

Congenital Chloride Diarrhea

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Congenital chloride diarrhea (CCD) [Synonyms Darrow Gamble syndrome(1), congenital chloridorrhea and congenital alkalosis with diarrhea] is a rare autosomal recessive disorder. The literature records 79 cases of CCD up to July 1986(2) after which there have been some stray reports(1,3-7). We report a case which we believe represents the first in Indian literature.

Case Report

A male baby was born of a non-consanguinous marriage to a 32-year-old 4th gravida at 34 weeks of gestation. The antenatal course was complicated by the presence of polyhydramnios. Antenatal ultrasonography had ruled out any renal pathology in the fetus.

Of the 3 elder sibs of the patient, only one, an eight-year-old female is alive. The other two, both born premature, had

expired in the neonatal period following diarrhea. Polyhydramnios was present during both these deliveries also.

At birth, the baby weighed 2.3 kg. The liquor amnii was noticed to be of light green color, albeit not typically meconium stained. It was not foul smelling. No obvious congenital anomaly was present.

It was observed that the baby was passing light green colored stools instead of meconium from the very first day of life. This suddenly transformed into watery stools of significantly large quantity and caused a greater than normal weight loss and severe dehydration by day four.

The baby at this stage had a distended abdomen, with dilated, visible coils of intestine in presence of diarrhea but without any vomiting. The baby was exclusively breast fed.

The hemogram, stool routine and culture did not reveal any abnormality. The serum electrolytes on day 4 were within normal range but there was metabolic alkalosis (pH 7.56), stool electrolytes showed chloride levels of 90 mmol/L on day 7 and confirmed our clinical diagnosis of CCD.

The patient was managed by adequate replacement of fluid and electrolytes given through parenteral and nasogastric routes. The fluid requirements reached as high as 800 ml/day (i.e., more than 400 ml/kg/day). The patient succumbed to sepsis, DIC and hemoperitoneum after 26 days.

Discussion

First described by Gamble *et al.* and Darrow in 1945, the largest series comprising 21 patients is from Finland(8). The basic defect lies in the active transport of $\text{Cl}^-/\text{HCO}_3^-$ in the distal ileum and colon resulting in fecal chloride loss and osmotic diarrhea. Sodium and potassium concentration in stool is not abnormally high, but

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the increased quantity of stool leads to an increased absolute loss manifesting as hyponatremia and hypokalemia besides hypochloremia. Also, acidity of the intestinal contents hampers sodium absorption and aggravates hyponatremia. Inadequate secretion of HCO_3^- in the ileum and colon, and excessive loss of H^+ through the kidneys lead to alkalosis. Hyperaldosteronism occurs as a compensatory mechanism to conserve sodium(8).

The condition is characterized by life-long, watery, 'urine like' diarrhea(9) of prenatal onset(2) resulting in polyhydramnios which in turn causes preterm delivery. The neonate passes soft or watery stools instead of meconium resulting in greater than normal weight loss and dehydration. The neonate develops a large and distended abdomen with visible coils of intestine, a situation often mistaken for intestinal obstruction and occasionally leading to unnecessary surgical intervention(9).

Investigations usually reveal an unusual combination of metabolic alkalosis with diarrhea. Hypochloremia, hypokalemia, hyponatremia hyperreninemia and hyperaldosteronism are the other features.

Stools are watery with a pH ranging between 4 and 6, their chloride content is high and is greater than 90 meq/L (when serum chloride levels are normal). The stool chloride content exceeds the sum total of stool sodium and potassium concentration after 3 months of age(8).

Urine has low or absent chlorides unless normal serum chloride levels are maintained.

No specific tests are available to diagnose CCD prenatally. On ultrasonography, the fetal abdominal cavity is filled with dis-

tended loops of intestines, often mistaken for intestinal obstruction(10).

Although ketoprofen, a prostaglandin synthetase inhibitor was used to curb hyperreninemia in one infant(11), the basic defect has no curative treatment. Fluid and electrolyte replenishment from day one forms the mainstay of therapy. After replacing the initial extracellular deficits, the patient needs an extra 10 mmol of chlorides 1 kg/day besides the normal requirement of this, 1-2 mmol are provided in the form of KCl and the rest as NaCl in an iso-osmolal solution.

Per oral electrolyte replacement can usually be started by day 3 or 4 to gradually replace the IV fluids over 3 to 4 weeks. For oral replacement therapy, a solution containing 0.7% NaCl and 0.3% KCl is used. This may be changed to 0.9% NaCl, 0.2% KCl in the event of hyponatremia and hyperkalemia.

The condition is usually fatal and left untreated. However, an adequate replacement therapy started early in life enables normal physical and mental development and prevents renal abnormalities. The patient gradually learns to cope with the diarrhea which persists life long. There are reports of a female affected with the condition successfully bearing a normal infant(12).

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REFERENCES

1. Lee YD, Lee HS, Moon HR. Congenital chloridorrhea in Korean infants. *Korean Med Sci* 1988, 3: 123-129.
2. Holmberg C. Congenital chloride diarrhea. *Clin Gastroenterol* 1986, 15: 583-602.
3. Tomaszewski L, Kelesza E, Sochav. Congenital chloride diarrhea. *Poland Materia Medica Polona* 1987, 19: 271-277.
4. Vermeylen D, Godart S, Moretto M, Janssen F, Bonton JH. Long term follow up of a case of severe congenital chloride diarrhea. *Eur Pediatr* 1988, 147: 649-652.
5. Wall BM, Williams HH, Cooke CR. Chloride resistant metabolic alkalosis in an adult with congenital chloride diarrhea. *Am J Med* 1988, 85: 570-572.
6. Jubani MM, Dondin KI, Sharda DC, *et al.* Congenital chloride diarrhea in Kuwaiti children. *Eur J Pediatr* 1989, 148: 333-336.
7. Abdullah AM, Shaheed MM, Katugam-pola SM, Patel PJ. Congenital chloride diarrhea: Case report and review of the literature. *Ann Trop Pediatr* 1990, 10: 71-74.
8. Holmberg C, Perheentupa J, Launiala K, Jallman N. Congenital chloride diarrhea: Clinical analysis of 21 Finish patients. *Arch Dis Child* 1979, 52: 255-267.
9. Lumdevist K, Anneran G, Essohor T, Ewald U, Hardell LI. Surgical implications of congenital chloride diarrhea. *Zeitschrift für Kinderchirurgie* 1983, 38: 217-229.
10. Kirkinen P, Jouppila P. Prenatal ultrasonic findings in congenital chloride diarrhea. *Prenatal Diagnosis* 1984, 4: 457-461.
11. Minford AM, Barr DG. Prostaglandin synthetase inhibitor in an infant with congenital chloride diarrhea. *Arch Dis Child* 1980, 55: 70-72.
12. Personal communication with Dr. K. Launiala, Department of Pediatrics, University of Kuopio, 70210 Kuopio 21, Finland.