Clinical Case Report

An unusual cause of failure to thrive in a child

PURNIMA SAMAYAM, RAVI CHANDER B., SUDHA REDDY V. R.

ABSTRACT

Classic Bartter syndrome, depending on the severity, presents during childhood or adolescence as failure to thrive and may be incorrectly labelled as protein–energy malnutrition, particularly in children from a low socioeconomic stratum. We encountered a 5-year-old boy who was asymptomatic till the age of 3 years. Despite adequate dietary intake, he was admitted and managed in various hospitals as a case of protein–energy malnutrition. On evaluation, he had unusual features in the form of persistent hypokalaemia and polyuria leading us to suspect a renal tubular disorder. Treatment of the condition resulted in good weight gain and normalization of serum electrolytes.

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INTRODUCTION

Failure to thrive in infants and young children can be due to many causes and may be the only manifestation of an underlying serious systemic disease. Bartter syndrome is an autosomal recessive disorder with a prevalence of 1.2 cases per million.[1] It may present in the neonatal period or early infancy with salt wasting. It can also present with failure to thrive, dehydration and muscle weakness in older children. The latter presentation is similar to that of protein–energy malnutrition with intercurrent infections, which are commonly seen in India. Unless there is a high degree of suspicion, patients may go undiagnosed or may be incorrectly managed for protein–energy malnutrition. Early diagnosis helps in improving the outcome by appropriate management.

THE CASE

A 5-year-old boy presented with a history of fever, vomiting and generalized weakness. In the past 2 years, the child had been admitted to other hospitals for similar complaints and had been treated as grade III protein–energy malnutrition with anaemia. He was born of a third-degree consanguineous marriage, and had an apparently healthy older sister. Maternal polyhydramnios was documented from the fifth month of gestation. He was born as a full-term vaginal delivery, weighing 2 kg. His postnatal period, infancy and first 3 years of childhood were uneventful with normal development, appropriate dietary intake and immunization.

M.V.J. Medical College and Research Hospital, Dandupalya, Kolathur Post, Kolar Highway, Hoskote, Bengaluru 562114, Karnataka, India

PURNIMA SAMAYAM, RAVI CHANDER B., SUDHA REDDY V. R. Department of Paediatrics

Correspondence to PURNIMA SAMAYAM; *drpurnimas@yahoo.com*

His weight at the time of presentation to us was 9.17 kg, height 92 cm (both <3rd centile) and orbitofrontal cortex (OFC) measurement 48 cm. He was febrile with some dehydration and pallor, normal blood pressure, distended urinary bladder and depressed deep tendon jerks. Investigations showed that his haemoglobin was 10 g/dl, the total leukocyte count was 3400/cmm with 80 neutrophils, 18 lymphocytes and 2 eosinophils. His serum sodium was 117 mEq/L, potassium 2.2 mEq/L, urea 34 mg/dl and creatinine 0.4 mg/dl. With treatment, his vomiting subsided and hydration status improved; but the serum sodium was 126 mEq/L, chloride 85 mEq/L and potassium 2 mEq/L. This was further investigated. A blood gas analysis showed metabolic alkalosis (pH 7.580, HCO_3 33.6, PCO_2 35.8, base excess 10.9). The urine output was 10 ml/kg/hour. Urine analysis showed the potassium to be 48.8 (normal <20) mmol/L, chloride 387 (normal 15–40) mmol/24 hours and calcium 171 (normal 50–150) mg/24 hours. As the child was normotensive and had persistent hypokalaemia in the absence of any drug history, an inherited tubular disorder such as Bartter/Gitelman syndrome was considered. His serum aldosterone was 1335.9 (range supine 10–160) ng/L. The serum magnesium was 1.7 mg/dl and calcium 9 mg/dl. Abdominal ultrasound and audiological evaluation were normal. Gitelman syndrome was excluded as his serum magnesium was normal and he had repeated episodes of overt volume depletion. The uneventful neonatal period, absence of nephrocalcinosis and a normal audiological evaluation were consistent with a diagnosis of classic Bartter syndrome (type 3).

The child was started on oral potassium supplements and ibuprofen along with appropriate dietary advice. On follow up, he had good weight gain and his electrolytes became normal with a serum sodium value of 136 mEq/L and potassium of 4.2 mEq/L.

