Case Report

Patent Ductus Arteriosus With Congenital Cytomegalovirus Infection: A Rare Presentation

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Introduction

Congenital cytomegalovirus (CCMV) infection has a worldwide incidence of 0.2% to 2.2%, and its seroprevalence ranges between 45% and 100%. Maternal transmission to the fetus of a new or reactivated latent infection may occur at any point during the gestation, leading to CCMV infection.

 Majority of infants born with CCMV infection are asymptomatic at birth. Asymptomatic CCMV infection is defined as the presence of cytomegalovirus (CMV) in any body secretions within the first 3 weeks of life, but with normal findings on clinical, laboratory, and imaging evaluations. Regardless of maternal immune status during pregnancy, 10% to 15% of neonates with CCMV have symptoms or signs at birth (eg, periventricular calcifications, intrahepatic calcifications, microcephaly, ventriculomegaly, echogenic bowel, meconium ileus, pleural effusion, and pericardial effusion). Only about 1 in 5 neonates with CCMV infection will be sick from the virus or have long-term health problems.

Here, we present an unusual case of patent ductus arteriosus (PDA) detected postnatally with CCMV infection.

Case Description

A 41-day-old female neonate with tachypnea and tachycardia, maintained at 94% oxygen saturation with FiO₂ of 40% was presented to the NICU of Meenakshi People Tree Hospital (Bengaluru, Karnataka, India). She weighed 2.79 kg (birth weight was 2.65 kg) and was...
born late preterm (at 36\(^{+1}\) wk of gestation) to a 34-year-old G3P2L1D1 mother through cesarean delivery. Her head circumference was 34 cm and length was 52 cm.

On examination, the neonate had tachypnea with respiratory rate of 64 breaths/minute. There were subcostal retractions with scattered crepitations. Cardiovascular examination revealed normal heart sounds, tachycardia, and grade 3 murmur at the left sternal margin, with palpable thrill. Furthermore, the liver was 4 cm below the right costal margin and the spleen was 2 cm below the left costal margin. Central nervous system (CNS) examination revealed anterior fontanelle at level, mild hypertonia of all 4 limbs, and poor newborn reflexes.

Chest X ray revealed cardiomegaly and > 60% cardiothoracic ratio with patchy nonhomogeneous opacities in the right as well as left middle and lower zones of the lung. The neonate was intubated and placed on mechanical ventilation in view of lower respiratory tract infection and congestive cardiac failure. She was kept under the recommended fluid restriction and intravenous antibiotics from day 1 of admission (Augmentin at a dosage of 20 mg/kg, BID, for 7 d, and Amikacin 15 mg/kg/d, for 7 d) and diuretics from when she became symptomatic (1 mg/kg/dose, BID, for 3 d) were started. A pediatric cardiologist’s opinion was taken and inotrope infusion was added. The neonate showed clinical improvement. She was extubated and put on oxygen support on day 5 of admission. Blood and urine cultures were sterile.

2-D ECHO was done on day 2 of admission. It revealed moderate PDA (2.6 mm) and a small atrial septal defect. A repeat ECHO after the third day of admission showed an increase in PDA size (3.5 mm).

The neonate had one episode of generalized tonic–clonic seizure in the second week of admission. Phenobarbitone injection was started after a second seizure, at a loading dose of 20 mg/kg stat, followed by maintenance.

The neonate continued to have multiple episodes of generalized tonic seizures, and levetiracetam was added after phenobarbitone but had no effect in controlling the seizure; it was given at a dose of 10 mg/kg stat followed by maintenance of 10 mg/kg/d.

A neurosonogram conducted at 42 days of life revealed diffuse cerebral edema. Brain MRI showed intracranial calcifications. She had hypertonia in all 4 limbs and neck. Cerebrospinal fluid (CSF) analysis showed normal results. Pyridoxine injection was administered as a single dose after phenobarbinate, but the neonate did not show any response. The repeat ECHO (3 d after the first ECHO) showed persistence of PDA size (3.5 mm), with bounding pulse and grade 3 murmur. The neonate remained oxygen dependent for 3 weeks, and gradually, oxygen was weaned to room air on day 23 of admission.

