Pseudo-Bartter syndrome in children with cystic fibrosis

Mojgan Faraji-Goodarzi

1 INTRODUCTION

Cystic fibrosis (CF) is a genetic disorder with autosomal recessive inheritance pattern due to the mutation in CFTR (cystic fibrosis transmembrane conduction regulator), which is responsible for transferring chloride ions into the epithelial membrane of the organ.1

Cystic fibrosis, due to multisystem engagement, may cause a wide range of symptoms and clinical findings, and therefore, it is found in the differential diagnosis of many childhood conditions.2 One of the clinical manifestations of CF is hypocalcemia metabolic alkalosis, which occurs more often in infants and young children, especially in warm weather conditions, which can result in high levels of chlorine and sodium ions in sweat.

Hypocalcemia metabolic alkalosis along with hyponatremia and hypokalemia is known as pseudo-Bartter syndrome. Biochemical manifestation of Bartter’s syndrome is similar to pseudo-Bartter syndrome, an exception to normal renal tubule in pseudo-Bartter, whereas disturbance of serum electrolytes is due to their excretion through nonkidney source (sweat).3,4 Pseudo-Bartter syndrome is a rare yet common in patients with CF and may occur repeatedly.5

2 CASE REPORT

A 4.5-month-old boy, presenting dry cough since two weeks that did not respond to antibiotics (amoxicillin-clavulanic acid), was admitted to the pediatric intensive care unit due to tachycardia and respiratory distress. He also presented anorexia and weight loss, without any episode of diarrhea and vomiting. The vital signs were as follows: RR = 30, HR = 90, BP = 80/60, and T = 37°C.

He was the first child of the family (no serious medical history of the mothers) and his birth weight was 3.5 kg, whereas at the time of admission he weighed 4.5 kg. The patient was calm during the examination and appeared normal with no sign of dehydration. Sodium electrolytes, blood gas analysis, and CBC were performed, and the patient was treated with fluid therapy and intravenous antibiotics

The test results of patient tests were as follows: PH = 7.60/PCO₂ = 48/HCO₃ = 46.1/BE = 24; Na = 122 mEq/L/K = 2.1 mEq/L/CL = 60 mEq/L/Mg = 1.2 mEq/L.

The patient had hypocalcemia metabolic alkalosis, hypokalemia, and hyponatremia. Urine electrolytes measured were as follows: Na = 67 mEq/L, CL = 63 mEq/L, and K = 14 mEq/L. Transtubular K gradient (TTKG) was found to be 2.5.
Sodium and potassium concentrations were measured after every six hours. Liquid therapy with half saline and 60 mEq/L potassium was prescribed to the patient. Since K urine excretion was <15 mEq/L, the cause of hypokalemia was nonrenal excretion. Barter syndrome was thus not the diagnosis.

Twelve hours after the initiation of the treatment with liquid therapy, Na and K were 136 mEq/L and 3.9 mEq/L, respectively.

The patient responded appropriately to Na and K administration. Serum potassium and chloride levels decreased to 40 mEq/L, and therefore, oral potassium was also administered. Sonography did not show any positive signs of nephrocalcinosis and hypertrophic pyloric stenosis.

In response to respiratory symptoms and underweightness and metabolic alkalosis presented by the patient, sweat test was performed twice. Initially, the sweat chloride and sodium were 58 mEq/L and 60 mEq/L, respectively, whereas, later, the levels of chloride and sodium were increased to 65 mEq/L and 68 mEq/L, respectively.

Two weeks later, tests were repeated: urine Na = 28 mmol/L/ urine K = 11 mmol/L/ urine CL = 16 mmol/L.

Liver enzymes were seen to be increased; however, urea, creatinine, glucose, albumin, potassium, sodium, and magnesium were normal in serum. During first examination, fat drop stool was not seen, but in the next test, fesses were seen with many fat drops, and the Sudan III test showed more than 100 fat drop.

