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ACUTE LIVER FAILURE IN A SEVEN-WEEK-OLD INFANT WITH GALACTOSAEMIA: CASE REPORT
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ACUTE LIVER FAILURE IN A SEVEN-WEEK-OLD INFANT WITH GALACTOSAEMIA: CASE REPORT

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SUMMARY

Galactosaemia is a rare metabolic disorder that presents in early infancy and affects multiple organs and systems and is potentially fatal if undetected early. We present a case of a seven week old male infant with jaundice from birth who presented with abdominal distension and feeding difficulties. He was ill looking at admission with moderate pallor, jaundice, hepatosplenomegaly and ascites. Investigations revealed anaemia, coagulopathy and deranged liver enzymes. A limited work up for cholestatic liver disease was suggestive of galactosaemia and the patient improved remarkably on institution of a galactose free diet.

INTRODUCTION

Galactosaemia is a rare autosomal recessive metabolic disorder affecting 1 in 30,000- 60,000 infants. Classic galactosaemia is caused by deficiency of the enzyme galactose-1- phosphate uridyl transferase (GALT) that prevents conversion of galactose to glucose (1). Most patients present in early infancy with jaundice, hepatosplenomegaly, hypoglycaemia, sepsis and cataracts. Hepatocellular insufficiency and acute liver failure are known but unusual presentations (2). There are no reports in the literature of infants presenting with acute liver failure in Africa. We present a case of a seven week old infant who presented with acute hepatocellular insufficiency and noted to have galactosaemia on investigations and who made a good recovery after eliminating galactose from his diet.

CASE REPORT

A seven week old male infant of Somali ethnicity was referred by a general physician with history of jaundice since birth and abdominal swelling for a few days. Jaundice was noticed from the first day of life and was progressively getting worse, with dark yellow urine but pigmented (light yellow) stool. He had been feeding well, on both breast milk and formula milk (Nan) until a few days earlier when he started tiring during feeds but without sweating or cyanosis. He was also described as being lethargic during the preceding 72 hours. No bleeding tendencies or rashes were reported although he did have an occasional low-grade fever.

The infant had been born at term by emergency Caesarean section secondary to cephalopelvic disproportion to a 26-year-old mother who had two previous first trimester pregnancy wastages. There was no history of liver disease or consanguineous marriages in the family.

Examination revealed a sick infant who was wasted, had moderate to severe pallor and moderate scleral icterus, was afebrile with mild pedal oedema but without any obvious dysmorphic features. He had a heart rate of 141 beats per minute and a respiratory rate of 42 breaths per minute. He was sleepy but rousable with mild hypotonia. The abdomen was asymmetrically distended more at the flanks with a girth of 38 cm at the umbilicus.

The liver was enlarged to 3 cm below the costal margin along the mid-clavicular line, he had a tipped spleen and there was moderate ascites. There were no petechial lesions or mucosal bleeds. The rest of the examination was normal.

His initial tests revealed a haemoglobin level of 7.8 grams/liter, white cell count of 15,000/mm^3, platelets of 326,000/mm^3 and a random blood sugar of 2.85 mmol/liter. Both mother and infant were blood group B+. The bilirubin and aspartate amino transferase (AST) levels were elevated and his initial international normalising ratio (INR) was 2.0 with a prothrombin time index (PTI) of 28% (Table 1).

An abdominal scan showed a hyperechogenic liver, non-dilated intrahepatic ducts, and oedematous walls of the gall bladder. Serology for VDRL, HIV, hepatitis B and C and IgM for cytomegalovirus was negative. Blood and urine cultures were sterile.

A limited work-up for prolonged cholestatic jaundice was done (Table 2). The most significant was a positive test for urine reducing substances (twice). A confirmatory test of reduced galactose-1-phosphate uridyl transferase (GALT) enzyme activity done at a referral laboratory confirmed the diagnosis of galactosaemia.

