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CASE REPORTS

# CYSTIC FIBROSIS IN AN INFANT PRESENTING WITH FEATURES OF PSEUDO BARTTER'S SYNDROME

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**ABSTRACT**

Cystic fibrosis (CF) is a progressive, genetic disease that causes persistent lung infections and limits the ability to breathe over time. Even though more than 1000 mutations have been identified in the cystic fibrosis transmembrane regulator (CFTR) gene, the data from India is limited. Facilities for diagnosis of CF is not easily available across various parts of India even today. A 3 months old male infant presented with severe metabolic alkalosis, hyponatremia and hypokalemia to our hospital with failure to thrive. The clinical presentation was similar to that of Bartter's syndrome and a diagnosis of CF was confirmed only through genetic analysis with mutations of compound heterozygosity c.1029delC (p.C343) in exon 8 and c.335C>T (p.S1118F) in exon 20 of CFTR gene.

**ARTICLE HISTORY**

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## Introduction

Cystic fibrosis (CF) is an autosomal recessive multisystem disease with significant morbidity and mortality in all parts of the world caused by a large number of mutations in the cystic fibrosis transmembrane regulator (CFTR) gene on chromosome 7. Recent review of all reported cases of CF in literature indicate that CF is far more common in people of India/ Indian origin than previously thought but is under diagnosed or missed in the majority of cases. (1) The type of mutations and their distribution varies widely between different countries and/or ethnic groups. It also needs to be emphasized that easy access for diagnosis through genetic screening in India is still limited. (2) We present a 3 months old boy who had severe metabolic alkalosis, hyponatremia and hypokalemia suggestive of Bartter's syndrome but was diagnosed as CF only on genetic testing.

## Case Report

A 3 months old male infant born of non-consanguineous marriage being exclusively breastfed, presented with two days history of cough, fever and feeding difficulty. He also had diarrhea one day prior to admission. Clinical examination revealed inadequate weight gain (birth weight 2.9 kg and only 3.3kg at admission) and respiratory distress. The baby was lethargic, febrile and dehydrated. The vital parameters recorded were, heart rate 128/min, respiratory rate58/min with chest retractions and capillary filling time more than 2 seconds. Respiratory system examination revealed tachypnea, equal air entry and no adventitious sounds. Other systems were normal. Investigations revealed severe metabolic alkalosis with hyponatremia and hypokalemia. Blood pH was 7.56, pCO2 - 22.2 mmHg, pO2 - 126mmHg, HCO3- was 29.1 mEq/L, serum potassium was 2.5mmol/L and serum sodium was 122mEq/L. Serum urea was 81mg/dL and creatinine was 0.6mg/dL. Urine creatinine levels were 10.9 mg/dl and urine potassium was 14.58mmol/L. Twenty-four hours urine sample showed low magnesium (5mg/24hrs). Chest X-ray and ultrasound (USG) abdomen was normal. He was managed with intravenous (IV) fluids, electrolyte corrections, oxygen and antibiotics. Based on the above presentation, a clinical diagnosis of Bartter's syndrome was suspected. He was started on spironolactone and oral potassium supplements. Mother's and child's blood was sent for genetic test for Bartter's syndrome. A whole exome screening of the CFTR gene was done at Centogene AG, Germany. Genetic analysis revealed mutations, c.1029delC (p.C343) in exon 8 and c.335C>T (p.S1118F) in exon 20 of CFTR gene in this infant in a compound heterozygous state. (3,4) Such compound heterozygous mutations in CFTR have already been implicated in cystic fibrosis, though not reported in scientific literature in Indian scenario. Validation of the variants in the proband and mother was done by Sanger sequencing, however segregation analysis could not be completed as father's sample was not available. Clinical findings observed in the proband were in accordance with cystic fibrosis. These variants were interpreted to be pathogenic for the clinical findings observed in the infant. The infant is currently being treated and managed for CF and has been hospitalized few times for repeated respiratory infections.

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## Discussion

In infancy, CF presents typically with combination of failure to thrive, steatorrhea and respiratory symptoms. Less commonly, it can also present as Pseudo-Bartters Syndrome (PBS) characterized by hyponatremia, hypokalemia, hypochloremia and metabolic alkalosis without renal tubular pathology (5,6). The frequency of ΔF508 mutation in Indian children with classical CF is reported to be between 19-44 percent. (7,8) Mutations 1161delC, 3849>10kbC-T and S549 N have been reported as other common mutations in Indian population beside ΔF508. (9,10) Our case report is in accordance with this finding though the compound mutations identified in our infant has not been cited in the Indian population as observed in the cited mutations list of CFTR gene in the above study. (11) In literature, the majority of children with CF and PBS are diagnosed around six months of age. (12) In CF, the excessive loss of sodium, chlorine and water through sweat can condition hyponatremia and hypochloremic dehydration, which results in reduced glomerular filtration and activates the renin-angiotensin-aldosterone system, which in turn leads to an increase in the reabsorption of sodium and potassium without affecting tubular excretion, known as PBS. (13) PBS is common in patients with CF, and it should be kept in mind in any patient with hypotonic dehydration and metabolic alkalosis. (14) CF is a clinical diagnosis, supported by genetic testing and the demonstration of abnormalities of CFTR function. A sweat test performed in a reliable laboratory is still a good measure of CFTR function in most cases. A good deal of clinical research remains to be done to understand the role of the sweat test for the diagnosis of CF in the genomic era. (15) We would like to conclude that it is worthwhile for clinicians to consider the possibility of cystic fibrosis in infants presenting with Pseudo Bartter's syndrome features.

## Compliance with Ethical Standards

**Funding:** None

**Conflict of Interest:** None

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