Type 1 glycogen storage disease presenting with distal renal tubular acidosis

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Case report

A one month old baby boy from Kandy, third child of consanguineous parents, was admitted to hospital with reduced feeding, excessive crying and difficulty in breathing of one day duration. On admission, baby was febrile with adequate hydration and good circulation. He was tachypnoeic and dyspnoeic but lungs were clear with good air entry. Abdomen was distended and liver was palpable 3 cm below the costal margin and the spleen 1 cm below the costal margin. There was no facial dysmorphism.

Investigations on admission revealed normal anion gap severe metabolic acidosis with hypokalaemia. Urinary pH was 6.5 and urinary anion gap was positive. Renal functions were normal. Blood sugar, white blood cell count and platelet count were normal. Haemoglobin was 9.5g/dl. A diagnosis of distal renal tubular acidosis was made and he was started on intravenous (IV) sodium bicarbonate with initial correction dose followed by maintenance (3 ml 4 hourly) doses which gradually normalized baby's blood gases. Tachypnoea improved and baby gained 350g within next 10 days. He was discharged on oral sodium bicarbonate with arranged clinic follow up.

A week later, baby was readmitted with an episode of severe metabolic acidosis precipitated by lower respiratory tract infection. At that time hepatosplenomegaly was persisting, random blood sugar (RBS) was normal and renal function tests were normal. Ultrasound scan (USS) of abdomen revealed hepatosplenomegaly. Oral sodium bicarbonate was increased to 8 ml 4 hourly to normalize blood gases and it was planned to investigate for glycogen storage disease. In addition, IV antibiotics were started for the respiratory tract infection. Metabolic screening came as negative. At the age of two months 3 weeks baby presented with four episodes of afebrile generalized tonic clonic fits which had occurred at midnight and early morning. On admission, RBS was low (50mg/dl), liver was palpable 4 cm below the costal margin and the spleen 1 cm below the costal margin (Figure 1).

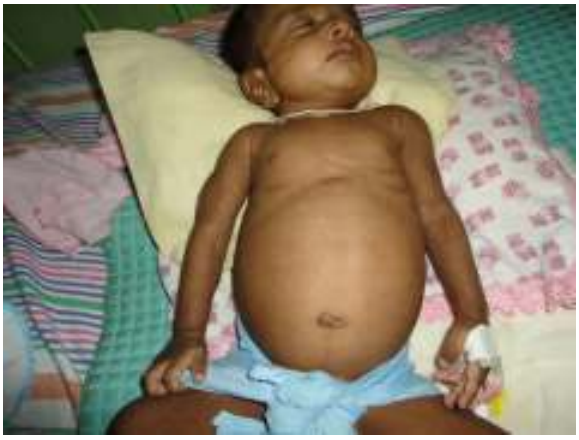

Figure 1: ***Baby at the age of 2 months and 3 weeks***

We investigated for glycogen storage disease (GSD). Serum triglycerides, serum uric acid, Liver transaminases (SGPT, SGOT) were high and repeat abdominal USS showed marked hepatosplenomegaly. Liver biopsy was done and findings were consistent with GSD type 1. No neutropenia was observed at any stage and no recurrence of infections. A diagnosis of distal renal tubular acidosis (dRTA) and GSD type 1a was made.

Discussion

Renal tubular acidosis (RTA) is a disease state characterized by a normal anion gap metabolic acidosis[1]. Glucose-6-phosphatase is part of an enzyme complex that regulates the final step of the production of free glucose from glycogen breakdown and gluconeogenesis[2]. GSD type 1 patients have inadequate hepatic conversion of glucose-6-phospate to glucose through normal glycogenolysis and gluconeogenesis[1]. The structural gene for glucose-6-phosphatase is located on chromosome 17q21; the gene for translocase is on chromosome 11q23[1]. Patients with type 1 GSD present in the neonatal

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period or early infancy with hypoglycaemic seizures, lactic acidosis or hepatomegaly[1]. These children often have doll like facies, thin extremities, short stature and a protuberant abdomen due to massive hepatomegaly[1]. Biochemical hallmarks of the disease are hypoglycaemia, lactic acidosis, hyperuricaemia, and hyperlipidaemia[1]. Our patient belongs to type 1a as he did not have recurrent bacterial infections from neutropenia and impaired neutrophil function.

Renal disease is a late complication and most patients with type I GSD older than 20 years develop proteinuria[1]. Many have hypertension, renal stones, nephrocalcinosis and altered creatinine clearance[1]. Glomerular hyperfiltration, increased renal plasma flow and microalbuminuria are often found in the early stages of renal dysfunction and can occur before onset of proteinuria[1]. In younger patients, hyperfiltration and hyperperfusion may be the only signs of renal abnormalities[1]. With advancement of renal disease, focal segmental glomerulosclerosis and interstitial fibrosis become evident[1]. In some patients, renal function deteriorates and progresses to failure, requiring dialysis and renal transplantation[1]. Other renal abnormalities include amyloidosis, a Fanconi-like syndrome, hypocitraturia, hypercalciuria, and a distal renal tubular acidification defect[1].

In dRTA there is impaired functioning of one or more transporters or proteins involved in the acidification process, including H^+/ATPase, the HCO_3^-/Cl^- anion exchangers or components of aldosterone pathway. Because of impaired hydrogen ion excretion, urine pH cannot be reduced below 5.5, despite presence of severe metabolic acidosis[1]. Loss of sodium bicarbonate results in hyperchloraemia and hypokalaemia. Hypercalciuria is usually present and may lead to nephrocalcinosis or nephrolithiasis. Chronic metabolic acidosis also impairs urinary citrate excretion causing hypocitraturia which further increases calcium deposition in tubules[1]. Our patient had non-anion gap metabolic acidosis, urine pH > 6.0 and a positive urinary anion gap ([urine Na^+ + urine K^+] – urine Cl^-) which is compatible with dRTA.

There are several case reports[3,4] and researches[5,6,7] which reveal that in type 1 GSD hypercalciuria and hypocitricaciduria increase with age and dRTA has been implicated in development of nephrolithiasis[8] and chronic renal disease. There are several case reports of GSD type 1 patients later presenting with renal stones who are found to have dRTA[3,4,5]. Furthermore, these studies concluded that citrate supplementation may be beneficial in preventing or ameliorating nephrocalcinosis and development of urinary calculi in GSD 1a[6]. One study states that chronic renal disease is a frequent and potentially serious complication of type 1 GSD and physicians should monitor renal function carefully in patients with this disorder[7]. But there were no reported cases of GSD type 1 initially presenting with dRTA.

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