Intractable diarrhoea caused by cytomegalovirus enterocolitis in an immunocompetent term neonate

by Amit Kumar Gupta, Arti Maria, Deepak Goyal, and Arushi Verma

Department of Pediatrics, PGIMER & Dr RML Hospital, New Delhi 110001, India

Correspondence: Dr. Amit Kumar Gupta, 74, Saakshara Apts, A-3 Block, Paschim Vihar, New Delhi 110063, India. E-mail <guptaamit@ymail.com; 4dramitgupta@gmail.com>.

Summary

Symptomatic cytomegalovirus (CMV) infection mainly affects preterm and immunocompromised infants and usually manifest as rash, pneumonia, hepatosplenomegaly or encephalitis. To our knowledge intractable diarrhoea at two weeks of age caused by postnatally acquired CMV in immunocompetent term neonate is not reported. An unusual case of postnatally acquired CMV enterocolitis manifesting as protracted diarrhoea in an immunocompetent baby in neonatal period is reported. We conclude that CMV should be considered in the differential diagnosis of intractable diarrhoea in neonatal period and treatment with intravenous ganciclovir for CMV enterocolitis is not only indicated but is therapeutic.

Key words: diarrhoea, cytomegalovirus, ganciclovir, neonate

Case Report

A previously healthy, top-fed, home-delivered term neonate, product of non-consanguineous marriage, presented at 15th day of life with lethargy, refusal to feed, neck retraction, tachypnea, jaundice and loose stools for 3 days before admission. There was no history of clay-coloured stools. On examination, the baby was normothermic, had tachycardia, tachypnea and poor cry activity. Baby was icteric and had hepato-splenomegaly. There was no rash or lymphadenopathy. Baby had a weight of 1.6 kg (weight for age less than third percentile), length of 46 cm (height for age less than third percentile, weight for height less than third percentile) and a head circumference of 32 cm (head circumference less than third percentile). Workup for sepsis was positive, with white blood cell count 4600/μl, platelets 1.6 lacs/μl, haemoglobin 20.6 g/dl, packed cell volume 56.3%, C-reactive protein 12.0 mg%, micro erythrocyte sedimentation rate (mESR) 18 mm, immature to total neutrophil ratio 35% and absolute neutrophil count (ANC) 1520. cerebrospinal fluid (CSF) cytology showed 300 cells (90% polymorphs), protein 175 mg/dl and sugar 24 mg/dl (corresponding blood sugar 73 mg/dl). Both blood and CSF cultures were sterile. Chest skigram showed bilateral infiltrates. Stool examination revealed full of pus cells. Urine routine microscopy was normal. Workup for neonatal hepatitis showed direct hyperbilirubinemia (total bilirubin 15.0 mg/dl, conjugated bilirubin 2.5 mg/dl), aspartate aminotransferase/alanine aminotransferase 39/73, alkaline phosphatase/gamma-glutamyltransferase 154/170, alpha fetoprotein level was 140 ng/ml and thyroid function test was within normal limits. Ultrasonography (USG) abdomen and hepatobiliary iminodiacetic acid (HIDA) scan ruled out surgical causes of neonatal cholestasis. General condition of baby improved over next 1 week; however, diarrhoea, features of encephalopathy and hepatitis persisted, for which baby was further evaluated. Immunoglobulin profile revealed a normal profile. Enzyme-linked immunosorbent assay (ELISA) 1 and 2 for human immunodeficiency virus (HIV) was non-reactive in the infant and parents. Metabolic workup for galactosemia, tyrosinemia and alpha-1 anti-trypsin deficiency was negative. Tandem mass spectroscopy was normal. Toxoplasma, Rubella, Cytomegalovirus, Herpes simplex virus (TORCH) titres and anti-hepatitis C virus antibiotic titres were negative. Repeat CSF showed total cells 480 (80% mononuclear cells, 20% polymorphs), low sugar and raised protein. Diarrhoea, encephalopathy and liver dysfunction persisted despite 2 weeks of broad-spectrum antibiotics. Stool culture sensitivity was negative. Fungal infection was ruled out. A diagnostic endoscopic biopsy was done, which was suggestive of enterocolitis, and tissue polymerase chain reaction (PCR) was positive.
for cytomegalovirus (CMV). At this point of time, urine PCR for CMV was positive. Repeat TORCH profile in the baby showed seroconversion with immunoglobulin M positive for CMV, whereas mother was negative. Computed tomography of the head did not reveal any intracranial calcification. Visually evoked potential and brain stem evoked response audiometry were normal. In view of encephalopathy and hepatitis, baby was started on intravenous ganciclovir (6 mg/kg/dose, 12 hourly for 6 weeks). There was definite improvement in those symptoms within 1 week of therapy. Sensorium and liver dysfunction normalized and diarrhoea settled down. Repeat CSF examination after 2 weeks of ganciclovir therapy was normal. There was complete recovery at the end of therapy. Diagnosis of postnatal CMV gastroenteritis was made on the basis of positive tissue PCR, seroconversion and therapeutic response, with complete clinical recovery after specific therapy with ganciclovir.

