RF) was studied in these diabetics, in normal children and in one adult population. The incidence of RF in 104 type 1 diabetics was 1.9% and that in 473 normal children was 0.6%. The incidence in childhood diabetics was higher than that in control children; however, there was no statistical significance. In 1,229 adult persons, the incidence of RF was 3.8%. 21/567 male subjects (3.7%) and 26/662 female subjects (3.9%) were positive for RF. In the population survey, the incidence of RF gradually increased with aging after the age of 50.

Thyroid microsomal antibodies, pancreatic islet cell antibodies and antinuclear antibodies were studied in childhood diabetics and in normal children. The incidence of these three autoantibodies in 104 childhood diabetics was significantly higher than that in the control children.

Almost all patients with autoimmune disorders have autoantibodies. Since Bottazzo et al. (1) and MacCuish et al. (2) first reported pancreatic islet cell antibodies (ICA) in diabetic patients with autoimmune endocrinopathies, diabetes mellitus was suspected to be an organ-specific autoimmune disorder. There are several reports (3-5) which show that the incidence of antithyroid antibodies in insulin-dependent (type 1) (6) diabetics is high; however, few reports show the relationship between type 1 diabetes

mellitus and non-organ-specific autoantibodies. Therefore, we measured rheumatoid factor (RF) and antinuclear antibodies (ANA) as non-organ-specific autoantibodies. As controls, a group of normal children and one adult population were studied.

SUBJECTS AND METHODS

Subjects; One hundred and four childhood diabetics from six to seventeen years of age participated in a childhood diabetes summer camp in the Kinki District in 1982. Serum samples were obtained from these participants, who had insulin-dependent diabetes mellitus. As controls, four hundred and seventy-three non-diabetics from six to sixteen years of age were studied. These individuals were normal elementary school children, junior and senior high school children. In these two groups, we studied rheumatoid factor (RF), antinuclear antibodies (ANA), thyroid microsomal antibodies (MCHA) and pancreatic islet cell antibodies (ICA). In order to study the age-dependency of the incidence of RF, we checked for RF in one adult population. A mass screening in Daiwa Village, Shimane Prefecture, was performed in July, 1982. One thousand two hundred and twenty-nine subjects took part in this survey and we measured RF in this population.

Methods; To detect RF we used latex-fixation kits (RA test; RA 77 Eiken). Standard indirect immunofluorescence methods were used to study ANA and ICA. As antigen of ICA and ANA, we used fresh human pancreas of blood type O. In the previous report (7), we showed that the incidence and the staining patterns of ANA were much the same between human pancreas and human peripheral leucocytes (8) as antigen. Therefore, ICA and ANA were studied by standard indirect immunofluorescence methods at the same time. MCHA were measured by the tanned red cell hemagglutination method, using commercially available kits, Microsome Test (Fuzi Zoki K.K., Tokyo). We regard the titers of elevated circulating thyroid antibodies to be significant when over $1:2^7$ (128) dilutions (9).

RESULTS

Table I shows the incidence of RF in childhood diabetics and in normal children. Two of 104 cases with diabetes (1.9%) and 3/473 normal children (0.6%) were positive for RF. The incidence

Table I. INCIDENCE OF RHEUMATOID FACTOR IN CHILDHOOD DIABETICS AND IN NORMAL CHILDREN

	Childhood diabetics (104)	Normal children (473)
Positive	2	3
Incidence (%)	1.9	0.6