The activity of trypsin was decreased by 1/24, where its normal rate is 1/96. Fecal elastase activity was 20 μg/g (normal > 200), seen as severe decrease in stool elastase.

Due to clinical and laboratory findings, such as positive sweat tests and other signs of metabolic alkalosis in infants, cystic fibrosis (CF) was diagnosed.

The patient was treated with fat-soluble vitamins, chest physiotherapy, antibiotics, MCT oil and pancreatic enzymes (due to gastrointestinal involvement and absorption of the patient), and amniotic nerve fibrosis and was discharged with good general condition.

3 | DISCUSSION

Cystic fibrosis (CF) manifests itself as a symptom of respiratory or digestive tract diseases. In CF, metabolic alkalosis and sodium electrolyte imbalance are also seen, as shown in Figure 1 6,7; therefore, it is important to differentiate it from pseudo-Bartter syndrome; and despite electrolyte test results are normal, kidney tubules dysfunction fails to maintain electrolyte balance. Conversely, in the CF, electrolytes are removed from the sweat, whereas, in the kidney tubules, electrolyte reabsorption occurs.

Pseudo-Bartter syndrome is one of the uncommon causes of metabolic alkalosis, although it occurs commonly in patients with CF. The most common cause of metabolic alkalosis is hypertrophic pyloric stenosis, whereas diuretics, cerebral palsy, and CF are uncommon causes. Pseudo-Bartter syndrome is characterized by hypocalcemia metabolic alkalosis, hyponatremia, and hypokalemia but kidney tubules function is normal. Pseudo-Bartter syndrome occurs in patients with CF for several reasons such as gastroenteritis and inadequate water and salt in the warm weather, leading to exacerbation of electrolyte excretion from the sweat. Patients with CF can compensate for increased electrolyte disturbances by increasing aldosterone secretion or salt intake. Some children are more sensitive to electrolyte disturbances than others, which may be due to excessive sweating and potassium intake. Pseudo-Bartter syndrome may be confused with a simple gastroenteritis or Bartter syndrome.8

Pseudo-Bartter syndrome is more common in the infants (about 3 months) during summers. Nonetheless, cases in adults have also been reported.

**FIGURE 1** illustrates imbalance in electrolytes, as a result of cystic fibrosis and pseudo-Bartter syndrome.
In 9% of children with CF, the first clinical manifestation of the disease is Pseudo-Bartter syndrome and 44% of patients who have had fetal bundle syndrome before the age of one, and premature colonization of Pseudomonas has been found. In patients over one year, 12% of cases have been reported.

Patients with pre-existing Pseudo-Bartter syndrome are diagnosed earlier (3 months compared to one year of age).

In the study by Muna, all patients with CF had hyponatremia in the early episodes of pseudo-Bartter syndrome and presented anorexia and cough before the onset of the disease with hypokalemia syndrome and arrhythmia as the most dangerous complications of this disease. Increased mucosal viscosity in the patient's airways may cause respiratory infections. Likewise, it is seen in other organs, such as the pancreas and biliary tract. Pseudo-Bartter syndrome is also characterized with pulmonary involvement and respiratory symptoms; however, its exact mechanism is unknown. In natural conditions, chloride ion is absorbed from the epithelial cells of the sweat pores and, by activating the sodium channels in the epithelial cells of the sweat duct, sodium re-absorption occurs and sweat is hypotonic. The defect in chloride reuptake prevents the opening of sodium channels and its reabsorption. As a result, large quantities of chloride and sodium ions are excreted in the patient with CF. Any factor that exacerbates sweating in the patient (such as being in a warm environment) will exacerbate the elimination of sodium and chloride ions from sweat. The result of this effect is the reduction of the volume of extracellular fluid that results in secondary hyperaldosteronism and metabolic alkalosis and activation of the renin-angiotensin system. On the other hand, this will accelerate the recovery of bicarbonate and the removal of potassium and hydrogen ions from the urine. Pseudo-Bartter syndrome treatment is essentially electrolyte modification and hydration.

