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Fetal Ventriculomegaly in Congenital Cytomegalovirus Infection (Cmv) – A Case Report and Narrative Review of Literature

Nargis Ara Begum[1*], Mohammad Abdur Rahman[2], Aminul Islam[3], Khodeza khanam[4], Suman Sharker[5], Runa laila[6]

[1]Senior Consultant Department of Pediatrics and Neonatology United Hospital Ltd. Dhaka, Bangladesh.
[2]Associate Consultant Department of Pediatrics and Neonatology United Hospital Ltd. Dhaka, Bangladesh.
[3]Senior Consultant Ever Care Hospital, Dhaka.
[4]Junior Consultant Obst. & Gynae Sarkari Karmachari Hospital, Dhaka.
[5]Specialist Department of Pediatrics and Neonatology United Hospital Ltd. Dhaka, Bangladesh.
[6]Department of Pediatrics and Neonatology United Hospital Ltd. Dhaka, Bangladesh.

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***Corresponding author:** Nargis Ara Begum, Senior Consultant Department of Pediatrics and Neonatology United Hospital Ltd. Dhaka, Bangladesh.

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Abstract:

Materno-fetal infection with cytomegalovirus is the most common congenital infection of newborn and leading cause of mental retardation and sensory-neural hearing loss. In case of congenital CMV infection, infant may be symptomatic or asymptomatic at birth. A symptomatic newborn is characterized by clinical signs like jaundice, hepatosplenomegaly, petechiae, microcephaly, hydrocephalus. Laboratory findings consistent with increase in transaminase level, thrombocytopenia, hyperbilirubinemia. The abnormalities of neonatal imaging's are found in 70% of symptomatic newborns, intracranial calcifications are the most frequent abnormalities. Mortality rate of such case approximates 30% & survivors can have mental retardation, sensoryneural hearing loss, choreo- retinitis & other significant medical problems.

Key Words: congenital cytomegalovirus (CMV) infection; ventriculomegaly; fetal ultrasound

Introduction

Cytomegalovirus is the commonest intrauterine infection having varied presentation with propensity for the central nervous system (CNS) [1,2,3]. Fetuses may remain asymptomatic or present with a wide range of brain pathologies. These findings are not always obvious antenatally but can be demonstrated by fetal ultrasound and MRI, to evaluate hydrocephalus, microcephaly, increased periventricular calcification and malformations of cortical development [4,5]. Brain involvement induced by congenital CMV infection may be the result of uncontrolled viral replication, immune-mediated damage by cytotoxic CD8+ T-lymphocytes and fetal hypoxia [6]. Ten per cent of congenitally infected newborns are symptomatic at birth and permanent neurological injury occurs in up to 60% of these infants [7,8]. Even with antiviral therapy, these injuries are often irreversible. Neurological outcomes may include cerebral palsy, mental retardation, sensorineural hearing loss, seizures, and visual impairments. Hydrocephalus, microcephaly, periventricular calcification, polymicrogyria have been found to be strong predictors of an adverse neurological outcome [9]. We reported a case of fetal hydrocephalus as a consequence of congenital cytomegalovirus infection, treated by valgancyclovir in the neonatal period.

Case Report:

A male baby was born at 36 wks of gestation by C-section due to severe oligohydramnios (AFI 3.8 cm). Mother (28 yrs old) is a primigravida with spontaneous conception and uneventful antenatal period. Ultrasound scan in first and second trimester were normal. Third trimester ultrasound showed mildly dilated cerebral ventricles, screening for maternal TORCHS was planned. As maternal CMV immunoglobulin (IgG) titre was high antenatally, planned for thorough postnatal evaluation of newborn. On physical examination, baby was low birth weight (LBW),

2016 gm (less than 10th centile), IUGR, supine length of 46 cm (25-50th centile), head circumference of 33.5 cm (50-90th centile), mildly pale, mildly jaundiced and tachypnoic. Haematological parameter showed 11 g/dl of haemoglobin and normal platelet count. Serum bilirubin on day four of life was 12.5 mg of indirect hyperbilirubinemia but other liver function test were normal. Other biochemical and coagulation studies were within normal limit. Evaluation of tachypnea showed normal lung finding, echocardiographic evidence of moderate patent ductus arteriosus (PDA) and persistent pulmonary hypertension of newborn (PPHN), resolved by oxygen and other supportive care. Ultrasound brain showed mildly dilated lateral ventricles with left germinal matrix hemorrhage (grade-1). CT scan of brain revealed dilated 3rd and lateral ventricles with periventricular calcification. Hearing test and opthalmological test were within normal limit. Urinary CMV DNA was done and found positive with high titre and treatment started within seven days of life by oral valgancyclovir at 16 mg/kg/dose, 12 hourly for next 6 months. Baby was discharged on day 10 of life with regular clinical, biochemical (liver function and renal function) and haematologic assessment. Neurodevelopmental follow up was planned routinely.