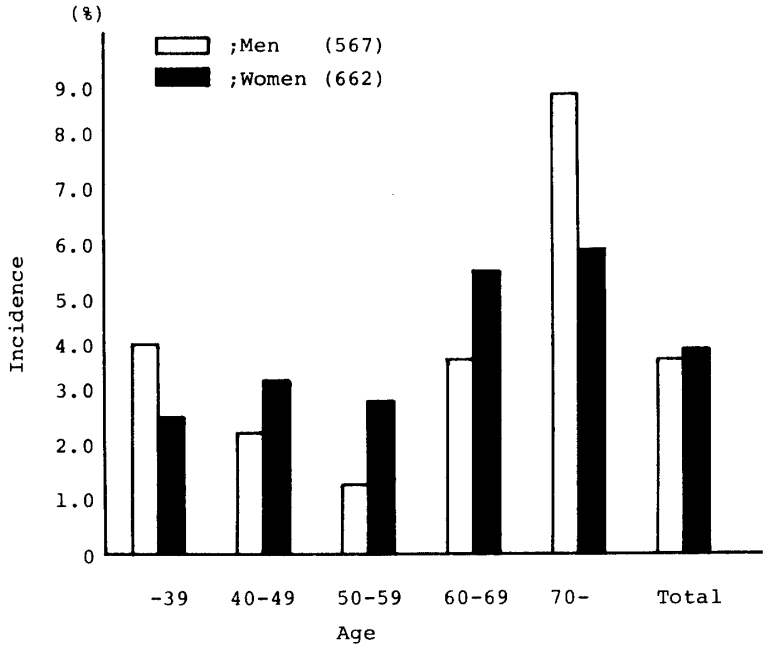

Fig. 1. Incidence of rheumatoid factor in relation to sex and age in one adult population.

in childhood diabetics was higher than in normal children; however there was no statistical significance. Two diabetics with RF suffered from neither rheumatoid arthritis nor liver disease. The duration from the onset of diabetes in these patients was two and six years, respectively.

Fig. 1 shows the incidence of RF in relation to sex and age in one adult population. 21/567 (3.7%) males and 26/662 (3.9%) females were positive. The incidence of RF in women was higher than in men and, in both sexes, the incidence gradually increased with aging after the age of 50.

In the survey of other autoantibodies in 104 childhood diabetics, the incidence of ICA, MCHA and ANA was 24.0%, 13.5% and 14.4%, respectively (Table II). The incidence of these autoantibodies in controls was 0.4%, 0.8% and 0.6%, respectively.

Table II. INCIDENCE OF ICA, MCHA AND ANA IN CHILDHOOD DIABETICS AND IN NORMAL CHILDREN

	Childhood diabetics(%)	Normal children(%)
ICA	24.0	0.4
MCHA	13.5	0.8
ANA	14.4	0.6

ICA ; Pancreatic islet cell antibodies
MCHA; Thyroid microsomal antibodies
ANA ; Antinuclear antibodies

In these three autoantibodies, the incidence in childhood diabetics was significantly higher than that in controls. No cases with RF had the other three autoantibodies.

DISCUSSION

Pancreatic islet cell antibodies (ICA) are detected frequently at an early stage after the onset of type 1 diabetes (10-12) and the incidence of ICA gradually decreases with a clinical course. However, the persistence of ICA in type 1 diabetes with other organ-specific autoantibodies was longer than that in diabetes without those autoantibodies. Rheumatoid factor (RF) is an age-depending (13) and non-organ-specific autoantibody. In our survey, the incidence of RF in normal children was lower than in the one adult population and gradually increased with aging after the age of 50. The incidence of RF in childhood diabetics was higher than in normal children; however, it was lower than in the one adult population. There were few reports regarding the relationship between the persistence of ICA and non-organ-specific autoantibodies. In this study, there were no cases with both ICA and RF. Therefore, there may be no correlation between the persistence of ICA and RF; however, we are interested in the occurrence, prognosis and complications of the two childhood diabetics with RF and of several diabetics and controls with both ICA and ANA as non-organ-specific autoantibodies.

In the recent paper (14), nonenzymatic glycosylation of serum IgG was presented. Glycosylated IgG in diabetics was shown. RF seems to represent an autoantibody to the Fc portion of altered or aggregated IgG. Therefore, if glycosylated IgG is a cause of

altered or aggregated IgG, RF in diabetics may be a result of abnormal glycosylation of IgG. In order to clarify this problem, we will study RF in many cases with diabetes.

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