PSEUDO-BARTTER SYNDROME IN AN INFANT: AS A PRESENTATION OF CYSTIC FIBROSIS

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ABSTRACT

Pseudo-bartter syndrome is characterized by hyponatremic, hypochloremic, hypokalemic metabolic alkalosis without renal tubular pathology. It may be the initial presentation of CF especially in infants. We report a 5 month old baby girl who presents with recurrent episodes of hyponatremic, hypochloremic and hypokalemic dehydration with metabolic alkalosis and failure to thrive. Initial sweat chloride concentration was 12 mEq/L whereas the repeated test revealed sweat chloride concentration of 70mEq/L. The cystic fibrosis mutation analysis revealed E1044G and D1152H compound heterozygosity. CF should be considered in infants presenting with recurrent episodes of hyponatremic, hypochloremic dehydration with metabolic alkalosis.

Kew words: Pseudo-bartter syndrome, children, cystic fibrosis

INTRODUCTION

Cystic fibrosis (CF) is the most common lethal inherited disease in Caucasians and occurs in approximately 1 of 3000 live births. CF is inherited as an autosomal recessive trait with a carrier frequency of 1 in 25. According to CF foundation, about 1000 new cases of CF are diagnosed each year. More than 70% of patients are diagnosed by age two. The major clinical characteristics of CF are progressive lung disease, pancreatic insufficiency and increased sweat electrolyte concentration due to exocrine gland dysfunction. In infancy, it presents typically with combination of failure to thrive and steatorrhea and respiratory symptoms. Less frequently, it can present as pseudo-bartter syndrome characterized by hyponatremia, hypokalemia, and metabolic alkalosis. In this study, we present an infant with history of recurrent hospital admissions due to hyponatremia, hypokalemia and metabolic alkalosis, diagnosed with cystic fibrosis.
CASE REPORT

A 5 month old baby girl presented to pediatric emergency department with vomiting, diarrhea, lethargy and cough. The baby was exclusively breast-fed with poor weight gain. On physical examination, the child was thin, the weight was 4.93 kg (below the third percentile) and the length was 63 cm (between 25th and 50th percentile). On lung exam, diffuse crackles on both sides were appreciated. The rest of the physical examination was unremarkable. Her medical history was only significant for a previous emergency room visit due to vomiting and lethargy which required admission to the ward 2 months ago. During that admission, the extensive laboratory workup was performed including sweat test which was reported as normal. The patient was given IV hydration and discharged home in 4 days. The family history was unremarkable. Laboratory tests were remarkable for the following values; serum sodium: 118 mEq/L, serum chloride: 65 mEq/L, serum potassium: 3.4 mEq/L, serum urea nitrogen of 53 mg/dL, serum creatinine of 0.46 mg/dL, urine sodium of 15.8 mEq/L, urine potassium of 15.8 mEq/L and urine chloride level of 6 mEq/L. Venous blood gas analysis revealed a pH of 7.61, pCO2 of 45 and HCO3 of 44.7 consistent with metabolic alkalosis. The patient was noted to have mild leukocytosis with white cells of 17800/mm3 with 67% of neutrophil predominance. The rest of the laboratory workup including blood glucose level, liver function tests, and stool exam were unremarkable. When we reviewed the patient’s laboratory workup in her previous admission with similar episode, it revealed sodium level of 122 mEq/L, potassium level of 2.6 mEq/L, chloride level of 64 mEq/L, blood urea nitrogen level of 46 mg/dL, creatinine level of 0.53 mg/dL and venous blood gas again consistent with metabolic alkalosis. In this admission chest x-ray revealed peribronchial thickening. The patient was admitted to the ward with diagnosis of dehydration with electrolyte imbalance and bronchopneumonia for IV hydration, electrolyte replacement and antibiotic therapy. The previous sweat test which was performed by pilocarpine iontophoresis method was reported normal (Chloride level of 12 mEq/L). Repeated sweat test with the same method following IV hydration was reported abnormal with chloride level of 70 mEq/L. The third sweat test and cystic fibrosis mutation analysis were ordered. Patient was diagnosed Cystic fibrosis and started on pancreatic enzymes, bronchodilator therapy and postural drainage for chest physiotherapy, and sodium replacement to breast milk. The cystic fibrosis mutation analysis revealed E1044G and D1152H compound heterozygosity.

