

Congenital Cytomegalovirus Infection in One Twin after Primary Maternal Infection

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ABSTRACT

Cytomegalovirus is the most common cause of intrauterine infection; it is a frequent cause of mental retardation and sensorineural hearing loss. We reported a congenital cytomegalovirus infection in one twin after primary maternal infection with a focus of dissimilarity in presentation, clinical course, and outcome.

Key words: Bichorionic, congenital infection, cytomegalovirus, twins

INTRODUCTION

The congenital cytomegalovirus (cCMV) infection occurs with a prevalence of 0.2%–2.0% (average of 0.64%) of pregnancies.^[1,2] The infection is the result of mother-to-child transmission, and it is due mostly to a primary maternal cytomegalovirus (CMV) infection which carries a risk of transmission from 24% to 75%.^[3-5] The incidence of CMV transmission due to non-primary infection is 1–2.2%.^[3,5]

About 10–15% of congenitally infected infants present symptoms at birth such as petechiae, chorioretinitis, anemia, intrauterine growth restriction, thrombocytopenia, hepatosplenomegaly, microcephaly, and jaundice, and a large percentage of them will die because of bacterial superinfection, hepatic dysfunction, or disseminated intravascular coagulation.^[3,6]

The majority of the congenitally infected infants have no symptoms or signs at birth, but 5% to 15% of them will develop sequelae such as delay of psychomotor development, sensorineural hearing loss, and visual impairment;^[3,7] that’s why CMV infection is an important problem in the developed countries.

CASE REPORT

The first-trimester laboratory screening of a biamnioticbichorionic twin pregnancy showed positive CMV IgM (29.20 Au/mL) and IgG antibodies (77.30 Au/mL) and positive CMV DNA in the urine (282 copies/ml). The determination of anti-CMV IgG avidity, performed at 24 weeks, documented a high-avidity index. The mother had no clinical signs of infection. During the counseling, she decided to not perform invasive tests.

At 25 weeks, fetal magnetic resonance imaging (MRI) was performed, and no signs of abnormalities were documented. Three doses of hyperimmune gamma globulin were used as potential antiviral therapy.

At 35 weeks, fetal MRI was repeated and revealed, in one of the twins, “alteration of white matter in the frontotemporal and parietal region bilaterally due to edema, temporal cysts, intraventricular and periventricular cyst formation, and caudothalamic groove cysts.”

At 36th week, two bichorionic, biamniotic female neonates were born after a cesarean section for abnormalities of fetal heartbeat.

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Anthropometric measurements, physical, laboratory, ophthalmological, and hearing assessment of the first neonate were normal.

The second born twin was apnoeic and hypotonic, with heart rate <60; neonatal resuscitation intervention was performed with a normalization of breath and heart rate. Arterial cord pH was 7.198. Body weight was 1630 g (<3th percentile), body length was 46 cm (25th–50th percentile), and head circumference was 33 cm (50th–75th percentile), respectively. Physical examination showed only multiple petechiae a few hours from birth. Neurological examination revealed major anomalies. Laboratory investigation showed thrombocytopenia (59,000 platelets/mm³). The CMV Immunoglobulin M (IgM) and Immunoglobulin G (IgG) were positive, respectively, 29.5 U/ml and 88 U/ml.

Liquor CMV DNA (331 copies/ml), serum CMV DNA (8377 copies/ml), and urine for CMV PCR (> 7.500.000 copies/ml) were positive. Congenital CMV was diagnosed. Ophthalmological and hearing assessment were normal. The brain sonography showed asymmetrical lateral ventricles and dilatation of occipital horn bilaterally, subependymal germinal matrix injury with pseudocyst, lenticulostriate vasculopathy, impaired myelination with hyperechoic matrix in frontal and periventricular zone, and cystic formation of temporal portion and of choroid plexus. Corpus callosum was normal [Figure 1]. Furthermore, MRI was performed and it documented a white matter injury in frontotemporal and parietal portions bilaterally; impaired myelination of internal capsule, temporal cystic formation, and subependymal ventricular hemorrhage are shown in Figure 2.

Antiviral therapy with 6-mg/kg intravenous ganciclovir (GCV) for a week followed by 16-mg/kg oral valganciclovir (VGCV) for other 5 weeks was administered. After discharge, both the twins underwent a follow-up on the basis of the Italian guidelines of Società Italiana di Neonatologia [Table 1].

