Congenital Chloride Diarrhoea: A Protocol for Antenatal Management

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Abstract: Chloride losing diarrhoea (CLD) is an autosomal recessively inherited disease characterised by lifelong chloride rich chronic diarrhoea which starts in-utero. Early diagnosis and proper replacement therapy are important to avoid serious complications of the disease. This series of cases present the tools used for in-utero diagnosis of CLD and the protocol for antenatal management adopted to achieve the best possible maternal and foetal outcomes.

Keywords: Chloride losing diarrhoea, Saudi Arabia.

INTRODUCTION

Of the many congenital chronic diarrheal disorders, chloride losing diarrhoea (CLD) is one of the most studied disorders. The disorder is commonly recognised in Finland, Saudi Arabia, Kuwait, and Poland [1]. The estimated incidences of CLD in Finland and Poland are 1 in 20,000 and 1 in 200,000, respectively. Consanguineous marriages in Saudi Arabia and Kuwait led to high local incidence of up to 1 in 5000 [1].

CLD is an autosomal recessively inherited disease as a result of mutation in the solute carrier family 26, member 3 gene (SLC26A3) on chromosome 7q31, which encodes for a transmembrane Cl-/HCO3- exchanger protein. The protein is mainly expressed in the brush border of ileal and colonic epithelium. The deficiency results in watery, Cl- rich diarrhoea, hypochloremia, hypokalemia, and metabolic alkalosis [2]. The diarrhoea begins in fetal life and causes polyhydramnios and premature delivery [3].The basic defect in CLD is the impairment of Cl-/HCO3- exchange in an otherwise normal distal ileum and colon. Active Cl- re-absorption is impaired and a large amount of Cl- is lost in the stool leading to hypochloremia. The associated defect in HCO3- secretion leads to metabolic alkalosis and the acidification of intestinal content, which further inhibit the absorption of Na+ through the Na+/H+ exchanger. In the intestine, the high concentration of electrolyte in the lumen, leads to impaired absorption of water and subsequent diarrhoea through osmotic mechanisms. Increased Na+ and water loss in diarrhoea causes secondary hyperaldosteronism and K+ wastage, resulting in both hyponatremia and hypokalemia. The postpartum diagnosis is confirmed by stool chloride content that exceeded the sum of faecal sodium and potassium. Usually stool chloride level exceeds 90 mmol /L. The objectives of this case series are to evaluate the spectrum of antenatal ultrasound and clinical findings of pregnancy complicated by CLD in Saudi Arabia and to present the antenatal protocol for the management of CLD in National Guard Hospital in Riyadh.

MATERIAL AND METHODS

The maternal antenatal records of 18 pregnant women diagnosed antenatally to carry a foetus with chloride losing diarrhoea were reviewed with respect to; the maternal demographic data, ultrasound findings, antenatal management and pregnancy outcomes. The neonatal records were reviewed for birth weight in relation to gestation age, and onset of diagnosis of CLD posnatally. The paediatric records of children diagnosed with CLD during the same period were reviewed to detect children who were not diagnosed in the antenatal period.

Protocol for Antenatal Management of Women Diagnosed to Carry a Foetus with CLD

As CLD is not uncommon in the Saudi community; antenatal diagnosis is based on the typical ultrasound appearance of dilated foetal bowel and the presence of polyhydramnios [4]. A history of previously affected child born to the same parents further confirms the diagnosis. Following the diagnosis, serial ultrasound examinations are usually done every 10-15 days to evaluate the amount of amniotic fluid and to perform cervical length assessment in anticipation of preterm labour. If the amniotic fluid index (AFI) exceeds 40 cm and/or the mother is distressed with the polyhydramnios, amniotic fluid reduction (AFR) is

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performed. A single course of dexamethasone (6 mg) every 12 hours for four doses is administered to the mother; if the cervix was found to be < 2cm long with painful uterine contractions and /or documented contractions on the elecromyogram [5] or before amniotic fluid reduction is performed, to women with gestation age between 24 to 34 weeks to enhance fetal lung maturation. Parents counselling is done as appropriate.

RESULTS

Eighteen women, with singleton pregnancy, were identified in the period between January1996 to December 2005 to carry a foetus with CLD. The demographic characteristics of these women are shown in Table **1**. The mean gestational age at the time of diagnosis was 30±3.8 weeks, 16 (88.8%) of the women had polyhydramnios and in 15 (83.3%) of the fetuses the bowel was dilated with the typical honeycomb appearance of the ultrasound image (Table **2**) (Figure **1**). In only 2 women the diagnosis was suspected during the second trimester anomaly scan. 14 (77.8%) women had AFR and 6 (33.3%) women had undergone the procedure more than once. The mean amount of amniotic fluid removed at each AFR procedure was 2.4±1.5l (mean ±SD). All women received one course of dexamethasone either before the first AFR or due to threatened preterm labour. The mean gestation age at delivery was 34.1±3.0 (mean ±SD) weeks and ranges between 25 and 40 weeks. All women had vaginal delivery. No complications were noted during labour or delivery except for one woman who started labour at 25 weeks gestation and delivered 560g infant who was diagnosed later with intestinal obstruction and who was alive at 1 month of life. The mean APGAR scores at 5 minutes were 8.0±1.0 (mean ± SD), range 7 to 9 and the umbilical artery pH was (mean ± SD) 7.39±2.1. In 16 neonates the birth weight was ≥ 50th percentile for the gestation age. The antenatal diagnosis of CLD was confirmed, in the postnatal period, by high concentration of chloride in the stool, in 17 out of the 18 newborns. One infant delivered at 25 weeks gestation was found to have intestinal obstruction. Two children were diagnosed in the postnatal period, one was delivered in another hospital and the second was delivered in NGH but missed diagnosed as intestinal obstruction, however the diagnosis of CLD was reached during the first week of life.

