Acute abdominal emergencies associated with cytomegalovirus infection in the young infant*

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Abstract. Gastrointestinal signs and symptoms have rarely been reported in association with cytomegalovirus (CMV) infection in young infants. However, in 1981 clear pathologic evidence was presented implicating this virus as a cause of hypoganglionosis and bowel dysmotility. We report our experience with four infants with CMV infection in whom gastrointestinal dysfunction was the reason for emergency abdominal operation. Since the association was made retrospectively, we were unable to demonstrate hypoganglionosis, but our experience underscores the need to include CMV intestinal infection in the differential diagnosis of the acute surgical abdomen in young infants.

Key words: Infections – Cytomegalovirus – Acute abdomen – Enterocolitis

Introduction

Cytomegalovirus (CMV) is the most common virus transmitted in utero, infecting approximately 33,000 newborn infants each year in the United States [18]. In addition to the transplacental route, an infant may acquire CMV during passage through the birth canal, from breast milk, or from blood transfusion [13]. Most infections are asymptomatic; only about 10% of infected infants have clinical disease. The characteristic features are hepatosplenomegaly, jaundice, petechiae, thrombocytopenia, pneumonia, chorioretinitis, and brain damage, including periventricular calcification and microcephaly. Infants with CMV usually are small for gestational age, reflecting intrauterine growth retardation. Gastrointestinal (GI) signs and symptoms have rarely been noted or emphasized. However, in 1981 Dimmick presented clear pathologic evidence implicating CMV as a cause of hypoganglionosis and bowel dysmotility in an infant [4]; a total of four cases have been documented to date [5, 17].

We report our experience with four infants with CMV infection who underwent emergency abdominal operations. GI dysfunction was a presenting feature in each. In two of the infants, the CMV infection was associated with or accompanied by an acute surgical condition. In the other two, the CMV infection mimicked an acute surgical condition.

Patients and methods

The four infants were treated at the University of New Mexico Hospital during a 10-year period (1976–1985). All of the virus isolations were made using standard tissue culture techniques (human fibroblast cells) in the virology laboratory of Dr. L. C. McLaren at the University of New Mexico Department of Microbiology.

Case reports

Case 1. A full-term male infant was born with hepatosplenomegaly, jaundice, petechiae, and thrombocytopenia. His urine was positive for CMV at birth. He developed intestinal obstruction due to ileal atresia, which was corrected within the first 24 h. The pathologic specimen showed typical ileal atresia without inflammatory change. Postoperatively he had feeding intolerance, failure to thrive, and required total parenteral nutrition (TPN) via a central venous line. He was discharged from the hospital at 3 months of age.
Case 2. A 28-week gestation, 680-g male infant had severe respiratory distress syndrome, requiring mechanical ventilation. At 2 days of age, he received a double-volume exchange transfusion for hyperbilirubinemia. His urine was positive for CMV at 5 weeks. He had three episodes of necrotizing enterocolitis (NEC). Pneumatosis intestinalis was present on X-rays of the abdomen. During the third episode of NEC, at 6 weeks of age, he developed pneumoperitoneum. At operation, a focal ileal perforation was exteriorized as an ileostomy. His postoperative course was characterized by prolonged ileus and thrombocytopenia. He died of a respiratory arrest 4 weeks after operation.

Autopsy examination showed focal chronic enterocolitis (Fig. 1). Enteric ganglion cells were present, without ganglionitis. Pneumonitis with CMV inclusions (Fig. 2) and hepatitis were also present. CMV was cultured from the lungs. Postoperatively his urine culture contained CMV and blood culture contained *Escherichia coli*. His prolonged recovery was characterized by persistent ileus, ascites, jaundice, thrombocytopenia, and bloody diarrhea. He tolerated feedings poorly and required TPN via a central venous catheter. He was discharged 7 weeks after operation. Since his mother had antibody to CMV, his infection may have been acquired in utero or from two blood transfusions he had received in the first 6 weeks of life.

Case 3. A 32-week, premature male infant was transferred to the University of New Mexico Hospital at 7 weeks of age because of suspected intestinal obstruction. At admission he had biliary nasogastric drainage, severe abdominal distention, and acidosis. Hematologic tests showed anemia, neutropenia, and thrombocytopenia. At emergency exploration the findings were massive small-bowel distention and a colon of normal caliber, suggesting total colonic Hirschsprung's disease. There was mild focal peritonitis at the terminal ileum, with a few nonobstructing adhesive bands. Biopsies of the appendix and the seromuscular layer of the sigmoid showed normal ganglion cells. Postoperatively his urine culture contained CMV and blood culture contained *Escherichia coli*. His prolonged recovery was characterized by persistent ileus, ascites, jaundice, thrombocytopenia, and bloody diarrhea. He tolerated feedings poorly and required TPN via a central venous catheter. He was discharged 7 weeks after operation. Since his mother had antibody to CMV, his infection may have been acquired in utero or from two blood transfusions he had received in the first 6 weeks of life.

