CASE REPORT

Gastrointestinal presentation and outcome of perinatal cytomegalovirus infection

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SUMMARY

A term infant presented at birth with bilious vomiting and abdominal distension. Multiple investigations were undertaken, including two laparotomies and a rectal biopsy, as no obvious cause for his symptoms could be found. This included testing for human cytomegalovirus (CMV) infection as part of a TORCH screen, which was negative at 10 days of age. However, a repeat screen at 3 weeks of age demonstrated positive findings of CMV in both urine and blood PCR. This subsequently led to the diagnosis of gastrointestinal pseudoobstruction associated with perinatal CMV infection. This case is of interest though there is limited information regarding the recognition of gastrointestinal symptoms in relation to CMV infection. This report aims to highlight our experience with an infant with perinatal CMV infection and severe gastrointestinal symptoms.

BACKGROUND

Human cytomegalovirus (CMV) is a member of the Herpesviridae family of DNA viruses and is found in saliva, urine, breast milk, cervical and vaginal secretions, semen, blood products and transplanted organs.¹ It is the most commonly recognised cause of congenital and perinatal viral infection worldwide.^{2–3} Congenital CMV infection occurs as a result of primary or recurrent maternal infection in pregnancy while perinatal infection occurs following exposure to infected maternal genital tract secretions at delivery or breast milk that contains the virus.^{1–2} Congenital infection affects 0.2–2.4% of all live births worldwide¹ and is defined by the isolation of CMV from urine or blood specimens within the first 3 weeks of life.⁴ About 10–15% of congenitally infected infants are symptomatic at birth and most experience serious long-term complications, such as cerebral palsy, cognitive impairment, epilepsy, optic atrophy and sensorineural hearing loss.⁴

Majority of infants with perinatal CMV infection are asymptomatic, which makes it difficult to provide accurate rates of infection but it is thought to be more prevalent than congenital infection.⁵ Perinatal CMV infection is not generally associated with symptomatic infection in term babies but can cause serious problems in preterm infants.¹

CASE PRESENTATION

A term, white male infant developed bilious vomiting and abdominal distension at 12 h of age. The baby was delivered by ventouse delivery weighing 3.68 kg and had an Apgar score of 9 and 9 at 1 min and 5 min, respectively. His mother was a

primigravida, had no complications in pregnancy and had started breastfeeding the infant.

An upper gastrointestinal contrast study showed a dilated small bowel with gasless rectum and small bowel, indicative of distal small bowel obstruction (figure 1). However, an exploratory laparotomy performed on day 1 of life demonstrated a healthy bowel with no evidence of malrotation or organic obstruction. Rectal biopsies of 2 and 4 cm depth showed the presence of ganglion cells with normal innervation, thus ruling out Hirschsprung's disease. Postoperatively, he continued to have bilious vomiting and total parenteral nutrition (TPN) was instituted. As vomiting and progressive abdominal distension continued, he underwent a repeat laparotomy at 2 weeks of age. This showed proximal small dilatation and scattered adhesions, but again no evidence of any organic obstruction and a gastrostomy tube was inserted. An ileostomy was also created at the transition from the dilated to non-dilated bowel.

Figure 1 An upper gastrointestinal contrast study showing a dilated small bowel with gasless rectum and small bowel.

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INVESTIGATIONS

Investigations, performed over the first 10 days of life, included a full blood count, full biochemical profile, parathyroid and thyroid function tests, TORCH screen (done at the age of 10 days), Parvovirus B19, immunoglobulin (Ig) profile, autoantibody screen including anti-Ro and anti-La antibodies, T-cell subsets including NK cells, CD4 and CD8 counts and a cranial ultrasound were all normal. The infant's mother had tested negative for HIV during routine antenatal testing, so this test was not repeated. Cystic fibrosis was also excluded by a negative neonatal blood spot test. In view of persistent symptoms, a repeat TORCH screen was performed when the infant was 3 weeks old and on this occasion, his urine and blood PCR tested positive for CMV, with urine titres of 90 818 copies/ml and plasma titres of 5418 copies/ml. The mother was subsequently tested and was found to be positive for both IgG and IgM antibodies. An upper gastrointestinal endoscopy confirmed a markedly dilated proximal small bowel and biopsies of the duodenum showed a histopathological evidence of CMV inclusion bodies with the typical 'owl-eye' appearance (figure 2). With these findings, a diagnosis of gastrointestinal pseudoobstruction associated with perinatal CMV infection was made.

