

## Case Report

# Congenital glucose-galactose malabsorption: A rare cause of chronic diarrhea

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Diarrhea present initially at early neonatal period is rare and is generally caused by congenital malabsorptive disorders. Congenital glucose-galactose malabsorption (CGGM) is a rare autosomal recessive disorder present as a protracted diarrhea in early neonatal life. A 3 month-old female infant present with chronic diarrhea, severe failure to thrive, hypernatraemic dehydration and nephrocalcinosis was studied. Early onset diarrhea in a patient with consanguineous parents should alert the pediatricians to think about a rare congenital cause of chronic diarrhea that can present with a life threatening condition.

**Key words:** Glucose galactose malabsorption, chronic diarrhea in infancy, congenital.

## INTRODUCTION

Diarrhea with an onset in the early days of life is rare and generally caused by congenital malabsorptive disorders (Guarino and De Marco, 2004). Congenital glucose-galactose malabsorption (CGGM) is a rare autosomal recessive disorder, which presents as a chronic refractory diarrhea in early neonatal life. It is due to a defect in sodium-coupled transport of glucose and galactose in the enterocyte (Abad-Sinden et al., 1997; Pascual et al., 2004).

In the Arab countries where consanguineous marriage is quite common, CGGM appears to be a common problem as compared to the western populations. There is no data about the incidence or the prevalence of this problem in the Arab world. Lebenthal et al. (1971) have reported an Iraqi adult with GGM and subsequently Abdullah et al. (1996) reported 8 Arab children with a similar problem in Saudi Arabia. Assiri et al. (2013) published five Arab children with GGM and one of them developed gangrene of both legs as a complication of hypernatremia and dehydration, necessitating bilateral

amputation. Two infants had nephrolithiasis (Assiri et al., 2013).

This study is presents an infant with chronic diarrhea, hypernatraemic dehydration and nephrocalcinosis, who was diagnosed as congenital GGM.

## CASE REPORT

A 3 months old Saudi girl presented to pediatric emergency department with the history of diarrhea since age of 2 days. She was a product of full term, normal delivery for primigravida mother with an uneventful pregnancy, with birth weight of 2.4 kg. At the second day of her life she started to have watery diarrhea around 10 times per day, yellowish in color not associated with mucous or blood with the history of abdominal distention and poor weight gain. No history of vomiting, skin rash, lethargy or poor feeding. There was no history of repeated infection.

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**Figure 1.** Severe muscle wasting and malnutrition.

She was admitted at the age of one week at local hospital for 5 days, treated as acute gastroenteritis and was discharged with little improvement. Another admission at the age of 2 months to private hospital investigated and was treated for 20 days with no improvement. She received birth vaccine, her development was appropriate to her age. She was the first baby of first degree cousin parents.

On examination, she looks unwell, conscious, pale, not cyanosed, cachectic, not on respiratory distress with moderate dehydration, no dysmorphic feature, and normal vital signs. Her growth parameters were below third percentile and the weight for age was 42%. She was with scanty hair with normal color, anterior fontanel, open and depressed measuring of  $2 \times 1.5$  cm.

She has diminished subcutaneous fat at the mid-arm with reduced muscle bulk at the gluteal region. She has mild abdominal distention with unremarkable systemic examination (Figure 1). Blood investigations showed serum sodium of 173 mmol/L, potassium of 4.2 mmol/L, urea of 223 mg/dl, creatinine of 0.9 mg/dl and pH of 7.20 and  $\text{HCO}_3$  of 11.6 with base excess of -16.1. Stool was acidic and showed no ova or cyst. No stool sugar chromatography was available. Ultrasound abdomen showed nephrocalcinosis in both kidneys (Figure 2). She

was admitted to pediatric ward, tried on many formulae, including lactose free, semi elemental and elemental formula with no change in diarrhea. Metabolic acidosis and pre-renal azotemia were treated with appropriate intravenous fluid. Patient kept NPO with marked improvement of diarrhea. The diagnosis of CGGM was contemplated based on the history of early onset of acidic osmotic diarrhea causing hypernatraemic dehydration that did not improve with elemental diet. The patient was started on galactomin 19 formula which was glucose-galactose free formula (fructose based formula), after the formula was started, the patient showed dramatic improvement, her diarrhea stopped, urea and electrolyte 2 days after introduction of formula was normalized: urea 31.9, creatinine 0.10, Na 134, and K 3.9. The patient was discharged with diagnosis of CGGM on galactomin 19 formula. After four weeks, she presented to gastroenterology clinic with weight of length, good muscle bulk and subcutaneous fat (Figure 3).

