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CASE REPORT

Hepatic metabolites and uric acid excretion in fructose-1,6-diphosphatase deficiency

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There have been a small number of patients reported with inherited disorders of gluconeogenesis. We studied a female patient with fructose-1,6-diphosphatase (FDPase; EC 3.1.3.11) deficiency (McKusick 22970), born of consanguineous parents (inbreeding coefficient 1/32). Since 4 months of age, she presented with many episodes of ketosis, lactic acidosis and hypoglycaemia, which, on two occasions, were accompanied by seizures. Blood uric acid was abnormally high (0.485 mmol L^{-1}) but below normal in urine (1.85 mmol g^{-1} creatinine). An open liver biopsy was performed on the patient under ether–nitrous oxide anaesthesia after an overnight fast, receiving 10% glucose i.v. solution. The sample was frozen in liquid nitrogen five seconds after its excision. FDPase activity was below the level of detection of the assay. Hepatic pyruvate kinase, total and active pyruvate dehydrogenase, phosphoenolpyruvate carboxykinase, glycogen phosphorylase, amylo-1,6-glucosidase ('debrancher'), acid α-glucosidase, glucose-6-phosphatase, fructose-1-phosphate aldolase and fructose-1,6-diphosphate aldolase were within normal limits. Liver metabolites were measured as described by DeVivo *et al.*, 1977. Compared with rat and with a human 'control' (a patient with partial deficiency of hepatic phosphorylase and debrancher enzymes), glucose was increased in our patient – probably due to its parenteral administration – as well as pyruvate and lactate, with a lactate:pyruvate ratio only moderately raised. Several Krebs cycle intermediates and the adenine nucleotides were greatly augmented (in mmol kg^{-1} wet tissue; citrate 0.708, α-ketoglutarate 0.696, malate 1.92, ATP 5.69 and AMP 3.00). Only in another patient with FDPase deficiency have hepatic intermediates been reported (Pagliara *et al.*, 1972). They were measured in that patient and in ours at the same laboratory, using the same procedures. However, glucose, pyruvate, lactate, Krebs cycle intermediates and adenine nucleotides were much higher in our patient, the lactate/pyruvate ratio being lower, near the normal range. Consequently, the significance of these obeservations is difficult to assess. This is compounded by the fact that normal levels in human liver are not adequately known.

A fructose tolerance test (FTT) was performed, giving fructose 0.25 g kg^{-1} as an i.v. solution after a 10 h fast. During the FTT, blood glucose and inorganic phosphate decreased markedly while lactate and uric acid increased; the latter

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from 0.327 mmol L^{-1} before to 0.506 after the load. Urinary uric acid was 0.302 mmol $(120\,ml)^{-1}$ (5.53 mmol g^{-1} creatinine) in the 4 h before and 0.033 mmol $(70\,ml)^{-1}$ (1.96 mmol g^{-1} creatinine) in the 4 h following fructose infusion. Our results of reduced urate excretion in a 24 h urine collection and of a sharp decrease in its renal clearance during the FTT suggest that, besides an increased uric acid production, there is an additional renal mechanism for uric acid elevation in blood, possibly caused by competitive inhibition of renal tubular urate secretion by lactate and ketone bodies.

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REFERENCES

DeVivo, D. C., Haymond, M. W., Leckie, M. P., Bussman, Y. L., McDougal, D. B. Jr. and Pagliara, A. S. The clinical and biochemical implications of pyruvate carboxylase deficiency. *J. Clin. Endocrinol. Metab.* 45 (1977) 1281–1296

Pagliara, A. S., Karl, I. E., Keating, J. P., Brown, B. I. and Kipnis, D. M. Hepatic fructose-1,6-diphosphatase deficiency. *J. Clin. Invest.* 51 (1972) 2115–2123

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CASE REPORT

Glyceroluria with adrenocortical insufficiency, developmental delay and early death

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Glycerol kinase deficiency (McKusick 30703) may present in infancy with massive glyceroluria, adrenocortical insufficiency, myopathy and developmental delay (Guggenheim *et al.*, 1980). We here report the presentation and diagnosis of a new case of this severe disorder. The case has been briefly mentioned elsewhere (Søvik *et al.*, 1986).

The male infant was born by forceps delivery following pre-eclampsia after 41 weeks of pregnancy. The boy was the first child of young and unrelated parents. The father was a drug abuser, but the mother denied any abuse of drugs or alcohol during the pregnancy. Shortly after birth, the infant (3840 g, 54 cm) was transferred to the neonatal intensive care unit, due to vomiting. Clinical examination revealed slightly dysplastic external ears, small palpebral fissures, hypognathia and reduced abduction of the hips. Chromosome analysis showed male karyotype XY. Low serum sodium (130 mmol/L) and high potassium (7.7 mmol/L) suggested adrenocortical insufficiency, and replacement therapy was started. The vomiting stopped

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