Short reports

Glycogen storage disease (type I) presenting in the neonatal period

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Summary Four Asian babies presenting with type I glycogen storage disease during the early weeks of life are described. In one child the symptoms, metabolic acidosis, and hypoglycaemia were so easily controlled that the diagnosis was not entertained, leading to a late diagnosis. In another child the diagnosis was reached only by investigation of a fortuitously detected hyperlipidaemia. The 3 babies in whom early treatment was started were thriving, and in one, the liver histology was so normal that doubt was cast on the diagnosis initially.

Presentation of type I glycogen storage disease during the neonatal period may be more common than has hitherto been thought. We report our recent experience of the early presentation of this rare metabolic disorder in 4 children born during the last five years.

Case 1

This girl was born in 1976 at term, the eighth child of healthy Pakistani parents, who were 1st cousins; 7 siblings were alive and well. Birthweight was 3.28 kg. Tachypnoea was noted at age 24 hours, there was a metabolic acidosis (base excess -15), asymptomatic hypoglycaemia (glucose 1 mmol/l; 18 mg/100 ml), and the liver was enlarged. Normoglycaemia was maintained by continuous intragastric infusion of milk and the acidosis required initial correction with oral bicarbonate. By 7 days normoglycaemia was maintained with normal 4-hourly feeds without bicarbonate. At discharge the only clinical abnormality was a palpable liver. She was seen monthly on 4 occasions, found to be thriving on a normal diet, with a normal acid base balance but with a persistently enlarged liver.

She was admitted to another hospital at age 5 months with pronounced tachypnoea, severe metabolic acidosis, and hepatomegaly (Dr J Insley). Glucagon and galactose stimulation tests suggested a type I disorder (Figure). Liver biopsy showed an excess of glycogen (10.7% of wet weight of liver) and no detectable glucose-6-phosphatase activity (Dr N Raine), confirming type I glycogen storage disease.

Despite a low lactose diet offered every 2 to 3 hours during the day she has done badly, suffering frequent episodes of metabolic acidosis, and poor growth (height 2 cm less than 3rd centile for age).

Case 2

This boy was born in 1979 at term; birthweight was 3.98 kg. At age 5 days, although only mildly icteric, a serum bilirubin level was reported as 325 μmol/l...
although not as great as described by Igarashi, supported the diagnosis of a type IB disorder. Liver histology showed as before a minimal abnormality, with normal liver glycogen and slight increase in fat deposition (Dr B Lake).

On a low lactose diet given every 2 hours he has remained well and is well grown. Continuous nocturnal tube feeding has been successfully introduced recently.

Case 4

This girl was born in 1980 at term, the second child of Indian parents who were 2nd cousins. Birthweight was 3.12 kg. A previous child born in 1978 at 28 weeks’ gestation had died of necrotising enterocolitis. Tachypnoea and metabolic acidosis (base excess -16) and hypoglycaemia (glucose 0.9 mmol/l; 16 mg/100 ml) were noted at 7 hours. A 10% dextrose infusion in addition to normal milk feeding was required to maintain normoglycaemia for the first few days.

At age 4 days an enlarged liver suggested the diagnosis of glycogen storage disease. Subsequent investigations confirmed this: results of glucagon and galactose tests were similar to those of the other patients (Figure). Liver biopsy (Dr M Tarlow) showed an excess of glycogen and the enzyme assay very low glucose-6-phosphatase activity, confirming type I glycogen storage disease (Dr A H Cameron, Professor D Patrick). At age 9 months she remains well on a 3-hourly round-the-clock low lactose diet, but with an obviously enlarged liver. Nocturnal tube feeding has recently been introduced.

Discussion

These 4 cases demonstrate some important points. Although rare, a neonatal presentation of type I glycogen storage disease may be more common than has hitherto been recognised. Symptoms may be transient, their significance not appreciated, and the diagnosis overlooked as in Case 1. We suggest that in the neonatal period, any unexplained metabolic acidosis, hypoglycaemia (often asymptomatic), hepatomegaly, or hyperlipidaemia merits the consideration of glycogen storage disease among the differential diagnoses. Fernandes et al.9 suggested that in type I glycogen storage disease the reduction of plasma lactate level after glucose may be a useful investigation without the potential danger of either a prolonged fast or galactose.

Although early reports suggested the neonatal presentation was associated with a poor prognosis it seems likely that the early diagnosis and institution of treatment may reduce complications and improve the subsequent prognosis. Case 1 suffered repeated
Glycogen storage disease (type I) presenting in the neonatal period 311

episodes of metabolic acidosis and is growth retarded, whereas the 3 diagnosed in the neonatal period are thriving. All our patients were Asian and consanguinity was a feature in every case.

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References


Liver damage in a neonate with alpha-1-antitrypsin deficiency due to phenotype PiZ null (Z–)

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SUMMARY An infant with neonatal liver damage had α-1-antitrypsin deficiency, having inherited the Z allele from the father and the rare null allele from the mother. This indicates that while a lack of serum antiprotease predisposes to early liver disease, homozygosity for the Z allele is not essential.

Alpha-1-antitrypsin represents the major serum protease inhibitor and can be quantified on this basis. The use of electrophoresis and isoelectric focusing has helped to identify at least 28 allelic variants, 4 of which are associated with low levels of clinical significance; these are labelled Z, S, null, and M malton in the Pi (protease inhibitor) classification. There is a complete lack of α-1-antitrypsin on the rare occasions that a homozygote for the null allele is identified.1–3 This allele produces no electrophoretic band; the heterozygous state can be deduced only by quantification and electrophoresis of parental blood.

The association of liver disease with α-1-antitrypsin deficiency has been known since 1969, nearly all cases being presumed ZZ homozygotes. The PiZ null (Z–) heterozygote is rare. Sveger4 found 2 Pi Z– neonates among 200,000 screened in Sweden, one of whom was normal; the other had slightly abnormal liver function tests. We could find no previous report of severe liver damage in a child with the Z– phenotype. We report one such case.

Case report

A girl was born weighing 2.08 kg at 37 weeks’ gestation, by caesarean section, performed because of cephalopelvic disproportion. She was the first child of unrelated parents, the mother having had 2 normal children by a previous marriage. Polyhydramnios was noted at delivery; the placenta was oedematous and weighed 750 g.

The patient required intubation at birth and regular respirations were not established until 7 minutes had elapsed. During the first 24 hours generalised abdominal distension and hepatosplenomegaly were noted. Her indirect bilirubin, on day 3, was 371 µmol/l (21.8 mg/100 ml) with a normal haemoglobin level, and one exchange transfusion was performed. A top-up transfusion was required on day 11. She failed to thrive and was referred for investigation at 8 weeks.