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TYPE I GLYCOGENOSIS WITH RENAL TUBULAR DYSFUNCTION (Presentation of Two Cases)*

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Two patients with hepatic glycogenosis associated with Fanconi syndrome are presented. Both patients were treated with a neutral phosphorus solution, an oral alkaline solution, cholecalciferol and uncooked cornstarch. The proximal renal tubular functions were corrected in the patient who used cornstarch properly, which may indicate a causal relationship between Fanconi syndrome and glycogenosis. *Key words: glycogenosis, Fanconi syndrome.*

The association of Type I glycogenosis with proximal renal tubular dysfunction (Fanconi syndrome) is known to be a rare entity [1,2]. Of the 171 cases of gycogenosis studied in our unit, only two cases of proximal renal tubular dysfunction were found. Since this type of association is rarely seen, we decided to present the clinical and laboratory findings of these two cases.

Case Reports

Case 1

A two-year-old boy born to consanguineous parents was admitted to the hospital for evaluation of growth retardation. Physical examination revealed a child with a doll-like face. His height was 72 cm (below the 3rd percentile) and his weight was 10 kg (below the 3rd percentile). He had a protuberant abdomen and the liver was palpable four cm below the right costal margin. Clinical findings of rickets were present.

Laboratory studies revealed normal hemoglobin and leukocyte counts but the results of urinalysis showed glucosuria and proteinuria. Generalized aminoaciduria, hypocalcemia (6.6 mg/dl), hypophosphatemia (1.4 mg/dl), elevated alkaline

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phosphatase level (18.8 BU, control < 14 BU), hypoglycemia (46 mg/dl), elevated blood lactate level (19.6 mg/dl) and metabolic acidosis (HCO_3^- 13.98 mEq/L) were detected. Hyperlipidemia (1180) mg/dl) and hypercholesterolemia (260 mg/dl) were present. Plasma urea, uric acid, alanine aminotransferase (ALT), aspartate aminotransferase (AST), electrolytes, protein, and albumin values were all within the normal range. X-ray of the wrist showed active rickets. A liver biopsy revealed swollen and vacuolated hepatocytes and minimal fibrosis in the portal areas, consistent with glycogenosis.

The patient was treated with a neutral phosphorus solution, an oral alkaline solution, cholecalciferol (5000 U/day) and uncooked cornstarch (2 g/kg/meal). Six years later, his liver was plapable 10 cm below the costal margin. Aminoaciduria, glucosuria, proteinuria and rickets were no longer present and the exhibited accelerated growth.

Case 2

A four-month-old girl, the product of a consanguineous marriage, was admitted to the hospital for evaluation of growth retardation. Physical examination, revealed that all anthropometric measurements were below the 3rd percentile (height 56 cm, weight 4100 g). She had a doll-like face and protuberant abdomen. The liver, had a soft consistency, and was palpable 3 cm below the right costal margin. She exhibited clinical manifestations of rickets.

Laboratory data revealed that the hemoglobin and leukocyte counts were normal. Glucosuria, aminoaciduria and a trace of proteinuria were present. Calcium was 10.2 mg/dl, phosphorus 2.4 mg/dl and alkaline phosphatase was found to be elevated (627 IU/L). Hypoglycemia (25 mg/dl) an elevated blood lactate level (71 mg/dl) and metabolic acidosis HCO_3^- 16.34 mEq/L) were noted. Total lipid (840 mg/dl) and cholesterol (242 mg/dl) levels were elevated. Plasma urea, uric acid, ALT, AST, electrolytes, protein, and albumin, however, were all within the normal range. Wrist X-ray showed active rickets. A liver biopsy revealed palely, stained, swollen hepatocytes, compatible with glycogenosis.

She was given a neutral phosphorus solution, oral alkaline solution, cholecalciferol (10000 U/day) and an uncooked cornstarch (2 g/kg/meal) diet. But she did not comply with the therapeutic measures. Therefore, persistent aminoaciduria, hypophosphatemic rickets and metabolic acidosis did not change in four years. Her liver became progressively enlarged, and was palpable 9 cm below the right costal margin. Her growth was significantly retarded.

Discussion

Both our patients had marked hepatomegaly, a doll-like face, fasting hypoglycemia, metabolic acidosis, hyperlactemia and hyperlipidemia. Although enzyme

studies could not be performed to determine the type of glycogenosis, clinical and laboratory findings were compatible with Type I glycogenosis[3]. In addition to glycogenosis, typical findings of Fanconi syndrome characterized by glucosuria, generalized aminoaciduria, metabolic acidosis and hypophosphatemic rickets were present in these two cases. Although this association has been known since Fanconi and Bickel's first reported such a combination[4], we diagnosed only two cases with this combination out of 171 cases of glycogenosis over the past fifteen years.

Nephropathy characterized by glomerulosclerosis and proteinuria without glucosuria and aminoaciduria has ben described in older patients with Type I glycogenosis[5]. However our patients were in the pediatric age group. Renal biopsies, were not available in our patients. Since they had glucosuria and aminoaciduria in addition to proteinuria, we believed the underlying pathology was most likely different from that resulting in glomerulosclerosis. Although rickets may cause generalized aminoaciduria, our patients also had proteinuria and glucosuria which are not expected in rickets.

Case I, who had used the therapy properly, showed signs of improvement in tubular dysfunction, and also in the amount of proteinuria. Chen et al[2] also reported improvement in tubular dysfunction of a patient with Type I glycogenosis who had received intensive cornstarch therpy. They suggested that the low incidence of Fanconi syndrome found in patients with glycogenosis may be due to prompt initiation of a cornstarch diet.

Cornstarch therapy was also found to be useful in controlling the clinical and metabolic manifestations of Type I glycogenosis and researchers have suggested that it be used as therapy at an early age[2,6].

Although Fanconi syndrome has been known to occur in association with various types of glycogenosis[1,2,7-11], the underlying defect of this metabolic association is unknown. Some of these patients also have a defective galactose metabolism[9-11]. The association of Fanconi syndrome and abnormal galactose metabolism in glycogenosis has been explained by a mitochondiral defect[9].

We conclude that tubular dysfunction occurs rarely in hepatic glycogenosis and therapy consisting of uncooked cornstarch may be effective not only in the controlling the clinical and biochemical abnormalities of the disease, but may also control proximal renal tubular dysfunction. Improvement in proximal renal tubular dysfunction was observed in one of our patients after initiation of uncooked cornstarch therapy with glycogenosis which may indicate that there is a causal relationship between hepatic glycogenosis and Franconi syndrome rather than it being a coincidental finding.

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