CASE REPORT

Antenatal Bartter syndrome presenting with vomiting and constipation mimicking subacute intestinal obstruction in a 20-day-old neonate

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SUMMARY

Antenatal Bartter syndrome is a rare condition that can present with different clinical features. These features include early onset maternal polyhydramnios, failure to thrive, prematurity and nephrocalcinosis. We are presenting this 20-day-old girl who had an antenatal history of polyhydramnios. She developed persistent non-bilious vomiting that was associated with constipation soon after birth. She presented with failure to thrive and features suggestive of intestinal obstruction. On the initial evaluation, she was noted to have hypokalaemic, hyponatraemic metabolic alkalosis. The initial work-up was done to exclude surgical and renal causes of her presentation, and the diagnosis was confirmed by gene analysis to be type III—classic Bartter syndrome. She was closely monitored for her growth and development with the appropriate salt replacement therapy.

BACKGROUND

They are four types of antenatal Bartter syndrome that have differences in phenotype and genotype.^{1 2} The clinical presentation of antenatal Bartter syndrome includes: prematurity, failure to thrive and nephrocalcinosis. Maternal polyhydramnios is a common feature in most of the cases.² Types I, II and III present with severe antenatal symptoms, prematurity and failure to thrive, whereas type IV presents with a mild salt-losing nephropathy and mild antenatal symptoms.¹

Type III Bartter syndrome (classic Bartter syndrome) is a rare genetic disorder that presents with salt wasting which occurs mainly in the ascending loop of Henle.¹ Patients with classic Bartter syndrome present with failure to thrive from infancy, with hypokalaemia and metabolic alkalosis. There is usually an increased renin–aldosterone activity and prostaglandin production.^{1 2} Treatment options for the electrolytes imbalance in patients with Bartter syndrome include potassium supplements, antialdosterone agents and indomethacin. However, the management of growth failure and hypokalaemia is reported to be difficult, and close monitoring of patients is usually needed.^{1 3}

CASE PRESENTATION

We report this case of a 20-day-old girl who presented to the paediatric emergency department with persistent non-bilious vomiting, occurring mainly after feeds. Vomiting started on day 5 of life and was initially occurring once per day then increased in frequency. She was eager to feed after the vomiting episodes. She stopped passing stool for 12 days before presentation and had mild abdominal distension. She was exclusively breast fed, sucking well and passing large amount of urine.

This newborn was a product of a consanguineous marriage and no maternal history of early miscarriages.

She was born at 38 weeks of gestation, with antenatal history of severe maternal polyhydramnios. Amnioreduction was done at 32 weeks (4 L was aspirated). She had a normal antenatal chromosomal study; however, the chloride content of the amniotic fluid was not done.

She was born in good condition with no resuscitation needed at birth. Birth weight was 3.09 kg (just below the 25th centile). She was discharged home well and presented later with the above-mentioned symptoms. Her weight on day 20 was 2.88 kg (2nd centile), and blood pressure was 71/40 (normal). She was moderately dehydrated with stable vital signs. Systemic examination was normal.

Radiological evaluation and surgical review were done to exclude possible causes of intestinal obstruction. This initial assessment excluded both intestinal obstruction and pyloric stenosis.

INVESTIGATIONS

Initial investigations showed severe hyponatraemia with hypochloreaemic, hypokalaemic metabolic alkalosis. Hypercalcaemia was also noted. pH: 7.564, sodium: 116 mmol/L, chloride: 53 mmol/L, potassium: 2.7 mmol/L, bicarbonate: 43 mmol/L, base excess: 43.7, calcium: 3.03 mmol/L, glucose: 8.5 mmol/L and magnesium: 0.86 mmol/L. Serum aldosterone: 725 pmol/L (normal range in neonates 471–4265 pmol/L). Serum cortisol (AM): 57 nmol/L (normal range in neonates 55–304 nmol/L). Parathyroid hormone: 41 pg/mL (normal range 10–65 pg/mL).

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Urine work-up: pH: 5.5, specific gravity: 1.005, urine creatinine: 681 µmol/L, urine calcium: 2.0 mmol/L, urine calcium/creatinine ratio: 7.06 mmol/mol of creatinine (normal range up to 1.5), urine protein: 0.2 g/L, urine sodium: 117.2 mmol/L, urine chloride: 130.8 mmol/L and urine potassium 17.2 mmol/L.

Whole exome sequencing essential for the baby and both parents; with the result of genetic assessment: chloride channel Kb (CLCNKB) causing CLCNKB-related disorder. Mode of inheritance: autosomal recessive; variant: p.G120V, coding DNA: c.359G>T, zygosity: homozygous, inherited from: mother+father; classification: likely pathogenic variant.