After the presence of cranial calcifications was observed, in view of congenital heart disease, hepatosplenomegaly, and neonatal convulsions, we checked for toxoplasma, syphilis, rubella, cytomegalovirus, and herpes simplex (TORCH) titers, and CMV IgM was found positive. After TORCH screening, urine polymerase chain reaction (PCR) was done, which was positive for CMV. The neonate was started on ganciclovir (GCV) injection at 6 mg/kg, for 4 weeks, followed by oral valganciclovir (Val-GCV) at 15 mg/kg, for 2 weeks. Blood counts, renal parameters, liver function tests, absolute neutrophil count, and urea and electrolyte levels were monitored regularly and closely.

Findings on otoacoustic emissions hearing screening were normal. Eye examination showed normal retina, with no CMV retinitis. The neonate’s further course in the NICU was uneventful, and she was discharged at 2 months and 27 days of corrected age. She showed features of failure to thrive at 4 months of age, with weight gain of 300 g/mo and persistent PDA. At 7 months of age, the neonate underwent PDA ligation and is presently thriving well with normal neurodevelopment.

**Discussion**

Primary CMV infection is reported in 1% to 4% of seronegative women during pregnancy, and the risk of transmission to the fetus is estimated to be 30% to 40%. Reactivation of CMV infection during pregnancy is reported in 10% to 30% of seropositive women, and, in this circumstance, the risk of transmission of the virus to the fetus is 1% to 3%.
About 40% to 58% of infants with symptomatic CCMV infection suffer from severe neurologic sequelae, and the mortality rate is 5% to 30%.

Neonatal infection is confirmed by culture, CMV DNA testing, or PCR of urine, blood, throat, and CSF samples, as in our case. Antiviral therapy in symptomatic CNS CCMV infection is effective in reducing the risk of long-term disabilities and should be suggested for affected newborns.2

GCV was the first compound licensed specifically for the treatment of CMV infection. GCV and its orally available prodrugs Val–GCV are the 2 most studied drugs that have been shown to be effective in the treatment of neonates with CCMV infection.3

A 6-week course of intravenous GCV at 6 mg/kg, BID, for 6 weeks should be considered in the management of newborns with symptomatic CCMV infection involving the CNS. Pharmacokinetic data currently also recommend a dose of 15 mg/kg, BID, for 6 weeks, which provides good concentrations of Val–GCV. GCV is associated with several drug toxicities, such as myelosuppression (granulocytopenia, anemia, and thrombocytopenia). This neonate received 1 dose of packed red blood cell transfusion to combat anemia in the course of treatment. There is growing evidence that newborns with CCMV infection would benefit from antiviral treatment.

CNS abnormalities are a common occurrence in CCMV infection and even cause epilepsy at a later stage of life. However, heart diseases are a very rare presenting feature in infants with CCMV. Few reports show the association of CCMV with vascular cell proliferation and increased arterial pressure.4 Some adults having CMV antibodies with atherosclerosis responded well to GCV, and the condition is regressed.

This neonate is one of the rare cases of CCMV infection presenting at, as late as, 2 months of age, with cardiac symptoms. It could be because of the relatively smaller size of the PDA initially, which became larger and caused the cardiac symptoms to develop gradually. Though the primary illness of CCMV was treated appropriately, the PDA did not close. It is well documented that PDA in term neonates does not respond to medical treatment, it is noteworthy that the neonate has responded well, as evidenced by the normal growth and development on follow-up.

Conclusion

TORCH screening was done late. We do not know the maternal viral status at the time of delivery. TORCH can present as late as 2.5 months.

- It is not common to have congenital heart disease with CCMV infection.
- PDA is a classic presentation of rubella infection, although it can be present in other TORCH infections.
- When a constellation of symptoms exists, among TORCH, CMV is one of the differential diagnoses for PDA, as it is a treatable condition.

References


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