CONGENITAL GLUCOSE-GALACTOSE MALABSORPTION - A CASE REPORT

W. S. Lee, A. Y. T. Goh
Department of Paediatrics, University of Malaya Medical Centre, 50603 Kuala Lumpur, Malaysia.

ABSTRACT: We report a case of congenital glucose-galactose malabsorption (GGM) in a Malay male infant who presented with protracted diarrhoea, severe metabolic acidosis, and marked hypernatraemic dehydration since the third day of life whilst on breast feeding. He was severely marasmic, requiring total parenteral nutrition to improve the precarious nutritional status. The course of illness was complicated by Staphylococcal septicaemia and catheter related endocarditis which was eradicated by a six-week course of vancomycin and fusidic acid. Subsequent carbohydrate tolerance tests showed impaired absorption of oral glucose but normal absorption of fructose. The child tolerated fructose-based modular feed well and had normal development. At fourteen months of age he still had failure to thrive despite an adequate calorie intake and normal appetite. *(JUMMEC 1997 2(1): 43-45)*

KEYWORDS: Chronic diarrhoea, glucose-galactose malabsorption, congenital.

Introduction

Glucose and galactose malabsorption (GGM) is a rare congenital disease resulting from a selective defect in the intestinal glucose and galactose/Na+ co-transport system. It was first described in 1962 by Lindquist in Sweden and Laplane in France respectively (1), (2). Since then this inherited form of carbohydrate malabsorption has been described in various communities. Quak *et al.* from Singapore described this condition in a Chinese family with two affected male children (3). We describe a Malay boy with this condition, from the Department of Paediatrics, University of Malaya Medical Centre, Kuala Lumpur. We believe that this is the first case reported in this country. It is a rare but an important cause of chronic diarrhoea in early infancy. Early diagnosis and appropriate dietary manipulation can prevent considerable morbidity and even mortality.

Case Report

MZ was born after a full term, normal pregnancy. His birth weight was 2.76 kg. He first developed watery diarrhoea on the third day of life whilst on breast feeding. Breast feeding was discontinued as advised by a general practitioner and an infant formula was started. However, diarrhoea persisted. He was admitted to a local hospital on the seventeenth day of life with severe metabolic acidosis (pH 7.07, bicarbonate 7.4 mmol/L, base excess -21 mmol/L); hypernatraemic dehydration (blood urea 28.5 mmol/L, serum sodium 183 mmol/L, potassium 4.5 mmol/L) and anaemia. He was also severely marasmic, with a body weight of 2.2 kg. He received intravenous antibiotics, blood transfusions, and two weeks of total parenteral nutrition. His weight improved to 2.55 kg. His diarrhoea stopped while he was kept nil orally but recurred when oral feeding was reintroduced. He was referred to this hospital at 51 days of life.

His parents were first cousins. Two of his male siblings, developed chronic diarrhoea since the third day of life and died two weeks later at a local hospital. No definite diagnosis was made. A female sibling died at five years of age, due to meningitis. He had four other living siblings, three girls and one boy, all of whom were healthy

Physical examination revealed a patient who had generalised wasting with loss of subcutaneous tissue. Apart from perianal excoriation, examination of the systems did not reveal any abnormality. The results of routine blood investigations, which included full blood count, urea and electrolytes were normal. Parasites were not detected on microscopic examination of fresh stools specimens on several occasions. Stool cultures were repeatedly negative for enteropathogens and no rotavirus and adenovirus were detected. Because of severe malnutrition, he was given total parenteral nutrition for two weeks. During this period when he was

Corresponding address:
Dr. W. S. Lee,
Department of Paediatrics,
University of Malaya Medical Centre,
50603 Kuala Lumpur.

not fed enterally there was complete cessation of diarrhoea. Diarrhoea recurred when oral rehydration solution which contained glucose was given. Based on these observations a presumptive diagnosis of congenital GGM was made.

To confirm the diagnosis of congenital GGM, glucose and fructose tolerance tests were performed. During the tests, the child was first given 1g/kg body weight of glucose solution (oral rehydration solution, Oralite® Poly Laboratories). Baseline and serial blood glucose levels were measured after the glucose was given. The child was observed for diarrhoea and clinical signs of dehydration. The stool output was charted, and the weights of the nappies before and after use were recorded. Watery stool specimens were sent for sugar chromatography. Fructose challenge was commenced 48 hours after the cessation of watery stools observed during the glucose tolerance test. During glucose challenge serial blood glucose levels were: 6.2 mmol/L at baseline; 6.3 mmol/L at 30 minutes, 6.3 mmol/L at 60 minutes, 6.1 mmol/L at 90 minutes and 6.7 mmol/L at 120 minutes after glucose loading showing no significant increase in the serial blood glucose levels after the oral glucose challenge. Serial blood glucose measurements during challenge with fructose showed a baseline of 6.1 mmol/L, 6.2 mmol/L at 30 minutes, 6.0 mmol/L at 60 minutes, 6.9 mmol/L at 90 minutes and 7.5 mmol/L at 120 minutes. There was significant rise in the blood glucose after the oral fructose load. Two episodes of watery stools were noted during glucose challenge and none during the fructose challenge. Sugar chromatography showed the presence of glucose on both specimens collected during the challenge with glucose.