DIFFERENTIAL DIAGNOSIS

The combination of recurrent vomiting in infants and hypochloreaemic, hypokalaemic metabolic alkalosis is a rare occurrence. Causes other than Bartter syndrome could be cystic fibrosis, initial presentation of pyloric stenosis and cases of pathologically increased aldosterone secretion.

TREATMENT

After stabilisation of the baby's condition and correction of electrolytes, diagnosis was established, and the family was updated. The baby was discharged after 10 days on oral potassium chloride, sodium chloride with follow-up with paediatric nephrology and genetic teams. She remained well and had close monitoring of her electrolytes, growth and development.

The use of indomethacin and spironolactone helped control the electrolytes imbalance.

OUTCOME AND FOLLOW-UP

She remained well after admission. Blood electrolytes improved, and her weight on discharge after 10 days of hospital admission was 3.2 kg (2nd centile), to be compared with the admission weight of 2.88 kg.

DISCUSSION

This case report presents a neonate with clinical features and investigations suggestive of type III Bartter syndrome. The initial blood picture showed normal serum magnesium, normal serum aldosterone for age, low blood chloride and low blood potassium in the presence of metabolic alkalosis. The presence of maternal polyhydramnios and hypochloreaemic, hypokalaemic metabolic alkalosis helped to guide the diagnosis of Bartter syndrome. This was confirmed later by the gene analysis.

The chloride channels that are found in the kidneys are encoded by the *CLCNKB* gene.⁴ The presence of any *CLCNKB* gene abnormalities including either gene mutation or deletion will affect the chloride channel function. These gene abnormalities have been reported in the literature as a cause of the autosomal recessive Bartter syndrome (type III).^{5,6}

The diagnosis of Bartter syndrome should be considered in children presenting with hypokalaemia, especially in the presence of growth failure.⁷ This rare syndrome presentation could be grouped into four variants or categories: antenatal Bartter that includes type I and type II, classic Bartter syndrome type III and classic Bartter with sensorineural deafness.⁷ The neonatal Bartter syndrome usually presents earlier in life when compared with classic Bartter syndrome. It is different from the classic form as it has high urinary calcium and sodium. This may be complicated later in life by nephrocalcinosis.⁷ It is reported that prostaglandin E1, when administered in high doses, can lead to pseudo-Bartter syndrome.^{8,9}

In our case report, serum aldosterone level was found to be within the normal range for the neonatal age group which is usually higher than the levels found in older children and adults.^{10,11} In children with antenatal Bartter syndrome, secondary hyperaldosteronism is usually present as a result of impaired sodium absorption in the ascending loop of Henle, which stimulates the renin-angiotensin-aldosterone axis leading to an increase in the blood aldosterone level.⁷

The parathyroid hormone level was noted to be within the normal range. This is despite the presence of significant hypercalcaemia which usually triggers a physiological response that results in reduction of the parathyroid hormone level. This abnormal response with relative hyperparathyroidism was noted on previous reports of cases with antenatal Bartter syndrome type I.¹²

Furthermore, the cortisol level was on the lower limits of normal. The expected level in the presence of stress and reduced body weight is to be on the upper limits of normal or even higher. This suboptimal response might be suppressed by the high blood sugars noted on the initial investigations, which could be explained by postfeeding and intravenous fluid therapy administrations responses.

The diagnosis can be suspected antenatally in the presence of polyhydramnios and growth failure.^{7,13} Amniotic fluid analysis is the investigation of choice and can confirm the high chloride content. Genomic DNA sequence can confirm the diagnosis of antenatal Bartter syndrome.

Other causes of hypochloreaemic, hypokalaemic metabolic alkalosis in infants includes infantile hypertrophic pyloric stenosis which usually presents with progressive non-bilious projectile vomiting that starts within the first 2–8 weeks of life.¹⁴

The long-term prognosis is dependent on the type of Bartter syndrome and satisfactory control of electrolyte imbalance. Close monitoring of growth and development parameters would be needed to achieve favourable prognosis.¹⁵

Learning points

- ▶ Bartter syndrome can be diagnosed antenatally with high index of suspicion in the presence of maternal polyhydramnios with high chloride content.
- ▶ Early diagnosis of Bartter Syndrome is important to establish good mineral replacement therapy, which could help in prevention of renal impairment in the future.
- ▶ Gene analysis is the gold standard test to confirm the diagnosis.

Contributors ISA conceived the idea of the case report, drafted the manuscript and made final changes. FE helped in the initial draft and literature search and updated the final version. KMS and BEJ revised and edited the manuscript as experts in the field.

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