A CASE OF GLYCOGEN STORAGE DISEASE TYPE III

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ABSTRACT

Glycogen storage diseases (GSD) are hereditary metabolic disorders leading to the storage in cells of glycogen of normal or abnormal structure.

We report a case of glycogen storage disease Type III which was diagnosed in October 1993.

Key Words: Glycogen storage disease

INTRODUCTION

The glycogen storage diseases (GSD) are hereditary metabolic disorders leading to the storage in cells of glycogen of normal or abnormal structure (1). The main types of hepatic GSD where storage is predominantly in the liver although not always restricted to this tissue are types I,III, IV and phosphorylase system deficiencies. We would like to report a case of GSD Type III which was diagnosed in October 1993.

CASE REPORT

N.T. a 16 year old female patient presented to the Marmara University, School of Medicine Hospital, Gastroenterology Division in October 1993 complaining of easy fatigue and growth retardation. She described convulsions occurring once or twice a month starting in infancy and continuing up until two years ago. She was delivered by normal spontaneous delivery with an unremarkable neonatal period. There was limited capacity to walk moderate distances because of easy fatigability starting in early childhood. She tolerated hunger badly describing a state of increased perspiration accompained by irrational behaviour on fasting. She had never menstruated. She did not continue her education after primary school and her family stated that physically she has always been less developed than her friends.

Scrutiny of her family history revealed that she had one sister and two brothers one of whom had very similar symptoms and had died at the age of 11 years old. The exact cause of her death was unknown by the family. Her mother also had frequent convulsions until late in puberty. The other sister and the brother were apparently healthy. Our patient was not on any medication currently although she had been prescribed anticonvulsant therapy in the past but was uncompliant to the therapy.

On physical examination the patient appeared much younger than her age with a short stature of 150 cms but did not have infantile body ratios. She had hypertelorism and the anteroposterior diameter of her chest was increased. On examination of the cardiovascular system second heart sound was slightly more prominent over the aortic area and there was a harsh 2/6 systolic murmur over the pulmonary area radiating downward towards the left side of the sternum. There was a nontender hepatomegaly of 17 cms total length. The liver was smooth with sharply demarcated edges on palpation. There was no splenomegaly. Her breast development was noted to start symmetrically as well as pubic and axillary telarche.

Initial laboratory investigation revealed a normocytic normochromic anaemia with a haemoglobin of 10.8 g/dl, haematocrit of 33.6%, mean corpuscular volume of 86.4, polymorphe nuclear leucocyte count of 5300/mm^3, platelet count of 247.000/mm^3; prothrombin and plasma thromboplastin times were normal as was the bleeding time. Blood biochemistry revealed a slight increase in the alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase as well as LDH but was otherwise normal. Urinalysis was also normal. On P-A chest X-ray a prominent pulmonary conus was noted but no other pathology was detected. The ECG revealed signs of left ventricular hyp rtrophy.

X-ray of wrist and hands was consistent with a bone age of 10 years old (2). An echocardiography was performed and showed conscentric hypertrophy of the left ventricle. Ultrasound examination of her abdomen and pelvis did not reveal any abnormal finding except hepatomegaly with smooth contours and homogenous parenchyma. The internal sexual organs were fully developed. Electromyography findings were consistent with axonal type neuropathy and the EEG was normal. We performed a prolonged oral glucose tolerance test which revealed symptomatic hypoglycaemia at 4.5 hours with a measured blood glucose level of 50 mg/dl. By this stage we had reached a preliminary diagnosis of glycogen storage disease but required specific liver and muscle tissue enzyme assays to make a definitive diagnosis. We therefore performed liver and muscle biopsies which were frozen and stored in liquid nitrogen and were transported to a specialized laboratory in Israel experienced in these assays (Pediatric Laboratory, Soroka Medical Center, Beer Sheva, Israel). Both specimens were assessed for their glycogen content according to the method determined by Johnson J.A., Nash J.D., and Fusaro R.M (3).

Amylo 1-6 glucosidase (debranching enzyme) activity was then determined according to Gutman et al (unpublished results) and both specimens were found to be deficient in amylo 1-6 glucosidase activity. The assays revealed 0% release of C14 glucose from radioactive glycogen / 0.3 mg protein/h in both the liver and the muscle specimens of the patient as compared to control specimens which showed 77% and 83% release of C14 respectively. On the basis of these results we were able to make a definitive diagnosis of GSD Type III where there is a total deficiency of both liver and muscle debranching enzyme, amylo 1-6 glucosidase.

DISCUSSION

GSD Type III is a rare autosomal recessive inborn metabolic disorder and is also known as limit dextrinosis, debrancher glycogenosis, Cori disease and Forbes disease (1).

With deficiency of debranching enzyme glycogen can be degraded only up to branch points in the molecule. Decreased production of glucose from the liver leads to hypoglycaemia which is largely compensated for by increased gluconeogenesis. Excessive glycogen accumulation occurs in liver, muscle and heart in various combinations. A number of patients with GSD Type III also have muscle weakness. In this group of patients rapid walking and climbing results in increased weakness without cramps. In some patients, however, there may be progressive myopathy (4). Marked hepatomegaly and growth failure are common although, spontaneous improvement occurs at puberty. Electrocardiographic abnormalities and moderate cardiomegaly are usually encountered. The serum concentrations of uric acid, lactate, ketones and lipids are normal which distinguishes this syndrome from GSD Type I. The patients with GSD Type III have only marginally impaired mental development and the prognosis changes from fair to good (1).

The diagnosis of the disorder is generally reached by liver and muscle biopsies in which debranching enzyme activity can be measured. It has been reported that peripheral tissue can also be reliably used for diagnosis. In this relatively novel approach debranching enzyme activity in erythrocytes (or leucocytes or fibroblasts) is measured. A normal activity however, does not exclude diagnosis. If a decreased activity is encountered, the diagnosis does not need to be confirmed by a liver biopsy and enzyme studies in liver and muscle biopsies may be restricted to patients with localized or atypical expression of the disease (5). In our case, since we were not able to study enzyme activity in peripheral tissues we had to perform liver and muscle biopsies.

Therapeutic approach to this syndrome still remains empirical. Nocturnal enteral feeding is used to overcome hypoglycaemia during prolonged fasting at night. Borowitz and Greene found that growth and transaminase and blood glucose levels were positively influenced by a high starch diet with a standard protein intake (6). Oral cornstarch therapy has also been reported to be effective in a few patients with GSD Type III (6, 7). This approach was

employed by Gremsa et al. (8) in three children with GSD Type III with decreased growth velocity, asymptomatic hypoglycaemia, hepatomegaly and elevated serum aminotransferase levels, and was found to be associated with maintenance of normoglycaemia, increased growth velocity and decreased serum aminotransferase concentrations in these three children (8).

We recommended our patient to have snacks between meals and to include cornstarch in her diet in order to overcome frequent attacks of hypoglycaemia and help to accelerate her growth and discharged her.

GSD Type III is an extremely rare disease and therefore controled studies of treatment are virtually impossible to conduct and for the foreseable future treatment will be empirical.

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