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Case Reports

A Rare Case of Cytomegalovirus Enteritis Transmitted Through Breast Milk in an Immunocompetent Term Infant After Gastrointestinal Surgery

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Abstract A full-term infant recovering from bowel resection for ileal atresia developed severe enteritis. Subsequent investigations confirmed the diagnosis of postnatal-acquired Cytomegalovirus (CMV) enteritis with the possible source of infection identified as CMV-positive breast milk. Postnatal-acquired CMV infection in preterm infants can cause significant morbidity, but is usually asymptomatic in term infants. This is the first report of life-threatening CMV enteritis in a term infant. Infants after major gastrointestinal surgery are at risk for CMV enteritis because of gut motility dysfunction, ineffective intestinal mucosal barrier, and impaired immune defense mechanisms. We suggest that breast milk screening should be performed in these cases, and feeding with CMV-positive breast milk should be avoided in the immediate post-operative period if possible. An effective method of CMV eradication needs to be established so that high-risk infants can receive the benefits of breast milk without the associated risks of CMV infection.

Key words Breast milk; Cytomegalovirus; Enteritis; Neonate

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Introduction

Congenital cytomegalovirus (CMV) infection is associated with significant morbidity in the neonatal period. On the other hand, postnatally acquired CMV infection, usually transmitted through breast milk, is common and asymptomatic in most full-term infants.[1,2] Postnatal CMV infection with gastrointestinal involvement has been reported in a small number of premature infants,[1] but is extremely rare in term infants. We report a case of severe CMV enteritis in an immunocompetent full-term infant after surgery for ileal atresia.

Case Report

A male infant was delivered by Caesarean section at 37 weeks gestation with birth weight 3195 g and Apgar scores of $9^{1}10^{5}$. He developed abdominal distension and bilious gastric aspirate on Day 1 of life. Abdominal radiograph

showed dilated bowel loops suggestive of intestinal obstruction which was subsequently confirmed by contrast study. Laparotomy revealed ileal atresia type III with segments of necrotic small bowel between the atretic segments. The proximal atretic segment was grossly dilated and hypertrophied. The necrotic and atretic segments were resected, and bowel continuity established by primary ileal-ileal anastomosis.

His post-operative course was initially uneventful. Feeding with expressed breast milk, frozen at -20°C, was started on post-operative Day 10 after return of bowel function, and gradually increased to full feeds after 7 days. He developed jaundice, dark urine and pale stools 4 days after establishment of full feeds. Liver function test revealed cholestasis with conjugated hyperbilirubinaemia, elevated alkaline phosphatase and deranged liver enzymes. Abdominal ultrasound showed increased periportal echogenicity suggestive of hepatitis. Urine detection of early-antigen fluorescent foci (DEAFF) test for CMV was negative. He deteriorated acutely 12 hours later with gastrointestinal haemorrhage and shock, requiring resuscitation and ventilatory support. Abdominal radiograph showed intraportal gas. A provisional diagnosis of severe enterocolitis was made. Emergency laparotomy was performed, which showed intact anastomosis and moderate amount of old blood in the dilated small bowel, but no necrotic bowel. Multiple yellowish plaques were found over the mucosa. The anastomosis was exteriorised to provide decompression. There was no need for bowel resection and so no bowel sample was sent for histological examination at that time. Post-operative course was uneventful, and closure of ileostomy was performed four weeks later.

Histological examination of the resected bowel (taken during ileostomy closure) showed ulceration and inflammation. Cells with intranuclear basophilic inclusions surrounded by clear halo were present, suggestive of CMV enteritis (Figure 1). Immunohistochemical staining was positive for CMV, thus confirming the diagnosis of CMV enteritis. This was compared with the proximal atretic bowel segment taken during surgery on Day 1, which showed no histological evidence of CMV infection. Repeat saliva and urine DEAFF test on Day 65 was positive for CMV (as compared to negative urine DEAFF test on Day 23), indicating postnatally acquired CMV infection.

Bacterial cultures from blood, peritoneal swabs and peritoneal fluid were negative. Mother's expressed breast milk tested positive for CMV. Human immunodeficiency virus (HIV) test was negative in both mother and infant.

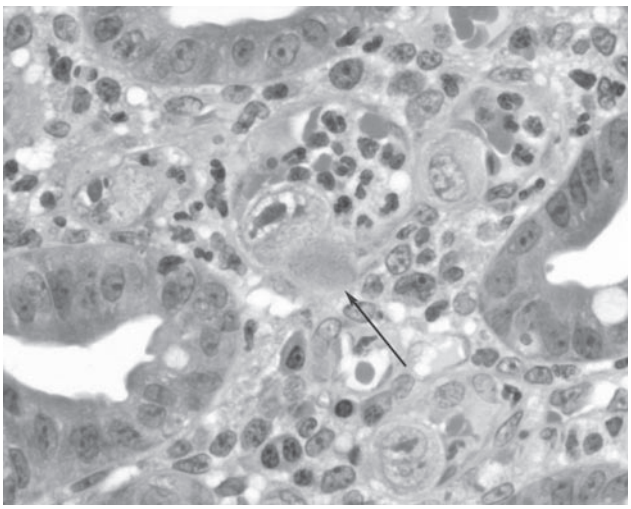

Figure 1 Microscopic appearance of section of small intestine. Scattered cells with prominent intranuclear basophilic inclusions surrounded by a clear halo are seen at the submucosa (arrow), which is diagnostic of cytomegalovirus (CMV) infection. Immunochemical staining for CMV showed positive results.