DISCUSSION

Pseudo-bartter syndrome is characterised by hyponatremia, hypokalemia, hypochloremia with metabolic alkalosis is infrequently reported in infancy. Although biochemical abnormalities were similar to those of Bartter syndrome, there was no pathology in renal tubules in PBS. Cystic fibrosis, surreptitious diuretic use, chronic administration of a chloride-deficient diet, pyloric stenosis, continuous gastric drainage without appropriate electrolyte replacement, cyclic vomiting, congenital chloridorrhea, abuse of laxatives can all cause PBS. In all of these conditions, except diuretic use, the chloride content of urine will be low, and this is contrary to all forms of Bartter syndrome.
It has been suggested that excessive salt loss with sweat predisposes the infants with CF to develop episodes of hyponatremic, hypochloremic dehydration with metabolic alkalosis. Secondary hyperaldosteronism resulting from water and salt losses, increased hydrogen and potassium ions waste via the kidneys. The preceding infections and/or inadequate sodium replacement can aggravate the metabolic alkalosis and electrolyte loss. In the literature, the prevalence of PBS in patients with CF was reported between 12-16.5% 4-5. The infants younger than 6 months of age can present with PBS as a presentation of CF. Pseudo-bartter syndrome was also reported in adolescents and adults with CF in a few studies mostly case reports 14-17. Fustik et al. investigated the incidence of PBS, possible risk factors for its occurrence in children diagnosed with CF before the age of 12 months. The prevalence of PBS was reported as 16.5%. All children with PBS had failure to thrive with history of loose stools and were exclusively breastfed. It was speculated that the hot climate during summer months, overheated houses during winter months, overclothing cause sodium and potassium loss due to excessive sweating in infants with CF. In another study published by Yalçın et al. from Turkey, the prevalence of PBS was 12% and no geographical or seasonal predilection to PBS was observed. They found no significant difference in age, gender, genotype or severity of PBS attacks between infants presented with PBS and diagnosed CF and those with known CF presented with PBS 4.

In our case, the patient with a history of recurrent admissions for similar episodes presented with vomiting, dehydration, electrolyte imbalance with metabolic alkalosis and failure to thrive as reported in the literature 4-5. We can speculate that hot weather, exclusively breast feeding and intercurrent infection were contributory factors aggravating the metabolic alkalosis in our patient. The sweat test is considered the best test to diagnose CF however our patient’s first sweat test was reported normal. We can speculate that the false sweat test was due to either inadequate sample or technical error. The causes of a false negative sweat test are as follows; edema due to hypoproteinemia secondary to pancreatic exocrine insufficiency, low sweat rate, inadequate sample and technical errors 18.

Hyponatremia is defined as serum sodium level of less than 135 mEq/L and is considered severe when the serum level is below 125 mEq/L. The serum electrolyte panel of the children presents with vomiting, diarrhea and dehydration to the pediatric emergency department mostly reveals low serum bicarbonate level, acidosis, low serum glucose level, hypernatremia very rarely severe hyponatremia. Wathen JE et al. evaluated the serum electrolyte panel in patients with dehydration. Out of 182 patients with dehydration, only 2 of them had serum sodium level of 130. Hyponatremia was defined as serum sodium level less than 130 mEq/L in that study 19. In literature, the mean serum sodium level in CF patients with PBS were reported 120-126 mEq/L 4-5. Our patient’s serum sodium level was 118 mEq/L. When we evaluate the patients with severe hyponatremia we certainly should consider CF.

Severe metabolic alkalosis if not treated causes apathy, confusion, cardiac arrhythmias and neuromuscular irritability. It also causes compensatory hypoventilation 20. Therefore early diagnosis and prompt correction with IV hydration in addition to sodium replacement and potassium replacement if necessary is crucial.

Infants with CF loose large amount of sodium in their sweat. Neither human milk nor standard infant formulas provides adequate sodium for CF infants. CF foundation
Pseudo-bartter syndrome in an infant

Evidence-based guidelines recommends 12.5 mEq of sodium from birth to 6 months of age and 25 mEq of sodium in the second half of the first year. Several mutations of the CFTR gene associated with PBS were reported in literature. Our patient had a compound heterozygosity for two mutations, E1044G and D1152H. To our knowledge the genotype found in our patient was not described before and PBS occurrence was not reported either of compound heterozygosity.

We would like to emphasis a few points in this case report. We should consider CF in patients with hyponatremic, hypokalemic dehydration and metabolic alkalosis especially in infants and be aware of the possibility of getting false negative sweat test. If the clinical presentation of the patient is consistent with CF, we should insist for another sweat test and consider mutation analysis.

COMPETING INTERESTS

The author declares that the author has no competing interest.

REFERENCES