

Severe, Prolonged Neonatal Hyperbilirubinaemia and Recurrent Hypoglycaemia: Can this be Galactosaemia?

TA Ogunlesi⁺, BO Ogunfowora⁺⁺, SA Sotimehin⁺

Summary

Ogunlesi TA, Ogunfowora BO, Sotimehin SA. Severe, Prolonged Neonatal Hyperbilirubinaemia and Recurrent Hypoglycaemia: Can this be Galactosaemia? *Nigerian Journal of Paediatrics* 2005; 32: 90. A case of prolonged severe hyperbilirubinaemia associated with persistent hypoglycaemia, features of proximal renal tubular defect and failure to thrive in a male preterm, low birth weight infant who was admitted at the age of 52 hours, is reported. Although the management was hindered by lack of diagnostic facilities, the positive outcome of a therapeutic trial with lactose-free diet was suggestive of galactosaemia. This case is being reported to create awareness of this clinical condition.

Introduction

CLASSICAL galactosaemia, due to the low activity of galactose-1-phosphate uridyl transferase (GALT), is a rare metabolic disorder.¹ The inability to metabolize galactose, a constituent of lactose, results in the accumulation of galactose-1-phosphate and its metabolites in the hepatic, renal, lenticular and cerebral tissues. Neonatal jaundice, hypoglycaemia, cataract and failure to thrive are the early features of galactosaemia, while liver cirrhosis and mental retardation occur later in life.¹ The diagnosis of galactosaemia is usually made from the identification of urinary galactose, thin layer chromatography of urine and PCR assays of erythrocytic enzymatic activity.² The latter two, which are specific and more reliable, are not available for routine use in clinical practice in most developing countries including Nigeria. It is likely that missed diagnosis may explain the apparent rarity and unknown incidence of galactosaemia in this part of the world.³ The incidence of 1/60, 000 live births in the United States of America was obtained from routine newborn screening programmes.^{1,3} Consequently, physicians practising in the developing world where diagnostic facilities are scarce need to be familiar with the clinical presentations of galactosaemia for early diagnosis and timely management.

Case Report

Baby AB was admitted to the neonatal unit of the Olabisi Onabanjo University Teaching Hospital, Sagamu, at the age of 52 hours. The chief complaint was difficulty with breathing of six hours' duration. The breathlessness was noticed soon after he was fed. The baby was delivered at an estimated gestational age of 36 weeks in a private clinic following pregnancy and labour which were uneventful. The birth weight was 1.8kg but the APGAR scores were not recorded at the place of birth. The mother was a 34-year old para 3⁺³. There was no history of preterm delivery or neonatal jaundice in the siblings. Physical examination revealed a preterm, low-birth-weight infant (weight, 1.7 kg; occipitofrontal circumference, 30cm; length, 42cm) with moderate icterus, weak cry, depressed primitive reflexes, generalized hypertonia, respiratory distress and harsh breath sounds. Prematurity, neonatal jaundice, neonatal hypoglycaemia and aspiration pneumonitis were diagnosed.

Initial investigations revealed venous haematocrit of 58 percent, random blood glucose (RBS) level of 0.5mmol/L, total and conjugated serum bilirubin of 302 μ mol/L and 18.7 μ mol/L, respectively but a normal cerebrospinal fluid. Both the baby and mother were of blood group B Rhesus positive. Chest radiography and glucose-6-phosphate dehydrogenase assays were not done.

The initial management comprised correction of hypoglycaemia with 10 percent dextrose-in-water, fluid maintenance with eight percent dextrose-in-fifth normal saline at 100ml/kg/day, *nil per os*, intravenous cefuroxime and gentamicin, and phototherapy. By the second day of admission, the baby was no longer dyspnoeic. However, double volume exchange blood transfusion (EBT) was carried out on the third day

