CASE REPORT

Congenital diarrhoea in a neonate with hypernatraemia and dehydration

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Abstract

Diarrhoea, vomiting, and dehydration are frequently encountered in neonatal emergency. However, it is challenging to manage resistant hypernatraemia and metabolic acidosis associated with it. Diagnosing the exact cause is even more difficult. Glucose-galactose malabsorption commonly presents with hypernatraemia and repeated dehydration. In the case described here, the baby started to have diarrhoea in the first week of life and presented in the neonatal emergency with severe dehydration and hypernatraemia. Higher sodium levels were difficult to manage throughout the course of illness. Hypernatraemia and diarrhoea worsened on feeding, whether formula or mother's feed, which raised suspicion of glucose and galactose malabsorption. So, genetic testing was performed and fructose based formula was started which led to improvement in the condition. Later, genetic testing confirmed our diagnosis. This case report emphasises that clinicians should consider the possibility that congenital diarrhoea could be due to glucose-galactose malabsorption while managing a case with loose stool and significant electrolyte imbalance in a neonate.

Keywords: Hypernatremia, dehydration, diarrhoea, glucose galactose malabsorption.

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Introduction

[1]Glucose-galactose malabsorption is a rare inherited disorder which results due to defect in transport enzyme proteins SGLT1 leading to failed transport of glucose or galactose across the intestinal lumen.[1] Glucose and galactose when remain unabsorbed, draw water out of the body along with them. The condition usually presents with intractable diarrhoea in early neonatal life and if left untreated can cause failure to thrive or infant's death.

Glucose-galactose malabsorption is an autosomal recessive disorder. SLC5A1 gene located on chromosome 22 encodes SGLT1 protein on luminal surface of the intestine.[2] More than 40 mutations have been recognised for glucose-galactose malabsorption.[3]

The glucose-galactose malabsorption improves by eliminating glucose, galactose, and lactose from the diet. Fructose-based formula is preferred to manage the symptoms of the disease.

In this case report, the baby had diarrhoea on the third day of life which was complicated with persistent hypernatraemia.

Case Report

A nine-day-old baby boy presented in the emergency department at the University of Child Health Sciences, The Children's Hospital, Lahore, in July 2021, with loose motion for one week with fever for four days. There were 8-9 episodes of loose motions per day of Grade III - IV on NCI grading and Type 6-7 on Bristol stool chart, without mucous or blood. The mother was a primigravida, had regular antenatal clinic visits, and had shown no risk factors. The child was delivered full term by LSCS due to intrauterine passage of meconium and remained stable in immediate postnatal period. He was breast fed for initial five days and was prescribed lactose-free formula and ORS by a general physician but there was no improvement. He was born to first degree related parents with no history of similar illness in the family. On examination, he was sick looking and lethargic with signs of severe dehydration. His heart rate was 170/minute, temperature 100°F, blood pressure 90/60mmHg, respiratory rate 66/minute and capillary refill time was more than three seconds. The rest of the physical examination was unremarkable. The baby was passing urine normally.

The patient was managed for acute watery diarrhoea, severe dehydration and neonatal sepsis. The baby was rehydrated. Empirical antibiotics were started. Initial investigations were retrieved and metabolic acidosis was corrected. Vitals and intake output record was monitored. Complete blood count showed Hb=15.2g/dL (11–17.3 g/dl), TLC 18.5×10^3/µL (4-21×10^3/µL), Neutrophils 34%, Lymphocytes 54%, Platelet 186×10^3/µL (152-472 ×10^3/µL), BSR 122mg/dL, CRP 1.3 mg/L (≤10 mg/L), Na 179 mmol/L (135-145 mmol/L), K 4.6 mmol/L (3.5 – 6.0mmol/L), Cl 161 mmol/L (96-106 mmol/L) , Ca 10.9mg/dL (7.6-10.4 mg/dL), Urea 200 mg/Dl(5-18mg/dl), Creatinine 1.1 mg/dL (0.2-0.9 mg/dl), ABGs revealed metabolic acidosis (pH 7.214, pO_2

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Table: Serial Serum electrolytes of the patient.