DISCUSSION

CMV is one of the most important causes of serious viral intrauterine infections.^[9]

The major risk of transplacental infection occurs in first trimester, but the fetus can be affected by CMV during all trimesters of pregnancy.^[9,10] Infants acutely symptomatic at birth are 10–15%, and among these babies, up to 80% will develop severe sequelae.^[9]

During cCMV, there is a spread of virus, fetal viremia, and subsequent T-cell response to CMV antigens expressed on the interstitial cells of different organs, so the clinical presentation of cCMV can involve all systems.^[11,12] In contrast, acquired

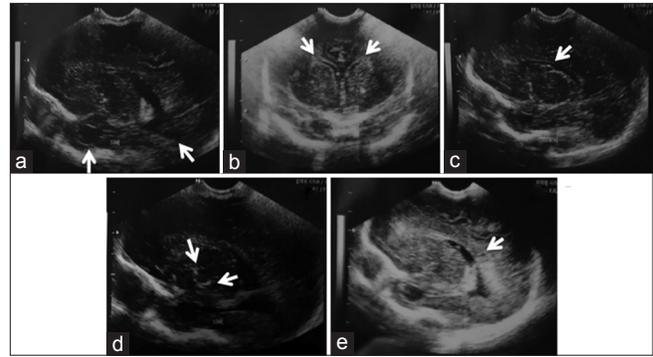


Figure 1: The brain sonography showed dilatation of occipital horns and cystic formation of temporal portion (a), dilatation of frontal horns (b), subependymal cyst (c), lenticulostriate vasculopathy (d), hyperechoic matrix in frontal and periventricular zone (e)

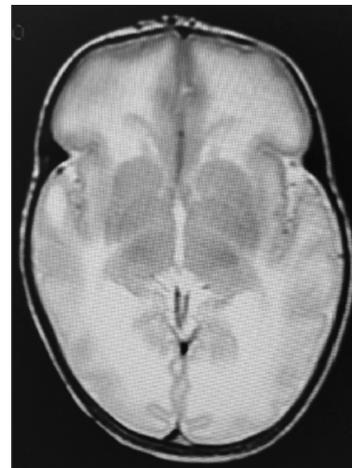


Figure 2: Impaired myelination of internal capsule

CMV infection (through contamination during delivery or through breastfeeding after delivery) rarely causes harmful sequelae.^[9,13]

The twin with cCMV infection had petechiae; the thrombocytopenia, defined by a platelet count of <150 × 10⁹/L, is a frequent hematologic disorder in cCMV infection.

The value of screening for fetal CMV infection is still controversial;^[14,15] it may help the prevention of congenital infections; seronegative pregnant women could be given basic information on how to avoid infection, and the opportunity of a prenatal diagnosis could be offered to those who acquire infection.^[14,15]

The determination of anti-CMV IgG avidity, performed before the 16th–18th week of pregnancy, identifies all women who will have an infected fetus/newborn (sensitivity 100%). After 20 weeks, sensitivity is drastically reduced (62.5%).^[3,16] A good indicator of a past infection could be a high-avidity index during the first 12–16 weeks of gestation.^[3] In our case,

Table 1: Follow-up congenital CMV infection

	Neonatal Age	3 months	6 months	12 months	18 months	24 months	36 months	48 months	60 months	72 months
Anthropometric measurements	X	X	X	X	X	X	X	X	X	X
Laboratory test	X	X								
PCR-RT (blood urine)	X	X								
Cerebral ultrasound	X									
Cerebral MRI	X									
Neurological evaluation	X	X								
Neuropsychological evaluation			X	X	X	X	X	X	X	X
ABR	X	X	X	X	X					
Audiometry examination tests						X	X	X	X	X
Fundus Oculi	X	X								
Ophthalmic evaluation				X		X				X

Modified from reference [8]. ABR: Auditory brainstem response

it was performed at 24 weeks and documented a high avidity, but its sensitivity was drastically reduced.

The gold standard for the diagnosis of cCMV infection in newborns remains the viral isolation in the urine and/or saliva during the first 14–21 days of life.^[3] The reason why only one twin has cCMV infection after maternal CMV infection is due to biamnioticbichorionic twin pregnancy. Twin fetuses simultaneously exposed to the same maternal stimuli may respond otherwise to maternal CMV infection; this suggests that fetus and placenta barriers can play a more important role in the protection of the embryo than maternal immunologic responses.^[17-19] Placenta represents a portal of entry for the virus and a reservoir in which the virus replicates before reaching the fetus as well as a barrier to fetal infection.^[17,19] Therefore, placenta limits the viral spread producing interferon.^[19]

In our report, only one of the twins had cCMV infection despite the fact that both of them were exposed to the same viral load at the same period of gestation. A few similar cases were reported.^[9,13,20-23] The infection in one twin was confirmed by positive histopathological findings in the placenta, while the non-infected sibling placenta was normal, it acted as a non-specific barrier to viral infection. The placental histopathology is one of the best procedures to confirm cCMV infection.^[9]

Several authors explain CMV transmission as the result of defective suppression of virus replication due to maternal ineffective immunologic reactions, while other authors

emphasize the role of the placenta as an important defensive mechanism against the virus;^[9] this may explain why in our case only one of the two twins had cCMV infection. It is known that the placenta is able to produce interferons that limit viral replication and HLA-G that protects fetal cells from CMV.^[9]

CONCLUSION

This report underlines the importance of early diagnosis to enable early clinical interventions and better neurological outcomes. It documented another experience in the use of GCV and VGCV in congenitally infected infants, supporting the usefulness of these drugs. It may be useful in the future to estimate the new incidence of the various sequelae after therapy.

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