

## Unusual case of failure to thrive: Type III Bartter syndrome

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### ABSTRACT

Bartter syndrome Type III is a rare autosomal recessive disorder resulting from an inherited defect in the thick ascending limb of the loop of Henle of the nephrons in kidney. The typical clinical manifestations in childhood are failure to thrive and recurrent episodes of vomiting. Typical laboratory findings which help in the diagnosis are hypokalemic metabolic alkalosis, hypomagnesemia and hypercalciuria. We report a case of Type III Bartter syndrome not responding to repeated conventional treatment of failure to thrive.

**Keywords:** Bartter syndrome; failure to thrive; hypercalciuria; hypomagnesemia; hypokalemia

### INTRODUCTION

Bartter Syndrome (BS) is a group of disorders characterized by hypokalemic metabolic alkalosis with hypercalciuria and salt wasting. The condition is named after Dr. Frederic Bartter, who along with Dr. Pacita Pronove, first described it in 1960.<sup>1</sup> BS is associated genetic defects in the loop of Henle transporters affecting sodium, chloride and potassium transport in the ascending limb. There is loss of sodium and chloride, with resultant volume contraction which instead stimulates the rennin-angiotensin II- aldosterone axis. Aldosterone promotes sodium uptake and potassium excretion, exacerbating hypokalemia. It also stimulates hydrogen ion secretion distally (from the distal limb of loop of Henle) affecting acid base balance in the body causing metabolic alkalosis. BS are of five types. It is inherited as an autosomal recessive disorder with the exception of type V which follows autosomal dominant pattern. Types I, II and IV are also called antenatal BS because the onset of illness is usually prenatally. Children with types I and II usually present to clinicians with maternal history of polyhydramnios, prematurity, nephrocalcinosis, polyuria, dehydration, and failure to thrive. Children with type III, the mildest of all BS, also known as classical BS, usually present with salt craving habit, low serum magnesium, dehydration and failure to thrive. Children with Type IV have clinical features similar to that of type I, except that they do not have

nephrocalcinosis but have sensorineural hearing loss instead. The most uncommon BS is of type V, the usual clinical features being low parathyroid hormone level, hypocalcaemia and hypercalciuria.<sup>2</sup> We report a case of BS not responding to conventional treatment of growth failure. We had also taken written consent from the mother for publication of this case report and inclusion of the photograph of the child.

### CASE REPORT

A 14 months old female child presented with history of unable to gain weight since 11 months and recurrent episodes of vomiting since 9 months. There was no history of consanguineous marriage, maternal polyhydramnios or premature birth. Her dietary intake was of adequate calories. There was no constipation. On examination the child looked sick and irritable. There were no obvious dysmorphic features. On anthropometry examination, head circumference for age was 42 cm, weight for age 5.5 kg, length for age 69 cm, all of which were below -3 Z score. There was no pallor, cyanosis, clubbing, icterus or lymphadenopathy. Pulse was 120 beats per minute, respiratory rate 36 per minute, temperature 98° Fahrenheit, blood pressure 95/60 mmHg and capillary refill time was below 3 seconds. Examinations of cardiovascular, respiratory, gastrointestinal and neurological systems were normal. Arterial blood gas

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examination showed metabolic alkalosis with pH of 7.56 which was persistently above 7.45 on repeated examinations. Likewise urinary chloride was elevated (40mEq/L). There was hypokalemia (serum potassium 2.3 mmol/l), hyponatremia (serum sodium 113 mmol/L), hypomagnesemia (serum magnesium 1 mg/dl), normal phosphate level (serum phosphate 3 mg/dl) and hypercalciuria (urinary calcium: creatinine ratio- 0.3). There was also high urinary excretion of sodium (55mEq/L), chloride (59 Eq/L) and potassium (44.2mEq/L). Abdominal ultrasonography was suggestive of Grade II medico-renal disease without evidence of nephrocalcinosis. Results of other investigations such as thyroid function test, echocardiography and Computer Tomography Scan of the brain were within normal limit. Although conformation of diagnosis required demonstration of genetic mutation that encode  $\text{Na}^+/\text{K}^+/\text{2Cl}^-$  transporter<sup>2</sup>, it was not possible in our setting.