Further immune function testing for the infant (at six months) showed no evidence of immunodeficiency. Cholestasis resolved gradually, and feeding with hydrolysed formula was tolerated well. He was discharged home at 4 months. Subsequent follow up for the infant showed that he was feeding well with normal growth, and detailed assessment at one year showed normal development.

Discussion

CMV enteritis is well-known in children with immunodeficiency, especially those with Acquired Immunodeficiency Syndrome or on immunosuppressive therapy. However, enteritis due to postnatal CMV infection is very rare, with only a few isolated reports and case-series in the literature. Reported gastrointestinal manifestations of CMV infection includes abdominal distension, diarrhea, cholestasis, necrotizing enterocolitis (NEC), ileal perforation, and ileal or colonic strictures.[3-6] One case-series of postnatal-acquired CMV gastrointestinal disease included 16 infants (15 premature; 1 term infant with immunodeficiency syndrome).[1] The most severe manifestations were found in the extremely premature age group. Another case report and literature review found that

most cases of CMV infection with gastrointestinal manifestations requiring surgical intervention occurred in preterm neonates, usually presenting with an NEC-like picture followed by intestinal obstruction due to stricture formation.[7] As far as we know, postnatal-acquired CMV enteritis in full-term infants with no evidence of immunodeficiency in the neonatal period has not been reported previously, and our case is the first report of this disease entity.

The diagnosis of CMV enteritis in this case was supported by a positive CMV test in a previously CMV-negative infant. The appearance of yellowish plaques on the intestinal mucosa is characteristic of CMV enterits. This was further confirmed by histology and immunochemical staining. CMV-positive breast milk is likely to be the source of infection.

There were several significant risk factors in our infant which predisposed him to CMV infection. Firstly, motility dysfunction of the small bowel is a known association of intestinal atresia. When enteral feeding was started, delayed transit and stasis of milk occurred, leading to prolonged mucosal contact with the gastrointestinal contents. Ingestion of CMV-positive milk with a large viral load increases the risk for regional CMV infection in the stagnant bowel, which could spread to other parts of the gastrointestinal tract. Secondly, the integrity of the normal gastrointestinal mucosal barrier may be less efficient because of the recent event of in-utero accident leading to intestinal atresia. Breakdown in mucosal defense increases the infant's susceptibility to CMV infection, especially in the presence of stasis. Thirdly, although the infant has no evidence of congenital immunodeficiency, major surgery and stress may impair his immune defense mechanisms, and predispose to overwhelming infection. Thus, the combination of gastrointestinal hypomotility, stasis of milk in the small bowel, possible breakdown of mucosal barrier and impaired immune mechanisms could lead to unexpectedly severe CMV enteritis in an otherwise normal term infant.

Postnatal-acquired CMV infection is usually transmitted through breast milk. 40-85% breastfeeding mothers are CMV IgG positive. A large proportion of CMV-positive mothers may experience reactivation of CMV infection and excrete CMV in their breast milk.[8] Postnatal-acquired CMV infection occurs in 58-76% of infants.[2] Term infants are usually asymptomatic due to the protective effect of maternally-derived transplacental CMV IgG. Therefore, breast feeding is still encouraged in CMV-positive mothers, and CMV screening in breast milk is not routinely performed. However, as illustrated in this case, severe infection can still occur in full-term infants with predisposing risk factors. Conversely, 15-25% of premature neonates develop symptomatic disease because of immature defense mechanisms and lack of protective immunoglobins. Over the past few years, postnatal-acquired CMV infection has received increasing recognition as a significant disease entity in extremely premature infants.

Breast milk contains many unique components including lymphocytes and immunoglobins, and is the best source of infant nutrition. The short and long term beneficial effects of breast milk have been extensively studied and well documented, and breast-feeding should be encouraged in all infants whenever possible. However, the benefits of breast milk must be balanced against the risk of CMV infection in susceptible infants. Postnatal-acquired CMV infection was previously described as a benign condition, but there is increasing evidence that life-threatening complications can arise. Ideally, breast milk should be screened and CMV eradicated for all at-risk infants. However, studies have shown that conventional methods of freezing breast milk to -20^{o}C does not effectively eradicate CMV.[9] Alternative techniques, such as pasteurization, may be more effective, but may damage lymphocytes and immunoglobins in breast milk.[10] So far, no standardised method for CMV eradication has been universally approved. With improved knowledge and standard of neonatal intensive care, survival rate of extreme premies has improved significantly in the past two decades. At the same time, improved surgical techniques and intensive care support has led to increased numbers of infants undergoing and recovering from major complicated gastrointestinal surgery. These infants would benefit greatly from the many unique properties of breast milk, and breast feeding should be encouraged when appropriate. However, these same infants are also extremely vulnerable to infection, because of poor defense mechanisms and motility dysfunction. As illustrated from our report, significant morbidity and mortality can result if CMV enteritis occurred. An effective method for CMV eradication needs to be established so that CMV-negative breast milk can be safely given to these infants.

Conclusion

We report an extremely rare case of CMV enteritis in a term infant. Infants after major gastrointestinal surgery are at risk of CMV enteritis in the post-operative period because of impaired gut motility, mucosal damage and decreased

immune defense. We suggest that breast milk screening should be carried out, and feeding with CMV-positive breast milk should be avoided in the immediate post-operative period if possible. Further studies are needed to establish an effective method for CMV eradication in breast milk, so that high-risk infants can receive all the benefits of breast milk without the associated risks of CMV infection.

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