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Case Report

A Rare Presentation of Anasarca with Congenital Cytomegalovirus Infection in a 6 Month Old Infant

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Abstract

Cytomegalovirus (CMV) is the most common congenital viral infection in the developed world, with an overall birth prevalence of approximately 0.6%. Approximately 10% of congenitally infected infants have signs and symptoms of disease at birth, and these symptomatic infants have a high risk for demonstration of subsequent neurologic sequelae, including sensorineural hearing loss (SNHL), mental retardation, microcephaly, development delay, seizure disorders, and cerebral palsy. Antiviral therapy of children with symptomatic central nervous system (CNS) congenital CMV infection is effective at reducing the risk of long-term disabilities and should be offered to families with affected newborns. Congenital cmv infection causes foetal hydrops. Anasarca in this age is rare.

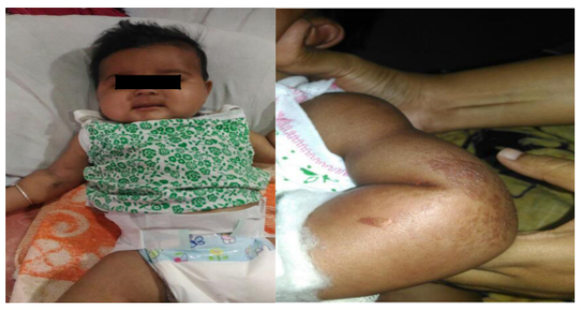
Keywords: *Cytomegalovirus (CMV); Sensorineural Hearing Loss (SNHL); Central Nervous System (CNS)*

Introduction

Cytomegalovirus (CMV) is the most common congenital viral infection in the developed world, with an overall birth prevalence of approximately 0.6%.

Case Report

A 6 months old female baby admitted with chief complaints of generalised swelling of whole body since 4 months of age. The swelling started from palm and soles and gradually progressed to involve the whole limbs, abdomen and cheek. There was no periorbital swelling. Urine output and colour was normal. There is a history of passage of pale coloured stool since last 2 months. The baby was born at term, of a primigravida mother by elective caesarean section, birth weight was 4 kg, cried at birth, postnatal period uneventful, immunization is up to date. The baby was exclusively breastfed for 4 months after which top feeds in proper dilution and frequency given. On examination baby was conscious, alert but irritable. On general examination pallor and anasarca was present. On examination of gastrointestinal system abdomen was soft, liver palpable 5 cm below right costal margin, liver span 8 cm, firm, margin round, surface smooth, moving with respiration. Spleen not palpable. Shifting dullness present but fluid thrill was absent. Other system within normal limits.



On examination of complete blood count Hb was 6.4, platelet 1.97 lakhs, WBC count 20,000 (neutrophil 60%, lymphocyte 37%, monocyte 2%, eosinophil 1%. Direct coombs test was negative, iron profile was normal. Stool for OBT was negative. CRP 22.7. Blood culture was negative. Urine routine and culture was normal. Renal function tests were normal. Liver function tests showed conjugated hyperbilirubinemia (bilirubin- 1.9 conjugated 1.4 unconjugated 0.5) hypoalbuminemia (albumin 1.6), globulin 2.3, alkaline phosphatase 289, SGPT 88, SGOT 320, normal HDL, VLDL, TG. Coagulation profiles showed inr 1.86, apt - no coagulation. Ultrasound of abdomen done which revealed hepatomegaly Viral profile (Hepatitis A, B, C, E and HIV 1, 2) was negative. The picture showed a baby with anasarca with anaemia with conjugated hyperbilirubinemia with dearranged coagulation with abnormal LFT with no blood or urinary infection. All pointed to a possibility of congenital infection. TORCH was sent which showed cytomegalovirus IGG and IGM positive. Urine for cmv PCR showed 4755 copies/ml. 2 units of FFP and 1 unit of PRBC given. Oral valganciclovir started and continued for 6 months. BERA done which was normal. MRI brain done which was normal. Ophthalmological examination was within normal limit.

Discussion and Conclusion

Cytomegalovirus (CMV) is a herpesvirus and commonest cause of congenital infections. Incidence is 0.2 - 2.4% of all live births. Perinatal infection has an incidence of 10 - 60% in the first 6 months of life. Immunocompromised patients and seronegative premature infants have a risk of infection as high as 30%. Perinatal transmission occurs mainly through genital tract secretions at the time of delivery and through breast milk. Approximately 6 - 12% of seropositive mothers transmit the infection through cervical-vaginal secretions, while 50% transmit through breast milk. CMV is mostly asymptomatic or mildly symptomatic in infants, children, however can be devastating to immunocompromised hosts including infected newborns, and results in the greatest long-term neurodevelopment morbidity of all the perinatally acquired viral infections. The most frequent sequel is sensorineural hearing loss (SNHL) [8].