**Discussion**

To our knowledge, this is the first reported case of postnatal CMV enterocolitis in an immunocompetent term neonate presenting with intractable diarrhoea at 2 weeks of age. Perinatal CMV infection has practically no consequences in term newborns, although it may cause, in some cases, a severe symptomatic disease in preterm newborns [1, 2]. Hampprecht et al have reported that the transmission of CMV from breastfeeding mothers to their preterm infants could result in symptomatic CMV infections, such as sepsis-like disease, and that the early onset of symptomatic infections occurs only in extremely immature preterm infants [3, 4]. In a previous study, all term infants shed CMV into urine over a long period, and all of them had normal clinical courses without sequelae [5]. Perinatal infection with CMV is asymptomatic but can present with pneumonitis, lymphadenopathy and hepato-splenomegaly [6]. This is rare presentation of intractable diarrhoea in a neonate because CMV gastrointestinal disease has been exceptionally observed in immunocompetent infants [2, 7–10]. We have ruled out HIV in this case, as CMV enteritis with ischaemic necrosis is common and well-recognized in patients with AIDS [10] and in immunosuppressed transplant patients [11]. Extensive immunologic evaluation of this patient revealed no evidence of any immunodeficiency.

CMV infection in this baby appears to have been postnatally acquired, as mother was never seropositive and baby demonstrated seroconversion 2 weeks after initial testing, while he was still symptomatic. The infant here described had no clinical signs of the disease at birth; moreover, absence of the stigmata of congenital CMV-like chorioretinitis, cerebral calcification and sensorineural hearing loss support postnatal acquisition of infection. No recognizable underlying illness or risk factors for CMV were found. Typically, incubation period for perinatal CMV is 4–12 weeks [10]; however, in this case, symptoms presented at 2 weeks of age, which remain difficult to explain with perinatally acquired infection. Also, difficult to explain is the likely source of infection. Horizontal CMV transmission from another close contact in the household may be possible, although we could not demonstrate source of infection. Tissue PCR assay confirmed intestinal CMV involvement, which promptly recovered after antiviral therapy.

Ganciclovir has proven efficacy in treating and preventing CMV infection in transplant recipients, yet little data about the use of ganciclovir in the paediatric age group exist [12]. Ganciclovir has been used in congenital infection [13] and in infants presenting with cholestasis [14]. However, there are no published controlled studies of the use of ganciclovir [13]. This neonate responded well to intravenous ganciclovir, without any adverse effect, resulting in complete resolution of diarrhoea, jaundice and meningoencephalitis within 2 weeks of starting it.

**Conclusion**

A case of intractable diarrhoea due to postnatally acquired CMV infection in a term, top-fed immunocompetent neonate is reported. Nevertheless, this case report contributes towards understanding CMV end-organ disease and related symptomatic infection of term infants during the first months of life. It is reasonable to workup for CMV aetiology in a case of protracted diarrhoea in neonates. Gastrointestinal manifestation should be considered in clinical spectrum of postnatal CMV infection in immunocompetent infants. It shows that severe disease may be acquired after birth, even in immunocompetent, formula-fed and full-term infants. Intractable diarrhoea may need ganciclovir therapy.

**References**