Question: 167

You are called urgently to the nursery to evaluate a newborn who exhibits possible seizures. The baby is a 2-day-old boy who has been healthy and breastfeeding well. Over the past 12 hours, he has become increasingly difficult to arouse and now is refusing to feed. Physical examination reveals a normally formed baby who has hypertonia and obtundation and responds weakly to painful stimuli. A bedside glucose determination is 60 mg/dL (3.3 mmol/L), and vital signs are stable. While arranging for further laboratory testing and transfer to the neonatal intensive care unit, you observe a generalized seizure.

Of the following, this presentation is MOST suggestive of a

A. fatty acid oxidation defect
B. glycogen storage disease
C. lipid storage disease
D. lysosomal storage disease
E. urea cycle defect
The signs of a progressive encephalopathy within days after birth described for the term newborn in the vignette could indicate the presence of a urea cycle defect (ornithine transcarbamylase deficiency, citrullinemia, carbamyl phosphate synthetase deficiency, argininosuccinic aciduria, or argininemia). The urea cycle, which is the primary pathway for the excretion of nitrogenous waste, contains five enzymes, any of which may be deficient. The first symptoms of this group of inborn errors of metabolism include poor feeding and lethargy that, if untreated, progress to coma. At the first signs of obtundation, it is important to measure plasma ammonia concentrations as part of a metabolic evaluation. If the infant does not display acidosis but does exhibit hyperammonemia, a urea cycle defect is likely. Amino acids should be measured for infants who have plasma ammonia concentrations greater than 210 mcg/dL (150 mcmol/L) to aid in diagnosis. Strong evidence suggests that the extent of neurologic damage in survivors is related directly to the duration of hyperammonemonic coma, so treatment should be initiated promptly. Treatment is aimed at removing ammonia from the blood and may include hemodialysis and arginine infusion. Initially, protein is removed from the diet, but it must be replaced slowly and limited thereafter.

Fatty acid oxidation defects typically present with hypoglycemia and metabolic acidosis with increased anion gap. If left untreated, hyperammonemia can occur. The normal bedside glucose determination reported for the infant in the vignette makes this diagnosis unlikely, although serum glucose also should be measured.

Glycogen storage diseases can present from days to years after birth. The major presenting features include hypoglycemia and hepatomegaly in type I and hepatomegaly in type III. Type II (Pompe disease) is a lysosomal storage disorder and may present with poor feeding and failure to thrive followed by progressive cardiac failure.

The lipid and lysosomal storage diseases typically do not present with early-onset obtundation. Clinical features include neurodegeneration and organomegaly. The findings of coarsening of the facial features or cherry red macular spots (as seen in GM1 gangliosidosis and Tay-Sachs disease, for example) may be helpful in diagnosing these conditions.

References:


