Pseudo-Bartter's Syndrome Associated With Cystic Fibrosis

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ABSTRACT

Cystic fibrosis is an autosomal recessive inherited generalized disorder of exocrine gland function that results in abnormal mucus production. There is a tendency in infants with cystic fibrosis to develop episodes of hyponatremic, hypochloremic dehydration with metabolic alkalosis and elevated plasma renin and aldosterone levels which are the biochemical picture of the pseudo-Bartter's syndrome. Here in, we report a 48 day old boy with Pseudo-Bartter's syndrome associated with cystic fibrosis and we emphasized the importance of the salt supplementation in these patients.

• ***Key Words:*** *Cystic fibrosis, Pseudo-Bartter, salt supplementation* **Nobel Med 2009; 5(1): 43-45**

ÖZET

KİSTİK FİBROZİSE BAĞLI PSEUDO-BARTTERS SENDROMU

Kistik fibrozis, egzokrin bez fonksiyon bozukluğu sonucu anormal mukus üretimi ile sonuçlanan otozomal resesif kalıtımlı bir hastalıktır. Kistik fibrozisli süt çocuklarında, Bartter Sendromu varyantı (Psödo-Bartter Sendromu) olarak bilinen, metabolik alkaloz ile birlikte hiponatremik, hipokloremik dehidratasyon ataklarıyla giden, artmış renin ve aldosteron düzeylerine rastlanır.

Biz burada, kistik fibrozis ile birlikte Psödo-Bartter sendromlu 48 günlük bir erkek bebek olgu bildirdik ve bu hastalarda tuz desteğinin önemini vurgulamak istedik.

• **Anahtar Kelimeler:** Kistik fibrozis, Psödo-Bartter, tuz desteği **Nobel Med 2009; 5(1): 43-45**

INTRODUCTION

Bartter's syndrome, is a rare inherited disorder characterized by growth deficiency, potentially resulting in short stature, muscle weakness, cramps, and/or loss of potassium from the kidneys (renal potassium wasting) and present with a history of failure to thrive, anorexia, vomiting, polyuria and hypotonia. Hypokalemia is almost always accompanied by hypochloremia and metabolic alkalosis.[1] Cystic fibrosis (CF) is an autosomal recessive disease caused by defects of the cystic fibrosis transmembrane regulator (CFTR) gene. Cystic fibrosis is also one of the disorders in which the metabolic findings may mimic those of Bartter's syndrome, so-called pseudo-Bartter's syndrome.[2] In this study, we present a case of cystic fibrosis with pseudo Bartter's syndrome.

CASE REPORT

A 48-day-old boy who was the third child of the second degree consanguineous (cousin) parents was admitted to our hospital because of poor feeding, troublesome cough, fever, vomiting and diarrhea. On physical examination, his weight was 4230 grams (10th percentile), his height was 60 centimeters (90th percentile), and head circumference was 39 centimeters (50th percentile). Respiratory system oscultation was normal, there was a 1/6 grade systolic murmur at the mesocardiac region. Suction reflex was depressed. On laboratory examination, leukocytosis (total white blood cell count: 31000/mm^3, peripheral smear: 60% polimorphonuclear leukocyte, 32% lymphocyte, and 8% band neutrophill) was detected. His serum electrolyte values included sodium 125 mmol/L, potassium 2.1 mmol/L and chloride 72 mmol/L. His urine electrolytes were as follows: sodium 16 mmol/L, potassium 13.4 mmol/L and chloride 8 mmol/L. Arterial blood gases showed metabolic alkalosis (pH 7.65, standard bicarbonate 34 mmol/L). Sweat chloride were 97 mmol/L and 93 mmol/L, respectively in two different measurements in two weeks interval. Immunoreactive tripsinogen level was detected as 45.8 ng/ml (in normal <50 ng/ml) and mutation analysis showed R117H/7T polymorphism (Non-classic cystic fibrosis). Plasma renin activity was measured as 20 ng/ml/h (normal activity is <16 ng/ml/h) and serum aldosteron level detected as >400 pg/ml (normal range is 3.8-31.3 pg/ml). In this clinical and laboratory pictures, diagnosis of cystic fibrosis, pseudo-Bartter's syndrome and suspected late neonatal sepsis were made. Vancomycin and meropenem were administered after blood culture was taken for suspected late neonatal sepsis and withdrawn at 10th day because of the negative blood culture and negative C-reactive protein. His electrolytes were regulated intravenously. Treatment with pancreatic supplements and chest physiotherapy were started. After 7 days of intravenous antibiotics administration and intravenous fluid and electrolyte replacement, his general condition improved and his serum electrolytes and acid-base status returned to almost normal levels (sodium 138 mmol/L, potassium 2,7 mmol/L, chloride 95 mmol/L, pH 7.53, standard bicarbonate 34 mmol/L). Oral supplements of sodium chloride and potassium chloride were started. He is now 4 months old and he remains on oral pancreatic supplements and chest physiotherapy.

DISCUSSION

Cystic fibrosis is an inherited multisystem disorder of children and adults, characterized chiefly by obstruction and infection of airways and by maldigestion and its consequences. Infants with cystic fibrosis can develop episodes of hyponatremic, hypochloremic dehydration with metabolic alkalosis and called as pseudo-Bartter's syndrome.

Pseudo-Bartter's shows presents the same clinical and biological characteristics as those of Bartter syndrome but without primary renal tubule abnormalities. In our patient, laboratory findings showed hypochloremic, hypokalemic metabolic alkalosis with normal urine electrolytes. In addition to cystic fibrosis, piloric stenosis, administration of thiazid diuretics, gastric drainage and chloride-losing diarrhea can lead to biochemical picture of low serum potassium, low serum chloride accompained by a metabolic alkalosis; so it is important to make a differential diagnosis of cystic fibrosis from these clinical conditions.

It has been suggested that the two principal factors contributing to the development of metabolic alkalosis are an increase in sodium delivered to the distal renal tubule and increased reabsorption of sodium in the distal tubule with exchange for potassium and hydrogen ions.[2] In cystic fibrosis, chronic loss of sodium and chloride ions in the sweat, predisposes young children to salt depletion episodes, especially during episodes of gastroenteritis and during warm weather.[3]

In this case, we detected high renin and aldosteron level (plasma renin activity was measured as 20 ng/ml/h and serum aldosteron level detected as >400 pg/ml) and we speculated that secondary aldosteronism was due to the increased renin release, resulting from depletion of the extracellular fluid volume caused by the excessive loss of salt in the sweat. Hyponatremia is common with cystic fibrosis in only breast feeding infants, especially during summer months. To avoid →

electrolyte depletion, 2-4 mmol/kg salt supplementation must be given daily to these patients. More than 1500 CFTR polymorphisms are associated with the cystic fibrosis syndrome. The most prevalent mutation of CFTR is the deletion of a single phenylalanine residue at aminoacid 508 (△F508).[4] One mutation that generates debate in the CF newborn screening community is R117H, a substitution of arginine for histidine at the 117th position in the CF transmembrane conductance regulator (CFTR) protein, which is in a membrane-spanning domain.[5] R117H is a missense mutation in exon 4 that reduces single-channel conductance and reduces chloride-ion transport[4] and mutation analysis of our patient showed R117H/7T polimorphism (Non-classic cystic fibrosis).

We concluded that cystic fibrosis must be considered in differential diagnosis in the in fants with hypochloremic, hypokalemic metabolic alkalosis with Bartter's syndrome and detection of urine electrolytes, sweat test and mutation analysis are the important laboratory works in differential diagnosis.

RESULTS

In the light of the present experience, we can emphasize the importance of the salt supplementation in cystic fibrosis patients with pseudo-Bartter's syndrome during episodes of gastroenteritis and during warm weather, to avoid electrolyte imbalance and hypochloremic alkalosis.

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REFERENCES

1 Rodriguez J.Tubular disorders of electrolyte regulation. In: Barratt TM, Avner ED, Harmon WE, eds. Pediatric Nephrology.-4th Edition. Lippincott Williams and Wilkins press; Pennsylvania 1999: 546.

2 Devlin J, Beckett NS, David TJ. Elevated sweat potassium, hyperaldosteronism and pseudo-Bartter's syndrome: a spectrum of disorders associated with cystic fibrosis. J R Soc Med 1989; 82 Suppl 16: 38-43.

3 Boat TF, Acton JD. Cystic fibrosis. In: Kliegman RM, Behrman RE, Jenson HB, Stanto BF, eds. Nelson textbook of pediatrics. -18th edition.Saunders-Elsevier press; Philadelphia, 2007: 1804-1808.

4 O'Sullivan BP, Zwerdling RG, Dorkin HL, Comeau AM, Parad R. Early pulmonary manifestation of cystic fibrosis in children with the Delta F508/R117H-7T genotype. Pediatrics 2006; 118: 1260-1265.

5 Sheppard DN, Rich DP, Ostedgaard LS, et al. Mutations in CFTR associated with mild-disease form Cl-channels with altered pore properties. Nature 1993; 362: 160-164.