THE INJECTOR 2022;1(1):40-43

Case Report

Congenital chloride diarrhea as a cause of congenital diarrhea: A case report

Yunus Coşar[1], Sibel Yavuz[2]

[1]Adıyaman University Faculty of Medicine, Department of Pediatrics, Adıyaman, Turkey

[2]Adıyaman University Training and Research Hospital, Department of Pediatric Gastroenterology, Adıyaman, Turkey

ORCID IDs of the authors

YC: https://orcid.org/0000-0002-9395-7156

SY: https://orcid.org/0000-0002-6768-238X

Correspondence

Author: Sibel Yavuz

Address: Adıyaman University Training and Research Hospital, Adıyaman, Turkey

Phone: +90 416 216 10 15

e-mail: sibel_5163@hotmail.com

Received: 1 March 2022
Revised: 6 March 2022
Accepted: 6 March 2022

Abstract

Congenital chloride diarrhea (CCD) is a rare cause of neonatal-onset diarrhea, which is associated with hyponatremia, hypochloremia and metabolic alkalosis. Despite its rare occurrence, CCD should be kept in mind in patients presenting with symptoms of congenital diarrhea. Here, a case of CCD diagnosed in a 12-month-old female patient, based on high fecal chloride concentration and genetic analysis is presented.

Keywords: Diarrhea, child, dehydration

 DOI: http://doi.org/10.5281/zenodo.6501661

INTRODUCTION

Congenital chloride diarrhea (CCD) is a rare, autosomal recessive disorder characterized by high fecal chloride concentration and chronic diarrhea. CCD is caused by mutations in the solute carrier family 26, member 3 (SLC26A3) gene, which disrupt intestinal $Cl^-/HCO3^-$ exchange and result in chloride-rich intractable diarrhea with neonatal onset characterized by hypochloremia, hypokalemia and metabolic alkalosis (1,2). The clinical course of the disease varies with age. In this report, a case of CCD as a rare cause of congenital diarrhea is presented.

CASE REPORT

A twelve-mount-old baby girl with a birth weight of 1950 grams who was born by cesarean section at 30 weeks of gestation to a 29-year-old mother (gravida 3, para 2) was referred with complaints of diarrhea and impaired oral intake which persisted since the first postnatal week. From her history, it was learned that she had watery, yellow colored stools 10-12 times a day that started after birth. The patient had a history of premature birth, polyhydramnios, and frequent hospitalizations due to her ongoing symptoms. On anthropometric measurements, her body weight and height were below the 3rd percentile. Physical examination showed signs of moderate dehydration, and systemic assessment findings were normal. Laboratory investigations showed Hb of 8.9 g/dl, WBC count of 12,740/mm^3 and platelet count of 485,000/mm^3. Arterial blood gas tests showed metabolic alkalosis, with a pH of 7.58, HCO_3 of 39 mEq/l, and PCO_2 34 mmHg. Serum electrolyte values were: Sodium 126 mEq/l, Potassium 2.9 mEq/l, Chloride 69 mEq/l (Table1). Investigations for the etiology of chronic diarrhea of the patient revealed: fecal sodium 100 mEq/L, fecal potassium 10 mEq/L, fecal chloride 95 mEq/L, fecal pH 6 (Table 2). Fecal reducing substances were negative, stool microscopy was normal and there was no growth of pathogens in fecal culture. Thyroid function tests, serum immunoglobulin levels and sweat test were normal, and celiac disease antibodies were negative. Regarding food allergy, total IgE was normal and specific IgE was negative. Her parents reported that the patient received a preliminary diagnosis of Bartter syndrome and has been followed at an external healthcare facility. Considering the onset of diarrhea immediately after birth and the presence of hypochloremic metabolic alkalosis, genetic testing was performed to confirm the probable diagnosis of CCD. Subsequently, a homozygous mutation in the SLC26A3 gene was detected on genetic analysis. Oral sodium chloride and potassium chloride supplementation was started. Currently, the patient is 36 months old, weights 13.3 kg and is being followed as an outpatient. Written consent was obtained from the parents of the patient participating in this study.

Table 1: Laboratory parameters of the patient

Parameters	Hgb (g/dL)	WBC ($X10^9$/L)	Plt ($X10^9$/L)	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	pH	HCO3 (mEq/L)	PCO2 (mmHg)	Sweat Cl (mmol/L)
Results	8,9	12,74	485	126	2,9	69	7,58	39	34	24

 DOI: http://doi.org/10.5281/zenodo.6501661

Table 2: Laboratory results of the fecal sample

Parameters	Fecal Na (mEq/L)	Fecal K (mEq/L)	Fecal Cl (mEq/L)	Stool microscopy
Results	**100**	**10**	**95**	Normal