TREATMENT

As the patient did not tolerate nasogastric tube feeding, postpyloric feeding with an elemental formula via a nasojejunal (NJ) tube was implemented. He tolerated his NJ feeds and a transgastric-jejunal (GJ) was subsequently inserted endoscopically. Since he was able to tolerate gradual increase of jejunal feeds, it was decided that the risks of using ganciclovir therapy outweighed the benefits and conservative management was implemented. The patient continued to improve with tolerance of enteral feeds and gradual weaning of TPN. A trial of erythromycin as a prokinetic agent was given to improve his intestinal motility but did not succeed.

OUTCOME AND FOLLOW-UP

The patient was discharged at 10 months of age with one quarter of his daily requirement provided via TPN and the remaining three quarters via enteral feeds using the GJ tube. The ileostomy fluid continued to be recycled into the colon with normal stool output. A hearing test and an ophthalmology review were normal.

Figure 2 A duodenal biopsy with immunohistochemistry for cytomegalovirus highlighting a viral inclusion body.

DISCUSSION

The understanding of CMV infection has improved in recent years with an increased awareness of this condition and improved diagnostic tests. However, the implications of having CMV infection remain significant as a result of increased morbidity and mortality.⁶ The most common presentations of the illness include intrauterine growth restriction, microcephaly, hepatosplenomegaly, jaundice, petechiae, thrombocytopenia or conjugated hyperbilirubinaemia, chorioretinitis, intracerebral calcification and evidence of hearing loss on newborn screen.^{1 3 4 6} Gastrointestinal involvement, however, is not thought to be a common manifestation of CMV infection in immunocompetent patients.

To the best of our knowledge, there are only two other case reports associating pseudoobstruction and CMV infection. Foucaud *et al* described a 2-month-old boy who had persistent abdominal distension and required total parental nutrition.⁷ A rectal biopsy showed hypoganglionosis with thickening of nerve processes and intranuclear inclusions in some neurons. CMV infection was subsequently confirmed by viruria and specific IgM and IgG antibodies.

Ategbo *et al*⁸ described a 2-month-old girl who had abdominal distension, vomiting and interstitial pneumonia who also required total parental nutrition. The presence of IgM anti-CMV antibodies and a biopsy of the small bowel that cultured CMV led to the diagnosis of CMV disease. Spontaneous remission occurred at 6 months of age and TPN was discontinued at 8 months of age.

Similarly, Bonnard *et al*⁹ reported a series of five neonates with gastrointestinal conditions requiring surgical intervention. These included necrotising enterocolitis, volvulus of a Meckel's diverticulum, perforation of a Meckel's diverticulum and distal ileal atresia. All patients had surgical specimens that showed typical nuclear inclusions consistent with CMV infection which led them to their conclusion that CMV infection could be an underlying factor in neonatal surgical conditions.

Our case adds to the limited information regarding the recognition of gastrointestinal symptoms in relation to CMV infection. In particular, this case is of interest as it is unusual to have an isolated intestinal manifestation of CMV without other clinical findings. Even with the positive findings of CMV from this infant's blood, urine and duodenal biopsy, the mechanism of the virus is unclear and it is difficult to know the exact role of the CMV infection in the extent of the pathology and clinical picture in this infant. Is CMV the direct cause for the pseudo-obstruction or is it an opportunistic superinfection in the presence of pre-existing inflammation?

A second point of discussion is that treatment options in neonates are limited. Clinicians have been treating symptomatic CMV with a variety of antiviral agents, ganciclovir being the most studied antiviral with the best treatment efficacy.^{3 10 11} However, studies have shown various side effects including neutropaenia, hearing loss, bone marrow suppression, raised liver enzymes, hypokalaemia and renal impairment.^{10 11} This significant profile of side effects has been a concern. Meanwhile, the development of a suitable vaccine remains a major public health priority.³ With conservative management, the outcome of patients appears to be good. In our patient as well as both patients described by Foucaud *et al* and Ategbo *et al*, all three cases recovered spontaneously without the use of antiviral therapy.

In summary, clinicians should be aware of the presentation of CMV in this infant and the good outcome despite the lack of

any clinical intervention that specifically targeted the virus. This case adds to the clinical spectrum of CMV infection and raises the question whether gastrointestinal presentations may be more common than recognised.

Learning points

- ▶ Human cytomegalovirus (CMV) infection is the most common recognised cause of congenital and perinatal viral infection in the developed world.
- ▶ The most common presentations of the illness include intrauterine growth restriction, microcephaly, hepatosplenomegaly, jaundice, petechiae, thrombocytopaenia or conjugated hyperbilirubinaemia, chorioretinitis, intracerebral calcification and evidence of hearing loss on newborn screen.
- ▶ CMV infection should be considered by clinicians as a cause of neonatal feeding intolerance.
- ▶ Conservative management should be tried first, before using ganciclovir therapy in view of concerns about side effects with ganciclovir and good prognoses in immunocompetent patients.

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