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CONGENITAL CMV MENINGITIS IN AN IMMUNOCOMPETENT INFANT WITH HIRSCHSPRUNG'S DISEASE – A CASE REPORT

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ABSTRACT Cytomegalovirus (CMV) is a common perinatal infection that tends to follow a silent course and only 5–15% of CMV-infected infants are symptomatic at birth, with signs and symptoms characterized by the involvement of multiple organs, particularly the reticuloendothelial and central nervous systems. (1,2)Gastrointestinal involvement is considered rare, and may vary depending on the location and extent of the disease, with different manifestations.(1,2,3,4,5,6)Few studies have also reported etiological association of Hirschsprung's disease with congenital CMV infection, due to damage of myentric plexus by the virus causing aganglinosis. (1,5,6) We report a case of coexistence of congenital CMV infection in the form of CMV meningitis with Hirschsprung's disease in a male infant born at 39 weeks gestation. The serologic data and DNA PCR report suggested a CMV infection of CNS and the pathologic findings of resected bowel specimens showed hypoganglionosis. Our report shows congenital CMV infection may be etiologically associated with Hirschsprung disease.

KEY WORDS : Congenital CMV infection, Hirschprung's disease, immunocompetent infant

Introduction

Cytomegalovirus (CMV) is the most common cause of congenitalviral infection worldwide, affecting 0.6- 6.1% of all live births in developing countries with high maternal seroprevalance ranging 84-100%.(7)InIndia prevalence of congenital CMV is 2.1% (8). Maternal primary CMV infection or reinfection during pregnancyare the cause of neonatal congenital infection, with a mean risk oftransmission of 40% (24-75%), lower in the first three months(36%) than in the last three months of gestation (78%). Mostof congenital infections (85-90%) remain asymptomaticamongthem, 8 to 15% will show developmental disorders or sensorial hearingloss (2,9,10,11) Possible signs and symptoms of congenital CMV infection withonset at birth are unilateral or bilateral sensorialhearing loss, visual loss, microcephaly, hepatomegaly and/or hepatitis, splenomegaly, thrombocytopenia, jaundice, petechiae, motor defects,mental disability, chorioretinitis, strabismus, optic atrophy, dentaldefects.(2,9,10) These are more severe when mother is affected in first trimester.

Gastrointestinal involvement is considered very rare in congenitaland acquired CMV infection (1,2) and manifestations may vary depending on the location and extent of the disease.(1,2,3,4,5,6)On the other hand, CMV gastrointestinalsymptoms could be an important manifestation of postnatalinfection in patients admitted to neonatal intensive care unitsora manifestation of CMV intestinal disease in immunocompromisedpatients or patients affected by inflammatory bowel disease (1,2) Arare presentation with intestinal polyps in immunocompetant healthypatients has also been described.(14)CMV infection can induce aganglionosis by damaging the myenteric plexus, as well as other organs. Therefore, through damage to the ganglion cells, CMV enteritis may produce a syndrome that can mimic Hirschsprung's disease. (1,5,6)
We present a case of congenital CMV meningitis in an immunocompetant neonate with Hirschprung's disease.

Case report

A 2500 g male was born at 39 weeks of gestational age through normal vaginal delivery with an insignificant antenatal and perinatal history. Due to an abdominal distension observed after birth and no passage of stool for 48 hours of life, Ultrasound abdomen was done which was suggestive of intestinal obstruction and the newborn was transferred to a tertiary care centre, where he was operated on day of life (DOL) 4 and an ileostomy was performed. The histopathology report of resected colon was suggestive of hypoganglionosis, likely due toHirschsprung's disease.Patient was discharged after 10 days of surgery on breastfeed. Child again got admitted at DOL 18 in the pediatric ward in view of loose stools and poor feeding. Childs weight on admission was 2500 g (less than -3SD) with length of 49cm (-1 to -2SD), and head circumference of 34cm (-2 to -3SD). On examination, child was afebrile; tachycardia was present with feeble peripheral pulses and cold peripheries. The capillary refill time was prolonged (5 seconds).

Systemic examination revealed hepatomegaly with liver span of 7cm.Child was kept in the Pediatric Intensive Care Unit (PICU) for management of dehydration with metabolic acidosis(p H 7.1, Bicarbonate 10,Base excess -18) and dyselectrolytemia (Serum Sodium 121 meq/L, Serum Potassium 2.4 meq/L). Child's hemogram showed leucocytosis(20,000/cmm) withnormal hemoglobin(11mg/dl) and platelet count(250,000/cmm).Liver and renal function tests were within normal limits. C-reactive protein was elevated (12mg/dl).Blood culture was positive for Methicillin Resistant Staphylococcus Aureus (MRSA) and antibiotic was changed to Vancomycin as per the sensitivity pattern.

