Congenital cytomegalovirus virus infection

Rana PVS
Professor and Head of Department, Department of Medicine, College of Medical Sciences, Chitwan, Nepal

Abstract

A 14 months old male child with psychomotor retardation and hypotonia is reported, where computerized axial tomography revealed multiple calcification and ventriculomegaly secondary to cortical atrophy. Investigation suggested the diagnosis of cytomegalovirus infection. Importance of early diagnosis is emphasized as the potential long term sequelae can be prevented or reduced markedly with available therapeutic options.

Key words: Congenital, Cytomegalovirus, Psychomotor retardation, Calcification, Ganciclovir, Hyper immune globulin

Infection by cytomegalovirus (CMV), a herpes virus, is common and is acquired in early life in developing countries, with seroprevalence approaching 100% by early adulthood. It remains latent reactivating to produce clinical illness in individuals with impaired immunological status. Congenital CMV infection is the most common of all congenital infections in developed world with reported incidence of 0.5-2% of all live births1 and parallels maternal seropositivity. A 30-40% infection to fetus is reported with primary maternal infection during pregnancy as compared to 1% with non primary infection2. However, the severity of congenital CMV infection is similar following primary and non primary infection3,4. The infection is apparent at birth in 10-25% of all children with congenital CMV infection. The illness with severity varies from a mild transient illness to a severe fulminant form with dissemination involving all the organs and has a perinatal mortality of 20%5. Those who survive have crippling complications in this communication a case of congenital CMV infection with predominant neurological manifestations is presented and literature is reviewed.

Case report

A 14 months old child presented to neurology services of College of Medical Sciences and Teaching Hospital Bharatpur (Chitwan) with history inability to stand or walk and poor vocalization. There was no history of natal or perinatal injury, fever or seizures. There was no antenatal check up of the mother. As stated he was born at full term with delivery conducted at home. Clinical examination revealed an ill nourished child. No significant clubbing, lymphadenopathy, icterus or neurocutaneous markers detected. He was afebrile. Central Nervous system (CNS) examination showed a floppy infant who was unable to hold his head. He could not sit without support but he could turn in the bed. Traction head lag response was positive. The response to loud sound was poor. The speech was poorly developed. Rest cranial nerves were normal. There was marked with hypotonia. No lateralized wasting or hypertrophy or abnormal movements noted. The reaction to noxious stimulation was normal. Deep tendon reflexes were symmetrical with plantar response extensor on both sides. No cerebellar signs detected. The fundoscopic examination was normal. There was no neck rigidity. Skull circumference was 40 cms with closed fontanelle. Rest systems were normal. Investigations revealed normal hematological and metabolic parameters. CT scan (Plain and contrast) revealed wide spread calcification in periventricular, subcortical and cortical regions ventriculomegaly (Figure 1 and 2). The mother had no evidence of active CMS infection. Test for HIV was negative in child and mother. TORCH test revealed significant titres diagnostic of CMV infections. A diagnostic PCR test and Ganciclovir therapy was advised. Parents other family member were counselled about the illness. However, he was lost for follow up.

Correspondence
Dr. P.V.S. Rana
Professor of Medicine & Neurology, Head Department of Medicine
College of Medical Sciences
Chitwan, Nepal
E-mail: rananirmalpvs@gmail.com
Fig 1: CT Scan showing multiple calcification (periventricular, subcortical and grey mater white mater junction), gross ventriculomegaly and mild cerebellar hypoplasia.

Fig 2: CT Scan showing multiple calcification (Periventricular & Subcortical region) and ventriculomegaly.
Discussion

The presentation as floppy child with psychomotor retardation with mild microcephaly, poor response to loud sounds suggesting hearing impairment, bilateral pyramidal signs and characteristic CT scan findings of wide spread intracranial calcifications and ventriculomegaly (Figure 1 and 2) suggested the child to be a case of congenital CMV infection, a diagnosis confirmed later by positive TORCH (TOxoplasma, Rubella, CMV, Herpes simplex) test for CMV infection in infant and mother. Confirmatory PCR (polymerase chain reaction) test was advised. However, the child was lost for follow up.

Congenital CMV infections are under recognised as a cause of morbidity in new born as statistics revealed that 4000-6000 infants are born with symptomatic congenital CMV disease every year in USA. New born with congenital CMV syndrome are small for gestational age. The clinical manifestations in severe cases include wide spread petechiae, hepatitis, pneumonitis, enteritis, nephritis, haemolysis and bone marrow suppression. Involvement of central nervous system (CNS) manifests as meningo-encephalitis, intracranial calcification, microcephaly, germinal matrix cysts, ventriculomegaly and cerebellar hypoplasia. Mortality of children with symptomatic disease especially with disseminated form is high and those who survive are likely to have late complications including hearing loss, Chorioretinitis, mental retardation, optic atrophy, seizures and learning disabilities. Even the 10-15% of asymptomatic children with congenital CMV infection are also at risk of developing these complications. Difficulty arises in distinguishing asymptomatic cases from disease. Though buffy coat culture is positive in symptomatic cases, detection of viral antigen (i.e. pp85 antigen) or DNA detection by PCR and DNA hybridization are more sensitive. Quantitation by DNA PCR is helpful in monitoring the progress of disease and response to therapy. The neuroimaging findings are diagnostic.

Ganciclovir, a nucleoside analogue, is the drug of choice for CMV infection. A non blinded randomized controlled phase III trial of Ganciclovir, to examine its benefit in infants with virologically confirmed congenital CMV infection, was initiated in 1991. The dose recommended was 12 mg/kg/day in 2 divided doses for six week. The end point was improved hearing or retention of normal hearing. A small but significant benefit was noted at six month. Present recommendation is to use Ganciclovir in infants with life threatening disease, CNS involvement or persistent of recurring disease (Class-I). Data whether Ganciclovir can prevent, delays or alters the onset of late onset or progressive sensory neuronal deafness in asymptomatic child with congenital CMV infection is lacking. No drug interaction was noted. As prong use of Ganciclovir can cause neutropenia, the use of G-CSF or GM-CSF can be considered. Renal insufficiency is the other side effect of the drug.

Other drugs available for treatment of CMV infection are a produg of Ganciclovir (Valganciclovir) and other antivirals (Foscarnet & Cidofovir) but there is lack of sufficient data in the setting of congenital CMV infection. In addition, trials are on for treatment of pregnant patients with primary CMV infection and fetal infection in utero with CMV specific hyper immune globulins - HIG. In the therapy group 3% of 55 women receiving HIG gave birth to symptomatic congenital disease as compared to 50% women who did not receive HIG. Similar figure in preventive group (120 patients) was 16% and 40% respectively. An improved outcome in fetus was noted. HIG can now be given for CMV infection during pregnancy. However, additional studies are needed.

In view of high incidence of acquired primary infection in women and possibility of its vertical and lateral transmission prenatal and natal screening with expanded screening of new born should be mandatory to detect cases at early stage especially when pregnant women with primary CMV infection and fetus with uterine infection, can be treated with effective medications.

References