Hence, the diagnosis of Bartter Syndrome Type III was made based on clinical findings of multiple episodes of vomiting, failure to thrive, normal blood pressure and supportive laboratory parameters of hypokalemic metabolic alkalosis (chloride resistant- since urinary chloride was above 20 mEq/L<sup>3</sup>), hypercalciuria and hypomagnesemia. The child was then treated with oral indomethacin (1.5 mg/Kg/day in 3 divided doses) along with other supportive management for failure to thrive and discharged. When followed up at 1 month from discharge, there was significant improvement in clinical and laboratory features including weight gain of approximately 25g/kg/day.



Figure 1. Shows the child before treatment. He was thinly built, sunken cheeks, relatively less muscle mass and visible ribs with prominent intercostal muscles.



Figure 2. Shows the child at 1 month after discharge. There is marked improvement in muscle mass, fullness of cheeks, decrease in ribs and intercostals muscles prominence .

## DISCUSSION

BS is a rare inherited defect in the thick ascending limb of the loop of henle of nephrons resulting in various tubular transport abnormalities of the kidney.<sup>4,5</sup> Although, patients with classic BS (Type III) may become symptomatic in the first two years of life, they are usually diagnosed at 6 years of age or even later. Similar to children with BS of neonatal subtype, patients with classic BS also have polyuria, polydipsia, and dehydration; however, they have slightly increased urinary excretion of calcium without developing renal calculi. They also have marked vomiting, dehydration and growth retardation. Although hypomagnesemia has also been reported to occur, it is typically seen in Gitelman Syndrome.<sup>6-8</sup> There is usually associated maternal polyhydramnios. Dysmorphic features present include triangular facies, protruding ears, large eyes and drooping mouth.<sup>9</sup> Older children may have recurrent episodes of polyuria with dehydration, failure to thrive and typical biochemical abnormalities. Urinary calcium levels are characteristically elevated.<sup>10</sup>

The typical features of hypokalemia, metabolic alkalosis, hypercalciuria and normal blood pressure present in our case suggest the child to be of BS. Age beyond infancy, features of dehydration and presence of low serum magnesium suggest it to be of type III. Although hypomagnesemia is also seen in Gitelman Syndrome, early occurrence of illness in infancy and absence of hypocalciuria are against it. Infants of type I or II BS are premature and usually have nephrocalcinosis. Absence

of sensorineural hearing loss and hypocalcemia also decreases possibility of it being type IV or V BS. Hence, based on the obvious clinical and laboratory findings, our patient was of type III BS.

Treatment of Bartter Syndrome is directed at preventing dehydration, maintaining nutritional status and correcting hypokalemia and use of potassium sparing diuretics. Magnesium is supplemented for hypomagnesemia. Indomethacin, a prostaglandin inhibitor, is effective and commonly administered, since BS is associated with increase in the renal excretion of prostaglandin E<sub>2</sub>,<sup>11-12</sup> which instead stimulates release of aldosterone.<sup>13</sup> Therefore, indomethacin would help correct hypokalemia by suppressing aldosterone release. On receiving definite treatment on time, the renal function gets easily corrected,<sup>14</sup> although some may go on to develop end-stage renal disease. Since the serum potassium level normalized with the use of Indomethacin during hospital stay and follow up, we did not give further potassium supplements, spironolactone or ACE inhibitors.

The diagnosis of Bartter syndrome not only helped the child to receive definitive treatment and gain weight during follow up but also became good learning curve for treating pediatricians to think of a rarer diagnosis of failure to thrive in our setup. There have been very few reported cases of Bartter Syndrome in the Indian subcontinent in past.<sup>15</sup> Therefore, our case highlights that a high index of suspicion is required to think of BS while managing child with failure to thrive specially if they are not responding to nutritional correction. In addition, simple and low cost treatment of NSAIDs could lead to remarkable improvement in the general well being of the affected children.

In conclusion, we report a 14 months old female child with inability to gain weight and recurrent episodes of vomiting with normal blood pressure, failure to thrive, normal systemic examination findings, hypokalemic metabolic alkalosis, hypercalciuria and hypomagnesemia suggesting type III BS. Unusual diagnosis of BS needs to be suspected, investigated and treated in all infants with failure to thrive including conventional high calories and protein diet.

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