He became febrile after two weeks of parenteral nutrition, and methicillin-resistant *Staphylococcus aureus,* was isolated from peripheral blood culture. Evidence of endocarditis with vegetation formation in the right ventricle was noted on echocardiographic examination of the heart. The central venous catheter was removed and the child was given intravenous vancomycin and fusidic acid. Methicillin resistant *Staphylococcus aureus* was isolated from the tip of the central venous catheter. His condition improved thereafter. He was then started on a modular feed, with fructose, whey protein (ProMod®, Abbott), corn oil, multivitamins and multiminerals (Vidaylin®, Abbott). Potassium, calcium and zinc supplements as well as iodised salt were added. He tolerated this feed very well with no further diarrhoea and started to gain weight. The cardiac vegetation resolved after six weeks of intravenous antibiotics. He was readmitted to the hospital at six month of age for introduction of solids under observation. He was able to tolerate a variety of weaning foods. Various weaning foods were introduced and the family was under the advice of an experienced paediatric dietitian. The child was to avoid normal infant formula and drinks which contained glucose.

At 14 month of age he was asymptomatic. Despite a voracious appetite and an adequate calorie intake, his weight gain remained slow and all his growth parameters were still well below the third centile. He was growing just below the third centile. His development was within normal range.

Discussion

Carbohydrate intolerance is a common cause of persistent diarrhoea following acute gastroenteritis. Commonly it is due to secondary lactose intolerance (4), although monosaccharide intolerance has also been reported (5). Such monosaccharide intolerance is often transient. Congenital glucose and galactose malabsorption (GGM) is a rare disorder resulting from a selective defect in the intestinal glucose and galactose/Na+ co-transport system. It causes long-lasting intolerance to glucose and galactose but not to fructose. It was first reported in Sweden and France in 1962 (1) (2), and has been noted to be an uncommon cause of chronic diarrhoea among children (6) (7).

In GGM, diarrhoea develops as a consequence of selective malabsorption of glucose and galactose. The defect is situated in the glucose/Na+ co-transport system in the brush border membrane of the small intestine (8). Disaccharides such as lactose, sucrose, and maltose are hydrolysed normally, but the absorption of glucose and galactose is absent or markedly reduced (9). This results in secretion of water and electrolytes into the intestinal lumen, thus causing diarrhoea. Characteristically, diarrhoea develops within four days of birth (10). This is rapidly followed by marked dehydration which is often hypernatraemic with metabolic acidosis and pronounced physical wasting (11). All these clinical features were present in our patient. Renal glycosuria, hypochromic anaemia and moderate steatorrhoea has also been described in this condition (10).

The inheritance of this condition was thought to be autosomal recessive in nature (10). The fact that the parents of our patient are first cousins supports this mode of inheritance. There were two elder siblings in the family who died of chronic diarrhoea with onset on the third day of life. It was likely that both of them also had congenital GGM and succumbed to the condition.

The diagnosis of this condition depends on the demonstration of the failure of absorption of glucose and galactose. This can be easily identified by the hydrogen breath test which was not available in our institution. Other methods such as measurement of serial blood sugars after administration of oral glucose and fructose loads are acceptable alternatives (11). In this patient, we have demonstrated a flat oral glucose tolerance test with normal absorption of fructose. Treatment is simple and consists of immediate rehydration and provision of a glucose- and

galactose-free diet. Oral rehydration solutions that contain glucose must be avoided. Commercially prepared glucose- and galactose-free formula (Galactomine19®, Nutricia) is costly and is not available in Malaysia. We had devised an alternative special formula by providing the major components of the nutritional requirement of the child separately. Fructose was the carbohydrate while whey protein (ProMod®, Abbott) was the main protein. Cornoil, potassium, calcium, zinc, multivitamins and multiminerals (Vidalyn®, Abbott) and iodised salt were added.

