failed to confirm the idea of reduced affinity for T₄ in TBG deficiency. This is the second reported case of TBG deficiency and growth retardation. The patient reported by Nikolai (1969) had been erroneously diagnosed as having isolated TSH deficiency and had failed to respond to several years of thyroid therapy. The true nature of his condition was subsequently revealed during a study of a family with X-linked TBG deficiency. As in our patient, no cause was found for his growth retardation.

Our patient differs, however, in having low but measurable levels of TBG and, as discussed above, probably represents a different mode of inheritance.

Summary

A 9-year-old boy was found to have constitutional growth retardation and thyroxine-binding globulin deficiency. He is the second child reported with this combination of defects and differs from the original patient in having low but not zero thyroxine-binding globulin levels.

He also illustrates the importance of assessing other parameters of thyroid function, such as the T₃ resin uptake, in children with low total thyroxine iodine (or protein bound iodine) levels, before embarking on thyroid replacement therapy.

References


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Growth Hormone Response to Oral Glucose Load in Untreated Diabetic Children

There have been contradictory reports of the plasma growth hormone levels to be found in children with untreated juvenile diabetes. Parker et al. (1968) and Drash et al. (1968) found normal fasting growth hormone levels after an oral glucose load. In contrast, Johansen and Hansen (1969) reported persistently high growth hormone levels fasting and throughout the day in untreated juvenile diabetics. In addition, Parker et al. (1968) found normal growth hormone responses during the arginine infusion test, while Drash et al. (1968) reported raised levels during this provocative test.

Patients and Methods

Twelve newly diagnosed diabetic children were investigated, before treatment with insulin was started. Five were girls and 7 were boys. Their ages ranged from 1 year 9 months to 14 years and none of the patients was overweight. All were fasted overnight (12-15 hours).

Control data were obtained from 9 non-obese, metabolically and endocrinologically normal children, with no family history of diabetes or coronary disease: 3 were girls and 6 were boys. Their ages were similar to the diabetic children, ranging from 2 years 7 months to 15 years 2 months. They were all on a normal diet. All were fasted overnight (12-15 hours) before blood collection.

They had been referred to the Endocrine Clinic because their parents were concerned about the child being much smaller than its sibs. All these children were on the 3rd to 10th centile for height and weight, while their sibs were on the 50th centile or above. Parent's permission was obtained from all cases before investigation. In the youngest child of the group, to avoid repeated venepunctures, an indwelling catheter was used.
Glucose tolerance test. After an overnight fast, oral glucose (1.75 g/kg body weight, up to a maximum dose of 100 g) was administered in 33% w/v solution in water flavoured with lemon juice. Venous blood was drawn from antecubital veins with minimal stasis. Blood samples were collected fasting and at ½, 1, 2, 3, 4 hours after the glucose load.

Blood glucose. Blood for glucose analysis was preserved by addition of fluoride oxalate and stored at 4 °C until analysed. All specimens were analysed within 48 hours of collection. Glucose was measured by an automated glucose oxidase method similar to that of Discombe (1963).

Plasma growth hormone. Heparinized plasma was stored at -18 °C until analysed. Growth hormone was measured by a double antibody radio-immunoassay procedure similar to that described by Hartog et al. (1964) using a British Medical Research Council growth hormone standard A preparation for standard reference solution. The level of sensitivity of the assay was approximately 1 ng/ml.

Analysis of data. Student’s t test was applied to determine the statistical significance of the means of the two groups of patients. The growth hormone response is considered as normal during peroral glucose tolerance test (PGTT) if levels of 7 ng/ml or more are found at any time during the test (Theodoridis et al., 1969).

Results

Blood glucose levels and means ±1 SD obtained from the diabetic children and the controls are shown in Tables I and II. The levels obtained from the diabetic children, as expected, were much higher throughout the test.

The mean fasting growth hormone level of the diabetic children (6.5 ng/ml) was higher than that
of the controls. This difference however, was not statistically significant. After oral glucose administration the mean growth hormone response of the diabetic children at 1, 2, 3, and 4 hours was lower than that of the control children; however, these differences were not statistically significant.

Only 7 out of the 12 children investigated with juvenile diabetes gave a normal growth hormone response of 7 ng/ml or more during the oral glucose tolerance test.

Discussion

The role of growth hormone (GH) in the pathogenesis of diabetes mellitus has been argued since Young (1937) first demonstrated the diabetogenic effect of anterior pituitary extracts. Our fasting GH results are in agreement with those of Parker et al. (1968) and Drash et al. (1968), but in disagreement with the results of Johansen and Hansen (1969).

The results presented here suggest that plasma GH concentrations in juvenile diabetes are not always normal, as suggested by Parker et al. (1968), or persistently raised, as suggested by Johansen and Hansen (1969). Only 7 out of 12 children investigated here gave a normal growth hormone response of 7 ng/ml or more during oral glucose tolerance test. 50% showed their maximum GH response during the fasting stage of the test, while in the normals this occurred 3 or 4 hours after the glucose load. It is possible that metabolic derangements and stress in the untreated diabetic children might have contributed to this phenomenon. The raised levels reported by Drash et al. (1968) after arginine infusion and the raised levels found during 24 hours by Johansen and Hansen (1969) may reflect increased GH secretion in the more severely ill untreated diabetic patient. We have previously reported normal GH levels in patients with mild diabetes, and raised levels in the more severely ill patients (Theodoridis et al., 1970). It appears that an increase of GH levels in untreated diabetic children is not an invariable finding, and that low levels can be found in some cases. This makes it unlikely that growth hormone is a causative factor in the pathogenesis of juvenile diabetes.

Summary

Blood glucose and plasma growth hormone levels were measured during peroral glucose tolerance test in twelve untreated diabetic children. Normal growth hormone responses were found in 7 out of 12 children investigated; in the remaining 5 the responses were subnormal.

We thank Professor C. M. Anderson for her support and the consultant staff of the Birmingham Children's Hospital for permission to study their patients.

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Maternal Histidinaemia

The hazards of maternal phenylketonuria are well documented (Stevenson and Huntley, 1967; Allan and Brown, 1968). A maternal blood phenylalanine above 15–20 mg/100 ml is almost invariably followed by impaired intelligence. Growth retardation, microcephaly, and abnormalities of the skeleton, heart, and eyes are also found. Next to phenylketonuria and homocystinuria, histidaemia is probably the most common inborn error of amino acid metabolism. We present here what we believe is the first case of maternal histidaemia to be recorded.

Case Report

The mother was aged 23 and the father 21 years at the birth of the patient. The father, a guardman, was healthy, but the mother had grand mal epilepsy from the age of 15 years. Her parents are alive and well, as are one brother and one sister. A second sister with spina bifida died at 7 weeks. A younger brother aged 16 years is mildly retarded (IQ 80) and at a school for epileptic children. He was found to have histidaemia, and when members of his family were examined the disorder...
Growth hormone response to oral glucose load in untreated diabetic children.
C G Theodoridis, G W Chance, B T Rudd and G A Brown

Arch Dis Child 1971 46: 117-119
doi: 10.1136/adc.46.245.117

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