## DISCUSSION

Differential diagnoses of any patient with early onset neonatal diarrhea are challenging, but fortunately, it has



Figure 2. Ultrasound abdomen showed bilateral nephrocalcinosis.



Figure 3. The patient 6 weeks after starting galactomin 19 formula.



limited causes which include congenital microvillus atrophy, tufting enteropathy, congenital GGM, congenital lactase deficiency, congenital malabsorption of chloride and sodium, bile acid malabsorption, and congenital enterokinase deficiency (Guarino and De Marco, 2004). CGGM is a rare autosomal recessive disease (Martin and Wright, 2004), first reported in Sweden and France by Linquist and Meeuwisse (1962). Currently, only about 300 cases have been reported worldwide (Martin and Wright, 2004). There are scattered cases reported in the neighboring countries like Oman and Malaysia (Lee et al., 2009; Al-Lawati and Vargees, 2008). In our country, thirteen cases have been reported in Saudi Arabia and all of them were presented with an early protracted diarrhea (Abdullah et al., 1996; Assiri et al., 2013), and this is the first case reported in southwest region of the Kingdom. Lactose, the primary disaccharide present in breast milk, is hydrolyzed by lactase on the external surface of the intestinal brush border (Martin and Wright, 2004). The liberated glucose and galactose are then transported across the brush border membrane by the Na<sup>+</sup>/glu co-transporter (SGLT1) and accumulate within the enterocyte. SGLT1 is responsible for the tight coupling of two Na<sup>+</sup> ions and one sugar molecule across the membrane (Martin and Wright, 2004; Linquist and Meeuwisse, 1962; Lee et al., 2009). CGGM is caused by a defect in the intestinal SGLT1 transporter due to mutation in the SLC5A1 gene (182380) which is located on chromosomal 22q13.1 (Martin and Wright, 2004). Lactose found in breast milk is hydrolyzed normally, but absorption of glucose and galactose is absent or reduced, leading to osmotic diarrhea. Undigested glucose and galactose are then delivered to the colon and fermented by colonic bacteria producing short chain fatty acids. The stools become acidic. Affected infants are usually present with diarrhea within the first few days of life with severe life threatening diarrhea with hyperosmolar dehydration and metabolic acidosis during the neonatal period (Martin and Wright, 2004; Lee et al., 2009; Al-Lawati and Vargees, 2008). As the pathogenesis of diarrhea is osmotic, the diarrhea resolves once enteral feeding is removed. The stool pH is usually <5.3 and stool reducing sugar is positive with large stool osmotic gap >40 mOsm. Our patient was having typical presentation of this disease and she improved dramatically after glucose and galactose were eliminated from enteral feeding and start her on fructose-based formula (Galactomin 19). The medium term prognosis of GGM is usually good. As the patients grow older, most can tolerate some amount of glucose with no diarrhea, the unabsorbed glucose being fermented by colonic bac-teria. The main concern for this group of patients is the compliance to these special formulae and the long term consequences of taking a high protein and fat diet (Martin and Wright, 2004). The required life-long glucose- and galactose-free diet may have significant renal and cardiovascular consequences (Lee et al., 2009).

While she is the first baby, her parents need to be counseled and to be seen in genetic clinic as soon as possible for the future pregnancies, fortunately our patient was accepted in higher center for that purpose.

## Conclusion

Early onset diarrhea in patient with consanguineous parents should alert the pediatricians to think about a rare congenital causes of chronic diarrhea that can present with a life threatening condition or serious long-term morbidity like renal failure and gangrenous legs which happened to one of the patients who were mentioned earlier and published by our colleagues in King Khalid University Hospital in Riyadh.

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