Congenital CMV infection has a different mode of transmission and pathogenesis. CMV spreads from sites of infection in uterine arteries to invade cytotrophoblasts, then to placental villi floating in maternal blood. IgG antibodies with a low neutralizing titre allow viral replication to continue in the villus cytotrophoblasts. The infection then spreads to the stromal fibroblasts and the fetal vasculature. It is associated with defective interferon-gamma and proliferative responses of CD4 T lymphocytes. Studies have suggested that CMV induced CD4 deficiency may be a factor for the slow clearance of the virus in children and its continued excretion in saliva and urine for upto 10 years.

Only 5% of congenital CMV infection present with the severe cytomegalic inclusion disease. Another 5% will have a mild involvement and the remaining will present with subclinical disease. Petechiae, hepatosplenomegaly and jaundice are the most common presenting features seen in 60 - 80% of cases. Microcephaly with or without cerebral calcification s, intrauterine growth restriction and prematurity are seen in about 30-50% of cases. Inguinal hernia and chorioretinitis are seen, but are less common. An important sequel of congenital CMV infection, whether symptomatic or asymptomatic is sensorineural hearing loss. CMV is a leading cause for sensorineural hearing loss, which is seen in 7% of all infants with the infection. The prognosis of severely infected infants is poor, with a mortality rate of 20 - 30%. Neonatal cholestasis is caused due to various conditions includes biliary atresia and a number of intrahepatic problems such as infections, metabolic conditions, and chronic familial cholestatic diseases. Several serologic studies suggest that various viral infections are associated with intrahepatic forms of neonatal cholestasis. Neonatal cholestasis gives rise to mainly two types of manifestations i.e. mechanical obstruction causing biliary atresia and functional impairment causing neonatal hepatitis. Congenital CMV infection as a cause of neonatal cholestasis is being seen with increasing frequency in the recent past. Although Cytomegalovirus (CMV) is known to cause intrahepatic bile duct destruction and paucity, its role as a cause of biliary atresia has been a topic of much debate. It has been suggested that neonatal hepatitis and biliary atresia represent two ends of a spectrum of a single disease process.

Congenital CMV is commonly diagnosed using serological tests. Maternal testing for CMV is desirable. Fetal infection is diagnosed by positive viral culture or PCR from amniotic fluid. Diagnosis in the neonate is made by viral detection in body fluids like blood, urine, sa-

liva, CSF, broncheo-alveolar lavage fluid and tissue biopsy specimens. via PCR, culture, or antigen testing (pp65 antigen) within the first 3 weeks of life.

Cranial ultrasound is a good screening tool, with subsequent MRI being recommended for definitive evaluation. Ophthalmologic assessment should be performed on all infants with congenital CMV infection. Ophthalmological signs are seen in a large percentage of symptomatic infants and include chorioretinitis, optic atrophy, and cortical visual impairment. Audiological assessment should be performed on all infants with congenital CMV infection: as noted, SNHL may be absent at birth, and progressive in nature, and frequent evaluations are required throughout childhood to evaluate for the possibility of hearing deterioration. At a minimum, audiological assessment should be performed every 6 months for the first three years of life, and annually thereafter. Hypoplasia and hypocalcification of tooth enamel is common in children with congenital CMV infection and regular dental visits are an important component of the long-term care of these infants.

Treatment of congenital CMV infection with antivirals should be instituted in infants with evidence of central nervous system (CNS) involvement, including SNHL, and should be considered in infants with serious end-organ disease (hepatitis, pneumonia, thrombocytopenia). The cornerstone of antiviral therapy is ganciclovir. Ganciclovir is a synthetic acyclic nucleoside analog, structurally similar to guanine. Following phosphorylation by a viral protein known as UL97, cellular enzymes phosphorylate the monophosphate form to di- and tri-phosphate metabolites; the ganciclovir triphosphate metabolite then exerts its antiviral effect in the CMV-infected cell.

An alternative to intravenous ganciclovir for neonates who can take enteral medication is the use of its oral prodrug, valganciclovir. This approach is attractive insofar as it obviates the need for placement of a central venous catheter for six weeks of intravenous therapy. Valganciclovir is very well absorbed following oral administration. It is rapidly metabolized following oral dosing into ganciclovir. Ganciclovir and its oral prodrug valganciclovir may have a useful role in Neonatal CMV cholestasis if given early in the course of the disease before severe liver cell damage occurs as has been used in few studies in Sweden and case reports. Untreated these patients can progress to chronic liver disease and portal hypertension.

Adverse effects profile of ganciclovir include bone marrow suppression. Other adverse effects include rash, fever, vomiting and neuropsychiatric disturbances [1-13].

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