DISCUSSION

In 1962, Bartter *et al*. published a report of 2 children with growth and developmental delay associated with hypokalaemic metabolic alkalosis and normal blood pressure despite high aldosterone production.[2] Bartter syndrome is an autosomal recessive disorder that affects the functioning of the thick ascending limb of the loop of Henle (Fig. 1). Different genetic types of Bartter syndrome are associated with different gene mutations.[3]

Neonatal Bartter syndrome (types 1 and 2) usually present in the newborn period or infancy. There is often preceding maternal polyhydramnios due to foetal polyuria and premature birth. Massive polyuria with life-threatening volume depletion and poor weight gain are seen. Nephrocalcinosis is universal in these types. The classic Bartter syndrome (type 3) phenotype is highly variable. The presentation may be like the typical 'antenatal' variant that manifests in the early neonatal period or the 'classic' variant that is characterized by childhood onset, fatigue, polyuria, polydipsia, salt craving, vomiting, dehydration, short stature and failure to thrive; nephrocalcinosis is absent and hypercalciuria is less severe/absent. Tetany and joint pains may result from chondrocalcinosis. Bartter syndrome type 4 is associated with sensorineural deafness. In contrast, patients with Gitelman syndrome have low serum magnesium levels with hypocalciuria and do not have signs of overt volume depletion.[4] Characteristic 'Bartter facies' has been

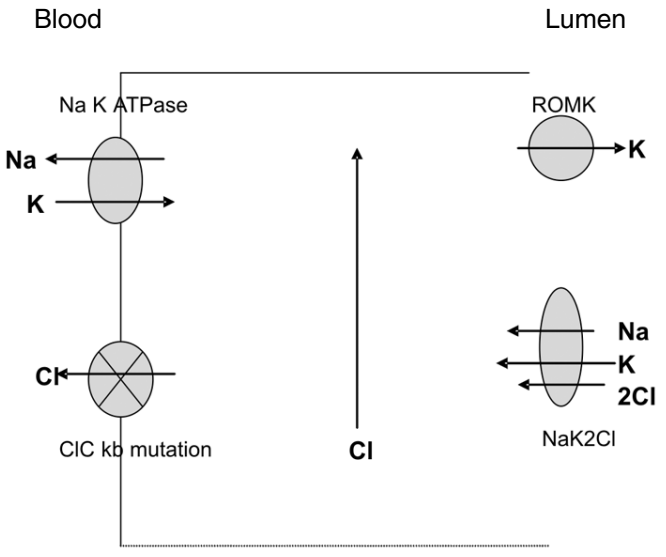

FIG 1. Classical Bartter syndrome is due to mutations in the chloride channel (ClC-kb). Inability of chloride to exit the cell leads to inhibition of sodium–chloride potassium– chloride transporter

described as a triangular thin face, large eyes, prominent ears and a drooping mouth.[5]

Laboratory assessment of patients with Bartter syndrome should include evaluation for hypokalaemia, hypochloraemia and metabolic alkalosis. Hypokalaemia is usually severe (1.5–2.5 mmol/L). Serum renin and aldosterone levels are elevated in all these patients, but their blood pressure is normal.[3] High urine chloride levels with low/normal blood pressure, high aldosterone secretion and high urinary potassium levels are found only with long term diuretic use and Bartter syndrome. Hence, diuretic abuse should be ruled out.[6]

Bartter syndrome presenting as severe failure to thrive in infancy has been reported.[1,7] Maternal polyhydramnios is usually seen in the neonatal forms. It may sometimes be seen in the classical variety,[3] as was seen in this case. In this case, the onset was mild, non-specific and after 3 years of age, with an apparently uneventful early life. Symptoms such as polydipsia, polyuria and salt craving, which are classical pointers to tubular disorders, were not noticed by the parents. In the absence of these pointers, children hailing from a low socioeconomic stratum are managed as protein–energy malnutrition before a diagnosis of the underlying disorder is made. Careful history, physical examination and attention to abnormal electrolyte patterns are hence vital in making a diagnosis.

The treatment includes oral potassium supplements, spironolactone and non-steroidal anti-inflammatory drugs (NSAIDs) such as indomethacin. Treatment may reverse the hypokalaemia and polyuria, and improves growth. If the condition is not diagnosed early, it can cause progressive tubulointerstitial nephritis. Early diagnosis and treatment improves the prognosis. Patients receiving pharmacological treatment have complications such as gastritis/gastric ulcers on long term follow up. There can be progressive deterioration of the glomerular filtration rate in some patients. Hence, surveillance of renal function and gastrointestinal endoscopy has been recommended for them.[8]

Conflict of interest: None stated

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