In most children, growth and development were normal once glucose and galactose were removed from the diet (11). However, in this case, despite an adequate calorie intake, the physical growth remained retarded although the development was within normal limits. This experience was similarly shared by Quak *et al.* from Singapore (3). The reason for this is not clear. In older children and adults, tolerance to the offending carbohydrates improves (11), although malabsorption of glucose and galactose in the small intestine remains unchanged.

Chronic diarrhoea among Malaysian children is commonly secondary to post-enteritis syndrome in which cow's milk protein and soy protein played an important role in prolonging the duration of diarrhoea (12), (13). Acquired carbohydrate intolerance is also important (14). However, chronic diarrhoea with onset during the first weeks of life is unlikely to be secondary to cow's milk or soy protein-sensitive enteropathy or acquired carbohydrate intolerance (15). This child developed chronic diarrhoea during the first few days of life while on breast feeding. He had two elder siblings who died under very similar situations. All this points to the possibility of a congenital malabsorptive disorder. The clinical features of severe metabolic acidosis, hypernatraemic dehydration, watery, acidic stools which contain the offending carbohydrate support the diagnosis of congenital GGM. It is of paramount importance for clinicians and other caregivers to realise that diarrhoea with onset within the first week of life especially in a breast fed infants is not due to acquired food protein or carbohydrate intolerance. Early recognition and referral should be made in order to prevent further deterioration of the nutritional status and to improve the outcome of the patient

References

1. Lindquist B, Meeuwisse GW. Chronic diarrhoea caused by monosaccharide malabsorption. Acta Paediatrica 1962; 51:674-85.
2. Laplane R, Polonovsky C, Etienne M, Debray P, Lods JC, Pissaro B. L' intolerance aux sucres a transfert-intestinal actif (ses repports avec l'intolerance au lactose et le syndrome coeliaque). Arch Fr Pediatr 1962;19:895-944.
3. Quak SH, Chong ASY, Low PS. Glucose-galactose malabsorption - a report in a Chinese family. J Sing Paediatr Soc 1989; 31:126-8.
4. Lifshitz F, Coella-Ramirez P, Gutierrez-Topete, Cornado-Cornet MC. Carbohydrate intolerance in infants with diarrhoea. J Pediatr 1971; 79:760-7.
5. Manuel PD, Mukhtar DJL, Walker-Smith JA. Transient monosaccharide intolerance in infants with acute and protracted diarrhoea. J Pediatr Gastroenterol Nutr 1984; 3:41-5.
6. Shaltout AA, Khuffash FA, Hilal AA, El Ghanem MM. Pattern of protracted diarrhoea among children in Kuwait. Ann Trop Paediatr 1989; 9:30-2.
7. Abdullah AAM. Aetiology of chronic diarrhoea in children: experience at King Khalid University Hospital, Riyadh, Saudi Arabia. Ann Trop Pediatr 1994; 14:111-7.
8. Booth IW, Patel PB, Sule D, Brown GA, Buick R, Beyreiss K. Glucose-galactose malabsorption: demonstration of specific brush border membrane defect. Gut 1988; 29:1661-5.
9. Meeuwisse GW, Melin K. Glucose-galactose malabsorption. A clinical study of 6 cases. Acta Paediatr Scand 1969 (suppl 188):3-18.
10. Desjeux JF. Congenital transport defects. In: Walker WA, Durie PR, Hamilton JR, Walker-Smith JA, Watkins JB. Eds. Pediatric Gastrointestinal Disease: Pathophysiology, Diagnosis, Management, 2ed. St. Louis: Mosby; 1996; 792-6.
11. Evans L, Grasset E, Heyman M, Dumontier AM, Beau JP, Desjeux JF. Congenital selective malabsorption of glucose and galactose. J Pediatr Gastroenterol Nutr 1985; 4:878-86.
12. Iyngkaran N, Robinson MJ, Sumithran E, Lam SK, Puthucheary SD, Yadav M. Cow's milk protein-sensitive enteropathy: an important factor in prolonging diarrhoea of acute infective enteritis in early infancy. Arch Dis Child 1978; 53:150-3.
13. Iyngkaran N, Yadav M, Looi LM, *et al.* Effect of soy protein on the small bowel mucosa of young infants recovering from acute gastroenteritis. J Pediatr Gastroenterol Nutr 1988; 7:68-75.
14. Iyngkaran N, Abidin Z, Davis K, *et al.* Acquired carbohydrate intolerance and cow's milk protein-sensitive enteropathy in young infants. J Pediatr1979; 95:373-8.
15. Walker-Smith JA. Intractable diarrhoea. In: Diseases of the Small Intestine in Childhood, 3ed. London: Butterworths; 1992; 390-413.