Olabisi Onabanjo University, Sagamu

Department of Paediatrics

⁺Lecturer

⁺⁺Senior Lecturer

Correspondence: Dr TA Ogunlesi
E-mail: tinuade_ogunlesi@yahoo.co.uk

of admission for severe unconjugated hyperbilirubinaemia (316 $\mu\text{mol/L}$). Enteral feeding with expressed breast milk (EBM) was also commenced on the third day of admission in addition to eight percent dextrose-in-fifth normal saline infusion. Despite these, the RBS levels remained persistently low (0.94 to 1.4 mmol/L) between the 7th and 30th days of admission. In addition, from the sixth day of admission (i.e. three days after the EBT), the serum bilirubin was mainly conjugated. Thus, phototherapy was discontinued. Other important findings at this stage included 4 cm hepatomegaly and deep yellow urine while the stools were normal. Blood culture yielded no growth and HBsAg screening was also negative. Hepatic ultrasonographic and enzymatic studies were not done for lack of funds. The thought of galactosaemia as a possible cause of conjugated hyperbilirubinaemia was entertained when urinalysis by *Clinitest*[®] showed the presence of reducing substances. Further urinalysis by *Multistix*[®] revealed glycosuria, proteinuria and acidic urine (pH 5–6). Serum electrolytes were within normal limits (Na^+ 131–134 mmol/L; K^+ 3.6–4.5 mmol/L; Cl^- 105–108 mmol/L; HCO_3^- 20–21 mmol/L) but the bicarbonate was low at 15 mmol/L on one occasion. This was corrected with intravenous 8.4 percent sodium bicarbonate.

The body weight gradually fell to 1.5 kg on the 30th day of admission despite provision of adequate calories. At that point, neonatal failure to thrive and Fanconi syndrome probably secondary to galactosaemia was diagnosed. Enzymatic studies of GALT were not available but a therapeutic trial of dietary manipulation was instituted. The mother was counselled to stop breast milk feeding while lactose free soy based diet (*Isomil*[®]) was commenced.

Remarkably, urinalysis done on the day following the commencement of dietary manipulation revealed no proteinuria or glycosuria. The RBS was also normal (3.5 mmol/L). The infant was discharged home at the request of the parents on the 41st day of admission (chronological age of 42 days) on 150 kcal/kg/day of *Isomil*[®]; his body weight on discharge was 1.5 kg. On review at the outpatient clinic at the age of 46 days, the baby's body weight was still 1.5 kg and he was still jaundiced, but had no cataract; the RBS was normal (3.4 mmol/L) and there was no proteinuria or glycosuria. At the chronological age of 11 weeks, the baby weighed 2.8 kg, having gained 1.3 kg over five weeks at the rate of 0.26 kg/week on *Isomil*[®] feeds. The jaundice had cleared and there was no cataract or urinary abnormalities. He was referred to the paediatric surgical unit for management of a left sided inguinoscrotal hernia.

Discussion

The paucity of local literature on galactosaemia in Nigeria suggests that the disease has probably not been extensively studied in the country. The early commencement of lactose-containing diet and the combination of prolonged, severe neonatal jaundice (unconjugated hyperbilirubinaemia which later evolved into conjugated hyperbilirubinaemia), hypoglycaemia and failure to thrive fit into the textbook description of galactosaemia.¹ Although the serum electrolytes, particularly potassium, were not remarkably abnormal, the presence of proteinuria and glycosuria were suggestive of renal Fanconi syndrome. Galactosaemia is a known secondary cause of this proximal renal tubular defect.¹ The renal leakage of glucose as well as hepatocellular damage may explain the persistent hypoglycaemia observed in this patient despite continuous dextrose infusion with or without supplemental EBM feeding. Thus, every baby with prolonged conjugated jaundice deserves to be investigated for galactosaemia as there is a known association between these disorders.^{2,4,5}

We acknowledge that we were not able to investigate this patient fully; this was due to lack of funds and facilities. However, the resolution of the metabolic, hepatic and renal abnormalities following the cessation of breast milk feeding and introduction of the lactose-free milk diet strengthened our suspicion of galactosaemia.⁶ It also helped to rule out other important differential diagnosis of conjugated hyperbilirubinaemia like biliary atresia, idiopathic neonatal hepatitis and metabolic disorders like tyrosinaemia.⁵

Galactosaemia is rare, even in places where routine screening is done.³ However, the morbidities associated with it are huge if left untreated. The absence of cataract in our patient was unusual^{1,2,4} but we speculate that the early initiation of dietary management may explain this. This also shows the gains of early detection and commencement of dietary manipulation. Although the gross features of galactosaemia are reversible following dietary manipulation, there is evidence that some neurological effects may persist despite the change in diet.⁷ Therefore, screening of newborn babies before exposure to lactose-containing diet is desirable.

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