*Case Report*

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# Congenital Chloride Diarrhea: A Case Report

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## Abstract

***Objective:*** Congenital chloride diarrhea (CCD) is a rare autosomal recessive disorder of intestinal chloride absorption. Pathognomonic features consist of watery diarrhea, failure to thrive, dehydration and hypokalemic hypochloremic metabolic alkalosis.

***Case Presentation:*** This is the report on an 8-month old Iranian girl with severe and complicated course of CCD and poor response to current treatment. In addition, she had a renal tubular defect in uric acid handling, resulted in persistent hyperuricosuria and hypouricemia.

***Conclusion:*** Specific characteristics of CCD in our population need additional investigation. But, it is recommended to consider CCD in any patient with severe resistant diarrhea to prevent its irreversible and long term organ damage.

***Key Words:*** Congenital chloride diarrhea, Metabolic alkalosis, Hypokalemia, Hypochloremia, Hyperuricosuria

## Introduction

Congenital chloride diarrhea (CCD) is a genetic disorder caused by a defect in Cl/HCO3 exchanger in terminal ileum and right colon[1,2]. It was first reported by Gamble et al and Darrow in 1945[2]. Currently, about 250 cases have been reported in literature. It is more common in Saudi Arabia, Kuwait, Finland and Poland[3].

CCD begins in fetal life. Delayed treatment leads to complications such as failure to gain weight, neurodevelopemental delay, and renal damage[1]. In this article, a severe and intractable case of CCD, resistant to recommended treatments is presented.

## Case report

The patient was an 8-month old girl admitted for intractable seizures. Parents were relatives, with no history of familial disorders. She was born prematurely (birth weight: 2300g) with a

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history of polyhydramniosis (PHA). Dilatation of intestinal loops was reported in prenatal ultrasonography. In addition to delayed meconium passage, she experienced constipation and intractable vomiting in neonatal period. Rectal biopsy was negative for Hirschsprung's disease at that time and gastroesophageal reflux was detected by barium swallow. She experienced severe watery diarrhea since the last days of neonatal period.

In her first visit at the age of 8 months, she had severe malnutrition (Weight: 2500g), dehydration, abdominal distension and neurodevelpoemental delay. Blood pressure was 70/50 mmhg. The urine output was 1-1.5 cc/kg/d. Serum electrolytes: sodium 117, potassium 1.6, chloride 65, calcium 9, phosphor 4, and magnesium 2.1 meq/L. Other laboratory findings included BUN 55, creatinine 0.7, uric acid 2.4 mg/dl, SGOT 138 and SGPT 84 IU. Renin level was more than 50 ng/ml and aldosterone more than 1000 pg/ml. Sweat test was negative in 3 measurements. Metabolic alkalosis was detected in arterial blood gas (pH 7.50; HCO3 38 meq/L).

Urinalysis revealed massive proteinuria. Urine sodium was 7, potassium 20, chloride 3 meq/L. Calcium output in urine was 4 mg/kg/d and urine uric acid 12 mg/dl. Stool was acid with normal trypsin activity; the levels of sodium, potassium, cholroide and bicarbonate in stool were 50, 40, 95 and 5 meq/L, respectively. No reducing substance or fat droplet was detected in stool examination.

Abdominal ultrasound showed thickened intestinal loops. Gastrointestinal series imaging was normal except for slow transit time.

These findings were in favour of CCD as the leading cause. Discontinuation of oral intake had no effect on stool volume. Treatment began with sodium and potassium chloride, omeprazole and nutritional supports. But the patient was resistant to recommended treatments, with poor weight gain, periodic metabolic alkalosis, repeated bouts of dehydration and hypokalemia. Finally, she died of a severe pneumonia in 18 months of age after 10 months of close follow- up.

## *Discussion*

Our patient was a case of intractable watery diarrhea with metabolic alkalosis. There are a few disorders characterized by intractable diarrhea in infancy, such as congenital glucose-galactose malabsorption and congenital sodium diarrhea. The former presents with metabolic acidosis, hyper-natremia and acidic stool containing sugar, and the latter has metabolic acidosis, and normal or slightly alkalotic stool[4,5]. These laboratory findings were contrary to our patient, who had hyponatremia, metabolic alkalosis and acidic stool.

Metabolic alkalosis could present in Bartter syndrome, characterized by hypo-kalemic hypochloremic alkalosis. Although, patients present during infancy, they do not experience intractable persistent watery diarrhea as CCD[6]. One of the other causes of metabolic alkalosis is cystic fibrosis. Sweat test and steatorrhea were negative in our patient and trypsin activity was normal[7].

CCD is an uncommon hereditary disorder characterized by severe watery diarrhea and metabolic alkalosis. It is caused by a defect in sodium independent Cl/HCO3 exchanger[8,9]. The result is a defect in intestinal chloride absorption and watery diarrhea throughout the life, resistant to withdrawal of oral intake [5]. Patients are born premature with prenatal PHA and dilated intestinal loops due to intra uterine diarrhea[10,11,12]. In neonatal period, intestinal obstruction, and distented abdomen may lead to rectal biopsy for excluding hirschprung disease[1,13], as our patient. Other presentations include malnutrition and failure to weight gain, hypokalemic hypochloremic metabolic alkalosis and dehydration. Diagnosis is made by high stool chloride content, more than 90 meq/L (normal values: 6-17), which is higher than the sum of fecal sodium and potassium[10].

Clinical course may be complicated by multiple organ damages. One of them is neurodevelopemental delay and recrrent seizures[10] due to metabolic derangements and impact of malnutrition on brain development.

The other is renal involvement. Prolonged dehydration leads to arteriolar changes, glomerular hyalinosis, diffuse sclerosis,

proteinuria and reduced renal function[14]. Renal hypoplasia, nephrocalcinosis and rare glomerulonephritis has also been reported in these patients[2].

It is expected that volume depletion leads to decreased urate excretion and hyperuricemia. But, the patient had persistent hypouricemia and uricosuria, which seems to be a primary tubular defect in uric acid handling. To our literature review, this complication has not been reported in CCD.

Malnutrition may induce further derangements of liver functions as our patient, because energy is required for a number of hepatic synthesis, storage and detoxification functions[15]. In addition, malnutrition may be complicated by recurrent infections due to acquired immune deficiency state. Our patinet finally died of a severe and resistant pneumonia.

On the other hand, prognosis has been reported appropriate in CCD with current treatments, and normal growth and intelligence could be expected in these patients[8,16]. But, the clinical course of our patient was protracted with poor response to current treatments, which suggests a severe penetration of its gene in this Iranian child. We need additional reports to confirm the characteristics of CCD in our population. Therefore, it is recommended to have CCD in mind as the leading cause of any severe resistant diarrhea to prevent its irreversible and long term organ damage.

## Conclusion

Clinical presentation of CCD could be different throughout the world. Specific characteristics of CCD in our population need additional investigation. But, it is recommended to consider CCD in any patient with severe resistant diarrhea to prevent its irreversible and long term organ damage.

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