Case 4. A 35-week gestation, 1730-g male infant required ventilatory assistance for respiratory failure. His urine was positive for CMV when tested at 3 weeks. At 3.5 weeks he developed GI bleeding, jaundice, and thrombocytopenia. NEC was suspected, although pneumatoses intestinalis was not present on X-ray. Exploratory laparotomy was performed because of worsening abdominal distention and a falling platelet count; no intestinal gangrene or perforation was found. A blood culture drawn just prior to operation grew *Klebsiella pneumoniae*. At 4 weeks, a cerebral ultrasonogram showed cystic abnormalities in the germinal matrix and at 6 weeks chorioretinitis was found. He also had poorly functioning diaphragms from birth.
He developed bilateral diaphragmatic paralysis, which failed to improve after bilateral diaphragmatic plications. Biopsies of the rectus muscle, diaphragm, and phrenic nerve showed no abnormality. He subsequently died of respiratory failure. The early, severe CNS involvement suggested that this infection was acquired in utero.

Discussion

CMV infections are very common throughout the world. Usually the acute infection is subclinical. Serum antibody survey in adults have shown an incidence of positive titers ranging from 38% in Rochester, NY, to 99% in Tanzania [8]. Clinical illness appears in 10%-15% of infected patients, primarily those with immature or impaired host defenses such as the fetus, newborn infant, or immunosuppressed patient [13]. Adults who have clinical disease typically have a mononucleosis-like syndrome; infants may have hepatosplenomegaly, jaundice, petechiae, thrombocytopenia, and brain damage. Recent reviews of human CMV infection have been published [6, 14, 18].

GI involvement with CMV is rare, and most reported cases are in adults following bone marrow transplantation [12] or associated with acquired immunodeficiency syndrome (AIDS) [9, 11]. Only a few pediatric cases have been reported. Victoria et al. described a 16-month-old child with AIDS who developed pyloric obstruction from an extensive inflammatory infiltrate of the pyloric epithelium and muscle by CMV [20]. Dimmick and Bove described three infants with CMV infection of the bowel. Infected enteric ganglion cells were found in two of the infants, one of whom had hypoganglionosis and colonic dysmotility. The third infant had classic short-segment Hirschspring’s disease and colitis by CMV [20]. The microscopic features of CMV infection consist of cytolysis, focal necrosis, and inflammatory response featuring the pathognomonic enlarged cells with intranuclear inclusions (cytopathic cells) [13] (Fig. 2). Healing results in fibrosis and often calcification, which may cause structural damage to developing organs in the fetus. Vasculitis and disseminated intravascular coagulopathy (DIC) may occur [18].

In two of our four infants, CMV infection coexisted with other documented gut pathology. In case 1, the jejunooileal atresia may have been related to intrauterine vasculitis of the developing midgut. In case 2, ileal perforation occurred in an infant with CMV and NEC. Other intestinal viruses that have been associated with NEC are Coxsackie B2 [7], rotavirus [15], and coronavirus [2]. The pathogenesis of NEC in these instances may be by mucosal injury from the virus, which then permits invasion of the gut wall by gas-forming enteric bacteria [10]. In case 3, the gastrointestinal manifestations of CMV mimicked total colonic Hirschspring’s disease and in case 4, NEC. The presentations in cases 3 and 4 were probably secondary to CMV colitis with superimposed Gram-negative bacterial sepsis. The postoperative course of three of our four infants was characterized by prolonged ileus, thrombocytopenia, GI bleeding, and failure to thrive. These manifestations led to clinical suspicion of intestinal obstruction or intra-abdominal abscess, but no obstruction or abscess was ever found on multiple contrast studies of the bowel or radiographic scans. Platelet transfusions caused only transient improvement in the thrombocytopenia. Two infants subsequently died with disseminated CMV infection. Proctosigmoidoscopy and biopsy might have documented CMV colitis, ganglionitis, or hypoganglionosis in all four infants, but we failed to perform the procedure because we recognized the association only in retrospect.

Our experience suggests that CMV intestinal infection should be included in the differential diagnosis of the acute surgical abdomen in the young infant. The diagnosis of CMV infection can be made by culture of the virus from urine, other body fluids, or tissue specimens. Serologic diagnosis is made by demonstration of IgM antibodies or persistent or rising IgG antibodies to CMV. Flexible proctosigmoidoscopy is feasible and indicated in infants with suspected colitis. Rectal suction biopsies should be evaluated for both the presence of ganglion cells and of viral colitis and ganglionitis. Repeat biopsies may be diagnostic in infants in whom abdominal distention persists. Because the reported cases of ganglion-cell infection and/or destruction have always involved the distal colon [5, 17], a decompressive colostomy or ileostomy might be beneficial in severe cases of CMV colitis.

Because CMV is widespread, and its GI manifestations are closely linked with pediatric surgical emergencies, this disease may assume increasing importance to pediatric surgeons. Preventive measures, handwashing in particular, are essential because nosocomial infection with CMV may occur [1]. Recent studies have shown that the use of frozen deglycerolyzed blood prevents transfusion-acquired CMV infections in neonates [16, 19]. A vaccine against the virus is being tested [14]. Al-
though presently there is no cure for CMV, a new drug 9-(1,3-dihydroxy-2-propoxymethyl)-guanine (DHPG) has shown promise in clinical trials in adults with CMV retinitis or GI disease [3].

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