Case Report

CEREBRAL EDEMA: A RARE COMPLICATION IN GALACTOSEMIA

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ABSTRACT

A 34 day-old girl infant was admitted for poor feeding and cholestasis. She had a bulging fontanelle, with no evidence of intracranial infection or hemorrhage. Investigations demonstrated that she had galactosemia. Computed tomographic scans demonstrated the presence of diffuse cerebral edema. After treatment the edema resolved.

Keywords: Galactosemia, cerebral edema, increased intracranial pressure.

INTRODUCTION

There are three distinct disorders of galactose metabolism. These disorders are transmitted by autosomal recessive inheritance and are expressed as a cellular deficiency of one of three enzymes in the metabolic pathway through which galactose is converted to glucose, including galactose 1-phosphate uridyl transferase, galactokinase and uridine diphosphate galactose-4-epimerase. Each enzymatic defect associated with galactosemia results in a distinctive clinical presentation. Clinical manifestations of toxicity in transferase deficiency galactosemia include jaundice, hepatomegaly, vomiting, hypoglycemia, convulsion, lethargy, aminoaciduria, cataracts, hepatic cirrhosis, mental retardation, and increased risk for Escherichia coli sepsis.\(^1\)

Galactokinase deficiency results primarily in cataract formation.\(^2\) In most cases of UDP galactose-4-epimerase deficiency, the defect is limited to erythrocytes and leukocytes, thus there are no clinical or laboratory manifestations of galactosemia.\(^3\) In a variant form a defect is more generalized and results in a severe clinical presentation resembling the classic form of the disease.\(^4\)

Treatment has remained essentially at minimizing galactose intake in affected individuals.

Increased intracranial pressure in patients with classic galactosemia was previously mentioned.\(^6,7\) In the literature only Belman et al.\(^8\) reported a neonate with signs of increased intracranial pressure demonstrated by computed tomographic brain scans (CT). The results of a metabolic screening program demonstrated transferase deficiency. Our article is about a 34 day old infant with poor feeding and cholestasis and signs of increased intracranial pressure without evidence of CNS infection or hemorrhage. The results of investigations for cholestasis demonstrated that she has transferase deficiency. Serial CTs showed a dramatic decline in cerebral edema accompanied by no deficit in developmental status.

CASE REPORT

A 34 day old girl infant referred to our hospital for poor feeding and cholestasis. She was 3.1 kg, product of a caesarean section because of placenta previa with appropriate Apgar. In the second day of life she was admitted to another center because of jaundice and poor feeding. In her laboratory exams from that center Hb was 10.5 g/lit, WBC count 12500, total bilirubin 13 mg/dL, conjugated bilirubin 0.5 mg/dL, CSF was clear and colorless with glucose 49 mg/dL, protein 70 mg/dL, with no RBC
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and WBC. Cultures of CSF and urine and stool were negative. After one week of systemic antibiotic therapy and phototherapy she was discharged. Her poor feeding and lethargy continued, so she referred to our hospital. On physical examination she had T=37°C, wt= 3.400 kg, HC= 36 cm. She was lethargic and jaundiced and the anterior fontanelle was 4x3 cm and bulged. She had hepatomegaly and ascites and also echymoses on her extremities. Her deep tendon reflexes were depressed, and had weak grasp and sucking reflexes and incomplete Moro reflex. Results of laboratory studies were: WBC 15000, Hb = 9.5 g/L, PLT=120000, pH=7.23, bicarbonate 14.2 mEq/L , Cl 108 mEq/L, Sodium 135 mEq/L, Potassium 3.6 mEq/L, total bilirubin 4.6 mg/dL, conjugated bilirubin 1.8 mg/dL, ALT 86 IU/L, AST 252 IU/L, total protein 4.1 g and Albumin 1.8 g/dL, Alkaline phosphatase 631 IU/L. Prothrombin time was 19.2 seconds (INR 2), PTT 52 seconds. Blood glucose was 40 mg/dL. The CSF was clear and colorless with no WBC and RBC, glucose was 30 mg/dL, protein 60 mg/dL. Blood and CSF cultures were negative. In urine pH= 6, specific gravity was 1014, glucose +2, and blood +, with no WBC and RBC. G6PD was sufficient, and direct Coombs was negative. She was treated for probable sepsis, hypoglycemia, hyperchloremic acidosis and hepatic failure and coagulopathy. In eye examination she had cataract with oil droplet appearance. On brain CT scan (Fig. 1) she had diffuse cerebral edema. For cholestasis initially tests for TORCH study and metabolic diseases were performed. Transferase deficiency was reported by the National Research Center for Genetic Engineering & Biotechnology one week after her admission.

Oral feeding with a lactose restricted formula was started and she tolerated well. Her general condition progressively became better and she was discharged from the hospital after 18 days. After the first month of a lactose restricted formula her weight was 3.950, HC = 37 cm.

The second CT scan performed after 3 months (Fig. 2) showed dramatic improvement in cerebral edema. At 5 months of age her weight was 6.500, HC = 41.5 cm with normal physical exams and normal liver function tests. She walked independently at 12 months and spoke a few words. At 15 months (last visit), her weight was at the 50th percentile, her height was between the 25th and 50th, and her head circumference at the 50th percentile. The neurological examination findings were normal.

**DISCUSSION**

Increased intracranial pressure in galactosemia is a rare complication of this disease. Galactitol accumulates in higher concentrations in brain tissue and appears to be a factor in the development of brain function abnormalities seen in transferase deficiency. Many symptoms and signs resolved after the early withdrawal of dietary galactose. However pathologic alternations in brain tissue may not be completely reversible through dietary galactose restriction.

The pathogenesis of CNS injury during galactosemia is unknown but diminished levels of ATP, reduced brain glucose and glycolytic intermediate concentrations, altered distribution of hexokinase, heightened fragility of neuronal lysosomes, and impaired fast exoplasmic transport has been mentioned. These changes seem to be associated with other conditions, namely hyperosmolality, alternation in energy metabolism, abnormal serotonin levels and interference with active uptake of glucose into neurons.

Because of the acute and fulminant nature of the ill-
The follow-up CT scan 2 months later does not define the white matter involvement, but demonstrates progressive mild diffuse volume loss.

In summary in the differential diagnosis of increased intracranial pressure in a jaundiced, ill infant the physician must consider galactosemia. More attention must be focused in countries in which screening tests for metabolic diseases are not performed routinely.

REFERENCES