Child developed high grade feverandone episode of focal seizures on fourth day of admission. Hypoglycemia andhypocalcaemia were ruled out. CSF showed 400 nucleated cells with 85% lymphocytes and elevated protein 400 mg/dL(sugar was within normal limits).CSF culture was sterile. Child was treated with Vancomycin for 21 days and CSF was performed on day 21 of antibiotic therapy which showed 650 nucleated cells with lymphocytic predominance, protein 350 mg/dL and sugar within normal limit. Tuberculosis was ruled out by appropriate tests. Mother was non-reactive for HIV antibodies by ELISA. CT brain was done to look for evidence of ventriculitis, butwas reported as having mild ventriculomegaly without evidence of ventriculitis.

Antibiotics were continued for 42 days and CSF was repeated, it showed 600 cells with lymphocytosis and moderately raised proteins (400mg/dL). Inspite of CSF pleocytosis, baby was not irritable, accepting feeds well and was gaining weight. As

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meningitis was not resolvingwith antibiotics and tubercular meningitis was ruled out, TORCH titers of baby and mother was sent to rule out congenital infections inspite of insignificant antenatal history.Table 1 shows serological data of mother and baby.

Table 1: Serological data of mother and baby:

Antibody against CMV	Mother	Interpretation	Baby	Interpretation
IgM	25	Negative	64	Positive
IgG	0.9	Positive	0.8	Positive

Results are given as numerical value, value>35 for IgM and >0.7 for IgG is considered positive.

CSF DNA PCR was positive for CMV. Child was screened for other manifestations of CMV. The opthalmoscopic examination showed no evidence of chorioretinitisand BERA was normal. CT brain at this point showed bilateral lateral ventricle enlargement with normal 3rd and 4th ventricles without intracerebral calcification. Thus, patient was diagnosed as a case of CMV meningitis in an immunocompetent host and was started on Gancyclovir for 6 weeks. Repeat CSF after 2 weeks of antiviral therapy showed marked improvement in CSF cell count, which decreased to 65 cells/cmm and also decrease in CSF protein to 100 mg/dL. Child required VP shunting due to development of hydrocephalus (head circumference-45cm, >3SD) at age of 3 months. Thereafter child was followed up till 6 months of age with repeat screening for ophthalmic, hearing, neurodevelopmental sequale of CMV infection which was found normal.

Discussion

Congenital CMV is a very common congenital viralinfection. In developing countries, the prevalence of congenital CMV infection is reported to be 0.6%–6% (7) with prevalence of congenital CMV in India is 2.1%.(8)Congenital CMV can follow a transplacentalroute or may be an ascending amnion infection derivedfrom a cervical infection.Most congenital CMVinfections are not clinically apparent, but if they are,they are characterized by the involvement of multipleorgans. Congenital CMV infection frequently manifest ashepatomegaly, microcephaly, intracranial calcification, hearing impairment, hemolytic anemia, thrombocytopenia,pneumonia,chorioretinitis(9,10,11) CMV involves CNS in form of microcephaly, neuronal migration defect, but CMV meningitis is rare entity and usually seen in immunocompromised host.

Congenital CMV-induced infections in the gastrointestinal tract are uncommon and only a few casereports have been documented. (1,2,3,4,5,6)A Porta et al showed association of different GI manifestation and congenital CMV infection (2),Huang et al(3) andReyes et al(4) reported one case each of CMV enteritis,Asabe K et al (1) and Hershlag et al (5) described a patient with coexistentHirschsprung's disease and CMV infection. Dechelotteet al(6) reported three cases of antenatal ileus associatedwith a CMV infection in both the fetus and placenta. Inall three cases, CMV was confirmed either in the ganglion cells or within the myenteric and submucosal plexuses along the small and large intestine. They thoughtthat the ileus was imputed to CMV, which caused aparalytic ileus. CMV infection probably induces aganglionosis by damaging the myenteric plexus, as well asother organs. Therefore, through damage to the ganglion cells, CMV enteritis may produce a syndrome thatcan mimic Hirschsprung's disease (1,5,6,12,13)

In our patient, cause of CNS infection was confirmed as CMV after DNA PCR report and serological analysis of mother and child. CMV meningitis is a rare presentation in immunocompetent host, as with our case and its occurrence with Hirschsprung's disease makes this case rarer. Also theclinical manifestation of Hirschsprung's disease can be considered to be due to hypoganglionosis caused by congenital CMV infection, but virus could not be isolated from the histopathological specimen of colon as CMV infection was not considered in this neonate at birth.

Conclusion

Gastrointestinal involvement during congenital and post-natal CMV infection is uncommon, in particular in immunocompetent newborns. Particularly rare is the onset of these manifestations in the first 24 h of life. The possible association between congenital infection and gastrointestinal involvement has to be suspected in newborns with specific symptoms and unknown origin. The role of invasive tests, such as the intestinal biopsy, and the necessity of a specific antiviral treatment should be considered accurately on each single case, basing on the review of the literature and recent scientific evaluations.

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