Discussion:

Cytomegalovirus, a double-stranded DNA virus, is the commonest cause of congenital infection. Mother-to-fetus transmission is usually secondary to maternal viremia or rarely by infected secretions following rupture of fetal membranes [10]. Upto 10% of congenital CMV infections are symptomatic, with predominant CNS manifestations. Sensorineural deafness is the commonest, followed by cerebral malformations like ventriculomegaly, lissencephaly, polymicrogyria, pachygyria, hypoplasia of cerebellum and hippocampus, and intracranial calcifications [11]. Ventriculomegaly is a common feature of congenital CMV infection in children. de Vries et al found mild to moderate ventriculomegaly in 10 out of 11 symptomatic children [12]. Some studies strongly support the association of fetal hydrocephalus with congenital CMV infection [13,14,15,16]. Intracranial calcification is considered the hallmark of intrauterine infections and have been described not only in congenital CMV infection but also in fetuses and newborn with congenital toxoplasmosis, rubella, herpes simplex and varicella [17, 18]. Two different types of calcifications have been reported in congenital viral infection; punctate calcifications, are small and disseminated in any part of the brain, including the basal ganglia and the cerebellum and a coarse, 'en plaque' calcification characteristically affect the periventricular zone, are associated with congenital CMV[13,19]. Our reported case was antenatally diagnosed as a case of fetal hydrocephalus with germinal matrix haemorrhage, antenatal screening of mother suggestive of high CMV titre and postnatal radiology (ultrasound and CTscan of brain) revealed dilated 3rd and lateral ventricles with periventricular calcification. Subsequently confirmed as a case of congenital CMV infection by urinary CMV PCR analysis. Similar to our case, Moinuddin et al reported a 35-week-old newborn, in whom third trimester ultrasonography showed enlarged cerebral ventricles and subsequent fetal MRI showed parenchymal hemorrhage in right posterior temporal and parietal regions with mild ventriculomegaly. Postnatal MRI demonstrated its progression to porencephaly. Polymerase chain reaction was positive for CMV [20]. Nigro et al reported a woman with CMV infection, whose abortion product at 20 weeks was a fetus with dilated occipital horn of ventricle with intracerebral hemorrhage [21]. Suksumek et al described a term neonate, who was found to have intraventricular hemorrhage in the third trimester ultrasonography. Postnatal MRI showed dilated ventricles, with bilateral occipital and subependymal cysts and residual bleed in the left lateral ventricle. Cytomegalovirus DNA PCR was positive, bleed was attributed directly to the pathological effects of the virus [22]. Our reported case, antenataly diagnosed fetal hydrocephalus case, postnatally presented with moderate PPHN, resolved conservatively with oxygen therapy and other supportive care. Similar finding was found in a study by Arun Babu et al, they reported a neonate with severe primary pulmonary hypertension, who was found to have multiple purpuric skin lesions and soft hepatosplenomegaly. Neuroimaging showed intraparenchymal and intraventricular hemorrhage along with periventricular calcification. Investigations showed thrombocytopenia and positive CMV IgM as well as urinary DNA PCR, and was started antiviral medication [23]. Interestingly, there was no hepatospenomegaly as well bleeding manifestations in our reported case.

Cytomegalovirus is thought to be directly neurotropic and affects nervous tissue development [23]. Central nervous system vasculitis can also occur due to infection of the endothelial cells, resulting in thrombosis or hemorrhage [24]. Cyst formation in the brain may be secondary to hemorrhage or virus-related cytopathic effects, and may not be demonstrable on early ultrasonography [25]. The diagnosis of fetal ventriculomegaly should be considered particularly worrisome and prompt a detailed investigation, not only in order to rule out congenital CMV but also chromosomal anomalies or syndromic malformations, particularly malformations of cortical development [26]. The treatment of CMV infection has developed significantly over the last 20 years, currently four antiviral drugs are marketed for treatment of CMV infection; valgancyclovir, gancyclovir, foscarnet, cidofovir. Collaborative antiviral study group (CASG) recommends treatment of intravenous gancyclovir or oral valgancyclovir should start within first three weeks of life. Our reported case of congenital CMV infection with mild ventriculomegaly was treated by oral valgancyclovir for six months course with regular follow up of haematologic, liver and renal function as well neurosurgical checkup of ventricular status of brain.

Cytomegalovirus infection in pregnancy is symptomatic in less than 25% of women but infects more than 40,000 newborns annually. In cases of unexplained fetal ventriculomegaly with intracranial hemorrhage, detected antenatally or postnatally, CMV should always be ruled out for early prediction of fetal infection or starting specific treatment immediately after delivery to reduce neurodevelopmental sequelae.

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