Galactosemia Detection from Phenylketonuria Screening

M. J. Henderson, L. Shapiro, and C. McCowan

We describe a case of classical galactosemia in which the diagnosis was first suggested by the finding of a moderately increased blood-spot phenylalanine concentration. The child was clinically unaffected at six days when the initial sample was collected. Prompt institution of dietary management averted a serious metabolic crisis.

Additional Keyphrases: blood-spot phenylalanine  galactose-1-phosphate uridylyltransferase

Children with galactosemia owing to deficiency of galactose-1-phosphate uridylyltransferase (EC 2.7.7.10; UTP-hexose-1-phosphate uridylyltransferase) usually develop symptoms within a few days of starting to consume milk (1), although this may be delayed if the baby's milk intake is initially low. If the diagnosis is not made promptly, severe and irreversible damage may occur in the liver and brain. The severity of the symptoms is variable, and the diagnosis may be difficult to make on clinical grounds.

An important clue to the presence of galactosemia in these circumstances may come from the unlikely source of the phenylketonuria screening test. This observation was first reported by Pollitt et al. (2) in 1982. They described 12 cases of galactosemia, in four of whom the diagnosis was first suspected because of abnormally high phenylalanine concentrations in the blood (180–730 μmol/L). Diagnosis in the other eight patients was prompted by the baby's illness.

We made a diagnosis of galactosemia in a case where the first clue was increased phenylalanine on routine Guthrie testing, and we present the case to confirm and publicize this benefit of the phenylketonuria screening program.

Case Report

Baby C.S. was delivered at 35 weeks in the obstetric regional referral unit by lower-segment caesarean section after the intra-uterine death of a twin. She was the product of the first pregnancy of unrelated parents. Her condition immediately after birth was satisfactory and she started taking milk by bottle soon after birth. At 48 h she was clinically jaundiced (serum bilirubin 174 μmol/L), and this persisted. She stopped taking nourishment by bottle and required tube feeds. At the age of six days a dried-blood-spot phenylalanine estimation by fluorimetric assay (3) as part of the neonatal screening program showed an increased concentration, 440 μmol/L, the upper limit of normal being 230 μmol/L by this assay. Repeat analysis two days later gave a phenylalanine value of 530 μmol/L.

At this point the child was transferred back to the district general hospital. On arrival she was mildly unwell, with lethargy and moderate jaundice. There was no hepatomegaly. A full infection screen was carried out and the baby was started on intravenous antibiotics, but milk feeds were continued. It was noted that she was slow to stop bleeding on venepuncture. Three days later, after an apparent improvement, the baby's condition deteriorated. She became more lethargic with pallor and jaundice. The abdomen was distended and the liver was enlarged 3 cm and firm. Because of the supranormal phenylalanine concentration, the possibility of galactosemia had been raised by the laboratory; the baby's diet was therefore promptly changed to a galactose-free milk. Reducing substances were found in the urine and a galactosemia screening test was positive. Further blood specimens confirmed the diagnosis of classical galactosemia with high values for galactose 1-phosphate (935 mg/L) and absent galactose-1-phosphate uridylyltransferase activity. Liver-function tests showed moderate abnormalities: bilirubin 122 μmol/L, alkaline phosphatase 391 U/L, alanine aminotransferase 41 U/L, aspartate aminotransferase 51 U/L, total protein 38 g/L, and albumin 23 g/L. Quantitative analysis showed that the concentrations of most amino acids in plasma were abnormally high, notably phenylalanine 449 and tyrosine 1200 μmol/L (upper limit for this age, 182 and 196, respectively).

After the feeding was changed, the baby's condition rapidly improved and she has remained well since. At the age of eight months she is growing normally and her development is within normal limits. She has classical oil droplets within the center of the lens in both eyes, but her vision appears to be normal. She has normal liver function and her most recent galactose 1-phosphate concentration was 76.3 mg/L (Table 1). Plasma phenylalanine and tyrosine concentrations are also now within normal limits at 82 and 117 μmol/L, respectively.

Discussion

The etiology of the hyperphenylalaninemia associated with galactosemia is not known. However, patients with severe liver-cell disease from various causes have increased concentrations of many amino acids in plasma, including phenylalanine (5). Thus, deranged liver-cell function, which is one of the common sequelae of galactosemia and was demonstrated in this case, is likely to be responsible for the hyperphenylalaninemia. Following reduction of galactose 1-phosphate concentration and improvement in liver function the plasma amino acid concentrations have returned to normal.

This case illustrates that galactose-1-phosphate uridylyltransferase deficiency should be considered in the differential diagnosis of neonatal hyperphenylalaninemia.

We would like to thank the Willink Biochemical Genetics Laboratory at the Royal Manchester Children's Hospital for the measurements of galactose-1-phosphate uridylyltransferase and galactose 1-phosphate; and Dr. H. Wilkinson for her efficient cooperation.
Table 1. Erythrocyte Galactose 1-Phosphate Concentrations (I) after a Lactose-Free Diet from Age 14 Days

<table>
<thead>
<tr>
<th>Patient's age, days</th>
<th>14</th>
<th>21</th>
<th>28</th>
<th>35</th>
<th>53</th>
<th>88</th>
<th>157</th>
<th>255</th>
</tr>
</thead>
<tbody>
<tr>
<td>I, mg/L of packed cells</td>
<td>935</td>
<td>348</td>
<td>254</td>
<td>244</td>
<td>128</td>
<td>102</td>
<td>63</td>
<td>76</td>
</tr>
</tbody>
</table>

References