Table 1
Baseline and in-patient follow up investigations

Test	Day 1	Day 6	Day 9
Total Bilirubin (mmol/L)	147	37	44
Direct Bilirubin (mmol/L)	87	32	17
AST (U/L)	108	94	66
ALT(U/L)	38	37	49
ALP (U/L)	772	495	220
Albumin (g/L)	26.1	34	32
PTI (%)	28	52	98
INR	2.08	1.6	1.0
Random Blood Sugar	2.85	4.0	3.8
Ammonia	932		
Creatinine (mmol/L)	21		

Table 2
Distinguishing and confirmatory tests

Test	Result	Normal values
Urine glucose	Negative	
Urine reducing substances	Positive (twice)	
Alpha-I-antitrypsin	1.32	0.88 - 1.74
Transferrin	<0.70	2.0 - 3.2
Ferritin	466	200 - 500
Thyroid function	Normal	
Galactose 1 PUT	10.9	15.1 - 34.3

The patient was commenced on intravenous fluids (dextrose saline), broad spectrum antibiotics (cefotaxime and amikacin) and diuretics (spironolactone). The patient had a stormy clinical course during the first 48 hours requiring admission to the intensive care unit for progressive respiratory distress needing therapeutic paracentesis as well as multiple blood transfusions. He was started on a lactose-free diet once the urine reducing substance result was known and gradually made a good recovery. His abdominal girth progressively reduced and was discharged after eleven days on a lactose-free soy formula.

The patient was later evaluated by an ophthalmologist and noted to have mild lens displacement but no cataracts. At 12 months of age, the patient had achieved all his major motor milestones, is now walking and making babbling sounds and has appropriate weight gain on a lactose-free (soy) formula.

DISCUSSION

Fulminant liver failure is defined as a multisystemic disorder in which severe impairment of liver function, with or without encephalopathy, occurs in association with hepatocellular necrosis in a patient with no recognisable underlying chronic liver disease (3). Liver failure is a rare presenting feature in the neonatal period and potential aetiologies include inborn errors of metabolism, infections, ischaemia and abnormal perfusion (4). Common metabolic causes include galactosaemia, fructosaemia, tyrosinaemia type 1 and bile acid synthesis defects (1, 2). Galactosaemia is the most common of these metabolic diseases in South Africa with an estimated incidence of 1 in 14,400 that is much higher than that reported in developed countries (5). Fateen *et al* (6) in Egypt showed that galactosaemia was present in 7% high risk neonates (jaundice, hepatomegaly and failure to thrive) compared to 0.05% amongst normal neonates.

The high rate of galactosaemia in South Africa and Egyptian neonates suggests that the scarcity of reports on this problem from Africa may be due to underreporting related to low levels of ascertainment. Lack of knowledge on this condition, low index of suspicion among clinicians, unavailability of diagnostic tests and the large burden of infectious diseases that present similar to galactosaemia may further complicate the ascertainment of cases.

Common clinical presentation of galactosaemia includes feeding difficulties, vomiting, cataracts, prolonged jaundice and failure to thrive. Jaundice is a more common presenting feature present in 77 - 100% in reported case series but liver failure has been infrequently documented as well (6, 7). Our infant had severe acute liver failure on presentation as evidenced by severe coagulopathy (INR of 2.0). There have been no reports from Africa on infants with galactosaemia presenting with acute hepatocellular dysfunction. In one case report of galactosaemia presenting at 11 months of age, the infant had persistent jaundice and no evidence of hepatocellular failure (8).

Correctly identifying the disease may be life-saving as treatment simply involves instituting a lactose free diet although there has been a report of blood exchange transfusion as a treatment option in the past (9). Our patient presented early with liver failure and underwent standard conservative management for liver failure but made a quick recovery once he was put on a lactose-free diet. He has had a complete recovery with normal synthetic function since discharge from hospital.

Other complications of galactosaemia include cataracts and neurological deficits (2). The seven week old infant was reviewed by an ophthalmologist and noted to have early cataract and is on regular follow up. The patient has also had normal neuro-developmental milestones so far and can now walk at 12 months. However, it is known that most children with galactosaemia, including those detected early by newborn screening methods do have some form of neurodevelopmental delay (2).

Nutritional counselling and appropriate advice plays an important role in the management of galactosaemia. Traces of lactose are found in several food substitutes and there is evidence that there is endogenous galactose production within the human body, which are thought to contribute to later complications of the disease (10). A recent study showed that an elemental diet may be more effective at controlling GALT1 levels (11). Our patient has done relatively well on a soy-based formula although we have not repeated his GALT1 assay. Unfortunately he has only seen the dietitian once since discharge but the parents have been diligent in avoiding lactose-containing foods. The exact duration of lactose free diet is not known although most experts agree that galactose should be restricted for life (2).

In conclusion, our report contributes to the limited data on galactosaemia in Africa, presenting as acute liver failure in an infant. Since routine neonatal screening is not done in Africa, screening for galactosaemia in high risk patients such as those with prolonged jaundice, hepatomegaly and failure to thrive may help diagnose this otherwise fatal disorder.

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