DISCUSSION

CCD was first described by Gamble and Darrow in 1945. CCD is a rare autosomal recessive genetic disorder caused by mutations in the SLC26A3 gene. Consanguineous marriage is the most important factor for the occurrence of CCD. Intestinal $Cl^-/HCO3^-$ exchange is impaired as a result of mutations in the SLC26A3 gene. Infants affected by CCD often present with profuse watery diarrhea, abdominal distention and recurrent vomiting episodes in the first hours of life (3). CCD is characterized by chronic secretory diarrhea resulting in polyhydramnios, dilated intestinal loops and prematurity prenatally, and lack of meconium, dehydration, hypoelectrolytemia, hyperbilirubinemia, abdominal distention and failure to thrive in the immediate postnatal period (4). The clinical diagnosis is based on the history, characteristic metabolic abnormalities and excessive fecal chloride concentrations. Signs and symptoms are usually confused with other conditions such as cystic fibrosis and Bartter syndrome. In addition to clinical history, urine and sweat chloride levels aid in the differential diagnosis of these diseases (5-7). In infancy, watery diarrhea often goes unnoticed in because the stool in diaper looks like urine, resulting in misdiagnosis or delayed diagnosis. In patients with suspected CCD, genetic testing is required to confirm the diagnosis (8). CCD is among the leading causes of diarrhea associated with metabolic alkalosis. In CCD, Cl^-/HCO_3^- exchange mechanism is either lost or defective, resulting in impaired intestinal chloride absorption. This causes increased fecal excretion of chloride and hypochloremia occurs in patients. The defect in HCO_3^- secretion causes metabolic alkalosis (2, 8). High renin and aldosterone, hypokalemia and metabolic alkalosis may also be associated with Bartter syndrome. As a matter of fact, CCD may be misdiagnosed as Bartter or pseudo-Bartter syndrome (6). Hyponatremia and hypochloremic and hypokalemic metabolic alkalosis were also present in our patient. The primary goal of CCD treatment is to reduce the severity of diarrhea and prevent its complications. Correction of electrolyte and acid-base balance is an important treatment method but diarrhea is often difficult to treat. In the early neonatal period, the management of CCD involves gradual switch from intravenous therapy to oral rehydration therapy. For the maintenance treatment of the disease, KCl and NaCl should be used together in order to avoid life-threatening complications. Failure to diagnose and treat the condition early results in chronic dehydration episodes, recurrent bowel infection, fluid and electrolyte imbalance and eventually retarded growth and development. In addition, the activation of renin-aldosterone system causes various complications including renal involvement, chronic kidney disease, hyperuricemia and male infertility (3). There is evidence that proton-pump inhibitors (PPIs) reduce gastric chloride secretion and reduce the severity of metabolic alkalosis (9). Moreover, some case reports suggest that butyrate may be effective in reducing the severity of CCD (10). Butyrate limits chloride secretion by inhibiting the activity of the $Na^+K^+2Cl^-$ cotransporter.

CONCLUSION

In conclusion, early diagnosis and treatment are crucial to ensure normal growth and development and to prevent other severe complications of CCD.

Informed consent: The author stated that the written consent was obtained from the parents of the patients in the study.

 DOI: http://doi.org/10.5281/zenodo.6501661

Conflict of interest: The author declares that there is no conflict of interest.

Financial disclosure: No funding was received in support of this study.

Peer-review: Externally peer-reviewed.

Authorship contributions: Concept, Design, Supervision: YC - Funding, Materials, Data collection &/or processing, Analysis and/ or interpretation, Literature search, Writing and Critical review: SY

References

1.Iijima S, Ohzeki T. A case of congenital chloride diarrhea: information obtained through long-term follow-up with reduced electrolyte substitution. Clin J Gastroenterol. 2008;1(1):28-31.

2.Holmberg C. Congenital chloride diarrhoea. Clin Gastroenterol. 1986;15(3):583-602.

3.Wedenoja S, Höglund P, Holmberg C. Review article: the clinical management of congenital chloride diarrhoea. Aliment Pharmacol Ther. 2010;31(4):477-485.

4.Kirkinen P, Jouppila P. Prenatal ultrasonic findings in congenital chloride diarrhoea. Prenat Diagn. 1984;4(6):457-461.

5.Shamaly H, Jamalia J, Omari H, Shalev S, Elias N. Congenital chloride diarrhea presenting in newborn as a rare cause of meconium ileus. J Perinatol. 2013;33(2):154-156.

6.Saneian H, Bahraminia E. Congenital chloride diarrhea misdiagnosed as pseudo-Bartter syndrome. J Res Med Sci. 2013;18(9):822-4.

7.Bhardwaj S, Pandit D, Sinha A, Hari P, Cheong HI, Bagga A. Congenital Chloride Diarrhea - Novel Mutation in SLC26A3 Gene. Indian J Pediatr. 2016;83(8):859-61.

8.Mäkelä S, Kere J, Holmberg C, Höglund P. SLC26A3 mutations in congenital chloride diarrhea. Hum Mutat. 2002;20(6):425-38.

9.Aichbichler BW, Zerr CH, Santa Ana CA, Porter JL, Fordtran JS. Proton-pump inhibition of gastric chloride secretion in congenital chloridorrhea. N Engl J Med. 1997;336(2):106-9.

10.Canani RB, Terrin G, Cirillo P, Castaldo G, Salvatore F, Cardillo G, et al. Butyrate as an effective treatment of congenital chloride diarrhea. Gastroenterology. 2004;127(2):630-4.