Pathological Case of the Month

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A 13-YEAR-OLD girl was seen for complaints of abdominal distention and inability to walk. Her abdominal distention began in infancy, and her parents noticed that her legs bowed when she walked. In the last few months, she became unable to walk because of pain. On physical examination, her height was 95 cm (<3rd percentile) and her weight was 19 kg (<3rd percentile). Her liver was palpable 8 cm below the costal margin. Enlargement in her wrist and ankle joints and bowing of her legs were noted. She could not stand up without help (Figure 1). Radiographs of the extremities revealed severe rickets (Figure 2). Results of liver needle aspiration biopsy showed glycogen accumulation in the hepatocytes (Figure 3).

Her serum calcium levels were 2.25 mmol/L (9.0 mg/dL); phosphorus levels, 0.52 mmol/L (reference range, 1.25-2.10 mmol/L); alkaline phosphatase levels, 2464 U/L (reference value, 0.85%); uric acid levels, 0.03 mmol/L (reference range, 0.12-0.42 mmol/L); and cholesterol levels, 6.88 mmol/L (266 mg/dL) (reference range, 0–5.17 mmol/L [0–200 mg/dL].) Her urine showed 4+ glucosuria, 4+ proteinuria, and generalized aminoaciduria. Tubular phosphate reabsorption was calculated as 52% (reference value, >85%).

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Diagnosis and Discussion

Glycogen Storage Disease With Renal Tubular Dysfunction (Type XI, Fanconi-Bickel Syndrome)

F anconi-Bickel syndrome is a rare type of glyco-
gen storage disease first described by Fanconi and Bickel in 1949.1 It is an autosomal recessive dis-
ease for which an enzymatic defect has not yet been iden-
tified. The disease is characterized by the association of a large liver with massive glycogen accumulation and se-
vere renal tubular dysfunction.2 Renal Fanconi syn-
drome, characterized by urinary loss of phosphate, amino acids, glucose, and bicarbonate, results in severe hypo-
phosphatemic rickets and markedly stunted growth.3

Affected children usually present in the first year of life with failure to thrive. A protuberant abdomen with hepato-
megaly and enlarged kidneys are noticeable by age 2 years.4 These children develop severe hypophospha-
temic rickets early in life unless they receive oral phos-
phate supplementation. Orally administering phos-
phate alone to the extent necessary for correction of hypophosphatemia may heal the florid rickets, but ade-
quate growth is not attained. At adolescence these chil-
dren have an extremely short stature. After puberty the hepatomegaly may recede although hepatic glycogen concentration remains increased. Some patients have additional muscular involvement.5

Proximal renal tubular dysfunction with glucos-
uria, phosphaturia, generalized aminoaciduria, bicar-
bonate wasting, and hypophosphatemia are characteris-
tic findings. Serum alkaline phosphatase levels are
increased, and there are radiological findings of rickets. Mild fasting hypoglycemia and hyperlipidemia may be present, but these are not consistent findings. Uric acid levels are low. Liver transaminases and plasma lactate are
usually normal. Results of tissue biopsy show marked ac-
cumulation of glycogen in the hepatocytes and prox-
imal renal tubular cells.

There is no known enzyme deficiency. All mea-
sured hepatic glycolytic enzyme activities are normal. Oral galactose tolerance tests typically show galactose intolerance, suggesting an impairment of galactose metabo-
lism. Defective galactose oxidation can be demon-
strated in vitro in fresh minced liver tissue and fibroblasts, despite normal activities of hepatic galactokinase, uridy-
lytransferase, and uridyl di phospho–glucose 4-epimer-
ase in homogenates of frozen liver.6

There is no specific therapy. Symptomatic replace-
ment of water, electrolytes, vitamin D, and phosphate, re-
striction of galactose intake, and adequate caloric intake
may improve growth. Long-term prognosis is not known.

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REFERENCES

1. Fanconi G, Bickel H. Die chronishe aminoacidurie (Aminosaure-diabetes oder ne-
phrotisch-glucosurisher zwergwuchs) bei der glykogenese und der cyst-
3. Kliegman RM. Defects in metabolism of carbohydrates. In: Behrman RE, Klieg-
5. Hurvitz H, Elpeleg ON, Barash V, et al. Glycogen storage disease, Fanconi ne-
6. Brivet M, Moatti N, Coriat A, Lemormier A, Odievre M. Defective galactose oxida-
tion in a patient with glycogen storage disease and Fanconi syndrome. Pedi-