Congenital Cytomegalovirus Infection Masquerading as Antenatal Ventriculomegaly With Intraventricular Hemorrhage in a Term Neonate

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Abstract

Intraventricular hemorrhage is an uncommon manifestation of congenital cytomegalovirus (CMV) infection and has been described in preterm neonates. We discuss a term neonate, who was referred because of intracranial hemorrhage and hydrocephalus detected in the antenatal ultrasound. She had cholestatic jaundice, hepatitis, and thrombocytopenia, with positive polymerase chain reaction for CMV. Neuroimaging revealed reduced sulcation, mildly enlarged ventricles, and multiple periventricular cysts, along with residual hemorrhage in occipital horn of left lateral ventricle. She was started on ganciclovir, following which there was improvement in platelet count, jaundice, as well as transaminase levels.

Keywords

cytomegalovirus, intraventricular hemorrhage, neonatal cholestasis, hydrocephalous

Introduction

Cytomegalovirus is the commonest intrauterine infection and can have varied presentation with propensity for the central nervous system (CNS). We report a term neonate, who was detected to have intraventricular hemorrhage and hydrocephalus during ultrasonography in the third trimester, which turned out to be congenital cytomegalovirus (CMV) infection, and received treatment with ganciclovir.

Case Report

The mother of our index case is a primigravida with spontaneous conception and uneventful antenatal period. Ultrasound scans in first and second trimesters, including level II scan for congenital malformations, were normal. Ultrasonography in third trimester showed dilated ventricles with intraventricular and germinal matrix hemorrhage.

The baby was delivered at term (37 weeks), with Apgar scores of 8 and 9. On examination, she was icteric with erythematous maculopapular rash over body. Anthropometry was within normal limits (weight: 2.7 kg [−1.42z], length: 46 cm [−2.26z], head circumference: 32 cm [−1.94z]).

Abdominal examination revealed firm hepatosplenomegaly; rest of the systemic examination was normal. Investigations revealed thrombocytopenia (platelet count: 19 000/mm³),

conjugated hyperbilirubinemia (total bilirubin: 14.1 mg/dL, conjugated fraction: 8.7 [61%]), and elevated transaminases (aspartate transaminase: 367 IU/L, alanine transaminase: 186 IU/L); coagulogram was normal.

Ultrasound of cranium showed multicystic lesions along lateral wall of frontal horns of lateral ventricle, and of the abdomen was suggestive of hepatosplenomegaly with normal echotexture. Magnetic resonance imaging (MRI) on D3 of life revealed reduced sulcation predominantly in bilateral frontal areas, mildly enlarged ventricles, and multiple periventricular cysts, along with residual hemorrhage in occipital horn of left lateral ventricle (Figure 1).

Polymerase chain reaction (PCR) of blood was positive for CMV, with a viral load of 279,560 copies/mL. Cytomegalovirus DNA polymerase chain reaction (PCR as well as CMV immunoglobulin (Ig) G was positive in mother. Serologies for rubella, syphilis, toxoplasma, and human immunodeficiency

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Figure 1. Magnetic resonance images showing. A, Axial T1 section showing reduced sulcation predominantly in bilateral frontal areas along with residual hemorrhage in occipital horn of left lateral ventricle (red arrow). B and C, Axial Fluid attenuated inversion recovery sequence (FLAIR) section showing reduced cortical sulcation and enlarged lateral ventricles. D, Axial FLAIR section showing enlarged temporal horns of lateral ventricles.

virus were negative. Thyroid function test was normal. She was started on intravenous ganciclovir (5 mg/kg administered intravenously twice daily), following which there was improvement of thrombocytopenia, jaundice, and transaminase levels (Table 1).

Discussion

Cytomegalovirus, a double-stranded DNA virus, is the commonest cause of congenital infection, with a global prevalence rate of around 2.5%.¹ Mother-to-fetus transmission is usually secondary to maternal viremia, or rarely by infected secretions following rupture of fetal membranes.

Upto 10% of congenital CMV infections are symptomatic, with predominant CNS manifestations. Sensorineural deafness is the commonest, followed by cerebral malformations like lissencephaly, polymicrogyria, pachygyria, ventriculomegaly, hypoplasia of cerebellum and hippocampus, and intracranial calcifications.² Intracranial hemorrhage has been rarely reported in congenital CMV infections and is limited to intraventricular hemorrhage in preterm infants.

Table 1. Investigations (Baseline and After Ganciclovir).

Investigation	Baseline	1 Week After Ganciclovir	2 Weeks After Ganciclovir	4 Weeks After Ganciclovir
Hemoglobin (g/dL)	14.4	14.5	12.7	13.6
Platelet (per mm ³)	19 000	64 000	174 000	296 000
Total leucocytic count	6340	8350	7600	8600
Total bilirubin (mg/dL)	14.1	13.1	10.9	4.6
Conjugated bilirubin (mg/dL)	8.7	7.6	7.1	1.2
Aspartate transaminase (IU/L)	362	327	196	66
Alanine transaminase (IU/L)	186	117	88	36

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 hydrocephalus. Postnatal MRI demonstrated its progression to porencephaly. Polymerase chain reaction was positive for CMV.³ 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.⁴

McDonald et al described a term newborn with CMV infection with intracranial hemorrhage involving the cerebellum, bilateral thalami, and extending to the ventricles, which was attributed to the thrombocytopenia.⁵ Suksumek et al described a term neonate, who was found to have intraventricular hemorrhage in the third trimester ultrasonography, although previous studies were normal. Postnatal MRI showed dilated ventricles, with bilateral occipital and subependymal cysts and residual bleed in the left lateral ventricle. Cytomegalovirus DNA PCR was positive, although platelet count, coagulogram, and liver function were normal, and bleed was attributed directly to the pathological effects of the virus.⁶

Ayadi and Ben Hamida reported a term neonate, with no abnormality detected on antenatal ultrasound, who was found to have thrombocytopenia and bilateral subependymal cysts and hydrocephalous. Polymerase chain reaction was positive for CMV; however, liver function test was normal. He was started on ganciclovir and discharged.⁷

Sobolewska-Pilarczyk et al described a term neonate, who was incidentally found to have a grade III intraventricular hemorrhage on postnatal ultrasound, which was confirmed on a Non-contrast computed tomography (NCCT), along with calcification of periventricular white matter and asymmetric ventriculomegaly with periventricular cysts. Coagulogram and platelet count were normal; PCR for CMV DNA was positive in both plasma and cerebrospinal fluid. Diagnosis of congenital CMV infection was kept, and treatment of ganciclovir was initiated.⁸

Arun Babu et al 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 on ganciclovir.⁹

Cytomegalovirus is thought to be directly neurotropic and affects nervous tissue development resulting in dysplastic changes, especially affecting the cerebellum and hippocampus.⁹ Central nervous system vasculitis can also occur due to infection of the endothelial cells, resulting in thrombosis or hemorrhage.¹⁰ Cyst formation in the brain may be secondary to hemorrhage or virus-related cytopathic effects, and may not be demonstrable on early ultrasonography.¹¹

Cytomegalovirus infection in pregnancy is symptomatic in less than 25% of women, but infects more than 40,000 newborns annually. In cases of unexplained intracranial

hemorrhage or cystic cerebral changes in newborns, detected antenatally or postnatally, CMV should always be ruled out.

Declaration of Conflicting Interests

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