In some developing countries, CF neonatal screening is not taken; for example, in some parts of India, children who were admitted with metabolic diarrhea and alkalosis are treated as CF even without a sweat test.

Our case report signifies the importance of critical diagnosis in patients with CF, particularly for metabolic abnormalities and providing timely treatment to alleviate the symptoms.

CONFLICT OF INTEREST

The authors deny any conflict of interest in any terms or by any means during the study. All the fees provided by Research Center Fund and deployed accordingly.

AUTHOR CONTRIBUTION

Dr Mojgan Faraji-Goodarzi: conceptualized and designed the study, drafted the initial manuscript, reviewed and revised the manuscript, designed the data collection instruments, collected data, carried out the initial analyses, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

ORCID

Mojgan Faraji-Goodarzi https://orcid.org/0000-0002-7494-2557

REFERENCES

1. Leoni GB, Pitzalis S, Podda R, et al. A specific cystic fibrosis mutation (T338I) associated with the phenotype of isolated hypotonic dehydration. J Pediatr. 1995;127(2):281-283.
2. De Gregorio F, Majo F, Buonpensiero P, et al. A missing early diagnosis of cystic fibrosis associated with a milder phenotype. Dig Liver Dis. 2008;40(10):A88.
3. Vilotijević-Dautović G, Stojanović V. Pseudo-Bartter's Syndrome in patients with cystic fibrosis: a case series and review of the literature. Srp Arh Celok Lek. 2015;143(11–12):748-751.
4. Ciki K, Esref S, Birbilen A, et al. Clinical features of pseudo-Bartter syndrome in cystic fibrosis. Eur Respir Soc. 2017;50 (suppl 61).
5. Salvatore D, Tomaiuolo R, Abate R, et al. Cystic fibrosis presenting as metabolic alkalosis in a boy with the rare D579G mutation. J Cyst Fibrosis. 2004;3(2):135-136.
6. Bates CM, Baum M, Quigley R. Cystic fibrosis presenting with hypokalemia and metabolic alkalosis in a previously healthy adolescent. J Am Soc Nephrol. 1997;8(2):352-355.
7. Al-Ghimlas F, Faughnan ME, Tullis E. Metabolic alkalosis in adults with stable cystic fibrosis. Open Respir Med J. 2012;6:59-62.
8. Kennedy J, Dinwiddie R, Daman-Willems C, Dillon M, Matthew D. Pseudo-Bartter's syndrome in cystic fibrosis. Arch Dis Childhood. 1990;65(7):786-787.
9. Dahabreh MM, Najada AS. Pseudo-Bartter syndrome, pattern and correlation with other cystic fibrosis features. Saudi J Kidney Dis Transplant. 2013;24(2):292.
10. Kintu B, Brightwell A. Episodic seasonal pseudo-Bartter syndrome in cystic fibrosis. Paediatr Respir Rev. 2014;15:19-21.
11. Priou-Guesdon M, Malinge M-C, Augusto J-F, et al. Hypochloremia and hyponatremia as the initial presentation of cystic fibrosis in three adults. *Ann Endocrinol*. 2010;71(1):46-50.

12. Yalcin E, Kiper N, Doğru D, Özçelik U, Aslan AT. Clinical features and treatment approaches in cystic fibrosis with pseudo-Bartter syndrome. *Ann Trop Paediatr*. 2005;25(2):119-124.

13. Beckerman RC, Taussig LM. Hypo-electrolytemia and metabolic alkalosis in infants with cystic fibrosis. *Pediatrics*. 1979;63(4):580-583.

How to cite this article: Faraji-Goodarzi M. Pseudo-Bartter syndrome in children with cystic fibrosis. *Clin Case Rep*. 2019;7:1123–1126. https://doi.org/10.1002/ccr3.2180