Na	179	176	177	170	162	156	146	148	168	175	150	146	144
K	4.6	5.4	5.1	5.0	4.0	4.6	4.1	4.1	5.2	4.0	4.7	5.5	5.8
Cl	161	130	140	138	139	134	121	139	145	125	123	120	112

60mmhg, HCO_3 6.9mmol, Anion gap was normal). The baby was managed for hypernatraemic dehydration. Maintenance intravenous fluids and feeding was continued. Urine output remained normal. But hypernatraemia, metabolic acidosis and loose stools persisted. Strict monitoring and management of hypernatraemia was continued in NICU. Diabetes insipidus was considered as a differential diagnosis. The baby was kept NPO in ICU and managed for hypernatraemia. Serum sodium normalised and loose stools settled. ABGs showed compensated metabolic acidosis. Antibiotics were discontinued when sepsis was ruled out. Diabetes insipidus was excluded based on normal urine output, high urine osmolality (425mosm/kg) in comparison to serum osmolality (329mosm/kg) in the setting of dehydration. On the ninth day of admission, after resuming feed, loose stools reoccurred. Serum sodium again rose to 168mmol/l. The feed was withheld again, and the baby was managed with intravenous fluids for hypernatraemic dehydration. Loose stools improved. Serum sodium normalised to 143mmol/l. Serial serum electrolytes are mentioned in Table.

Simultaneously, work up for malabsorption was performed due to association of diarrhoea with feeding. Stool complete examination showed Osmolality 286 mosm pH 5.2 and presence of reducing substances were confirmed with Clinitest. Stool culture was negative for any organism. As there was a high index of suspicion for glucose-galactose malabsorption diarrhoea, genetic testing was sent for glucose-galactose malabsorption. Intestinal biopsy could not be performed because testing facilities were not available in our institute. Meanwhile, fructose-based milk formula (Galactomin 19) was arranged and started after gastroenterology consultation. The patient's condition improved with no recurrence of diarrhoea on special formula, and he was discharged after 21 days of hospital stay. The parents were counselled for strict compliance to formula avoiding carbohydrate-based products. The baby was called for follow-up after two weeks and it was noted that he remained well on fructose-based dietary formula with adequate weight gain. In the interim, genetic testing was followed which identified a homozygous likely pathogenic variant in SLC5A1 gene, c.875G>A p.(Cys292Tyr). The result was consistent with genetic diagnosis of autosomal recessive glucose-galactose malabsorption. Parent-targeted genetic analysis was also performed which confirmed the homozygosity of the patient by the presence of carrier state in both father and mother.

Discussion

Glucose-galactose malabsorption, though a rare disease, needs a high index of suspicion for diagnosis in neonates who have severe diarrhoea, dehydration, acidic stool, and positive reducing substances. SLC5A1 mutations impair intestinal glucose and galactose/Na^+ cotransport system resulting in unabsorbed glucose and galactose from intestinal lumen.

It leads to osmotic diarrhoea and excess water loss which causes hypernatraemia. Similarly, raised serum sodium concentration was observed in this case due to severe diarrhoea and dehydration. In GGM findings of small bowel biopsy include villous architecture and normal enzyme (disaccharidase) activity. In this case, the baby was admitted with diarrhoea on the third day of life. Diarrhoea at early neonatal life raises speculations for congenital diarrhoeal disorders. Paediatricians also need vigilance to anticipate the manageable condition. Once the glucose-galactose malabsorption is managed in neonatal age, the infant can enjoy a normal life.[3,4] However, in untreated patients GGM can cause severe life-threatening repeated dehydration and associated complications such as electrolyte imbalance, cerebral haemorrhage, thrombosis, and weight loss. Thrombocytopenia and gangrene are also associated with this complex carbohydrate intolerance.[5] Renal stones and glycosuria can also be sometimes noted in glucose-galactose malabsorption.[6,7]

Lactose is broken down to glucose and galactose, both absorbed through luminal surface by SGLT1 Protein. Hence, any substrate which contains glucose and galactose can lead to malabsorptive diarrhoea in GGM. Excessive loss of water leads to dehydration and hypernatraemia. In the index case, the patient was having diarrhoea even on lactose-free milk due to the use of ORS, because ORS also contains glucose. But when the patient was kept NPO and managed with IV fluids, diarrhoea improved. As soon as the feed was started again, loose stools reoccurred, and the challenge of managing severe hypernatraemia was faced. This became the decisive moment to perform genetic testing for glucose- galactose malabsorption. Further arrangement of fructose-based milk formula was also an extremely difficult task because it had to be imported as it is not readily available in our country.

The start of fructose-based formula resulted in resolution of diarrhoea and hypernatraemia as in our case. The principal key in managing GGM is avoidance of glucose and galactose in diet.[3,8] However, the disease may get less severe at a later age and low content of sugar can be added.[8,9]

Conclusion

Glucose-galactose malabsorption is an infrequent cause of diarrhoea in neonates and diagnosis needed a high index of suspicion in a 9 days old baby who was timely managed with fructose-based formula, correction of electrolyte imbalance and dehydration and which saved the life of the neonate.

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Conflict of interest: None.

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Abbreviation: GGM= Glucose-galactose malabsorption; NPO= Nil per oral; ORS= Oral rehydration solution

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