DISCUSSION

The early diagnosis and treatment of children with CLD is vital for a favourable long term outcome [6, 7]. The previously documented high prevalence of the condition in Saudi Arabia and other Arab countries [6] can be explained by the high frequency of

Table 1: Maternal Demographic Characteristics for Women with Pregnancies Complicated with Chloride Losing Diarrhoea

Maternal Characteristic	Mean ± SD	Range
Age (years)	26.4 ± 4.6	18-36
Parity	2.0 ± 2.49	0-11
Consanguineous marriage [n (%)]	10 (55.6%)	
History of previously affected child [n (%)]	6 (33.3)	

Table 2: Ultrasound Examination Findings and their Frequency in Pregnancies Complicated by Chloride Losing Diarrhoea

Ultrasound examination findings	Mean ± SD	N (%)
Gestation age at the time of diagnosis (weeks)	30.0±3.8	
Amniotic fluid index (cm)	34.6±8.5	
Women with polyhydramnios (AFI > 24cm)		16 (88.8%)
Fetuses with dilated bowl		15 (83.3%)
Findings of polyhydramnios and dilated bowl		14 (77.7%)
Structural abnormalities		0 (0%)

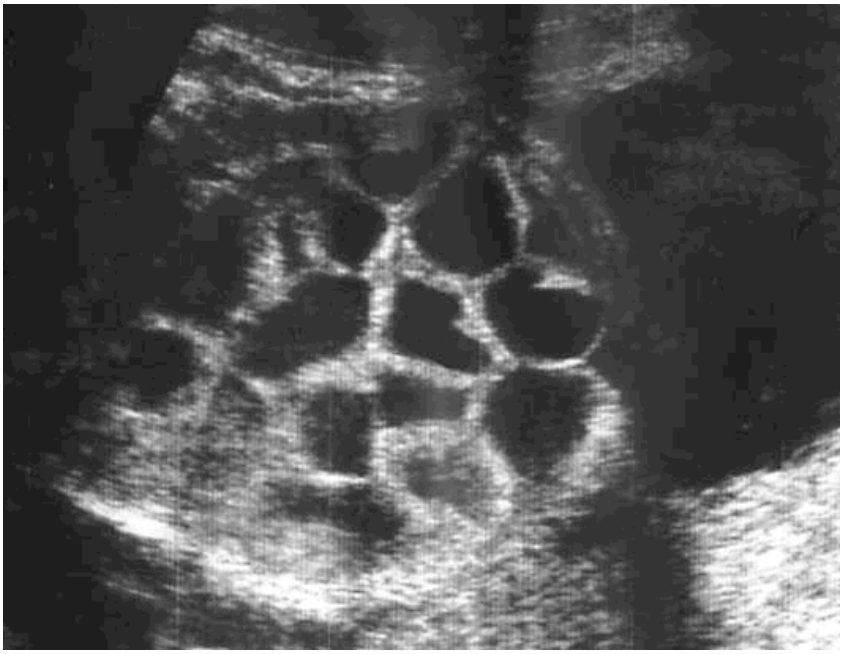

Figure 1: Ultrasound appearance of fluid filled dilated foetal intestines in a case of chloride losing diarrhoea.

consanguineous marriages which was a feature of 55% of marriages in this series. Consanguineous marriage is associated with the emergence of autosomal recessive disorders including CLD.

The high antenatal detection rate of CLD in this series and the availability of an established protocol for antenatal management for affected pregnancies; facilitated prolongation of pregnancy to an average of 34 weeks and improved the outcomes form preterm deliveries by the timely administration of dexamethasone for foetal lung maturity. Late diagnosis of the children with CLD was associated with chronic diarrhoea, dehydration, failure to thrive, renal failure and death [3, 7].

The ultrasound examination, in our protocol, was the main tool for diagnosis of CLD by the findings of the typical honeycomb appearance of the fluid filled foetal intestines and polyhydramnios [4]. Confidence in the diagnosis was supported by high level of suspicion due to the relatively high incidence of the condition in the Saudi community and the presence of positive family history in one third of the series. Similar sonographic appearance can be found in cystic fibrosis complicated by meconium ileus however the condition is rare in Saudi Arabia [4]. Although foetal bowel obstruction appears in ultrasound scan image as dilated bowel caudal to the obstruction, CLD can be distinguished by the generalised dilatation of the foetal bowel and the presence of polyhydramnios [4]. One case in the current series was misdiagnosed as CLD and turned to have intestinal obstruction. It is worth noting that the typical ultrasound findings were not all present till the late second trimester or early third trimester however most of the women in this series were followed up closely either because of the presence of history of previous pregnancy complicated with CLD or because of the appearance of early signs of the disease usually dilated foetal bowels.

Another important use of ultrasound in our protocol is for the assessment of the uterine cervix, as a validated method for early prediction of preterm labour [5]. Early prediction of preterm labour facilitates timely administration of steroids and improves outcomes [8].

CONCLUSION

Ultrasound examination and the findings of dilated foetal bowel and polyhydramnios are strongly suggestive of CLD due to the high incidence of the disease in Saudi Arabia. Family history is an important clue to the diagnosis. Antenatal detection and proper antenatal management of CLD improves the maternal and neonatal outcomes.

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