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Case Report

Role of Oral Valganciclovir in Sick Preterm with Cytomegalovirus Virus Infection and Ventilation Dependence

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Abstract

Cytomegalovirus (CMV) is the most common congenital viral infection in neonates. Postnatal infection regarding infants rarely has significant clinical consequences. However, preterm may be at higher risk of developing symptomatic postnatal CMV disease. A multipara woman delivered vaginally a male preterm infant at 30 weeks' gestation who was suspected of early-onset sepsis in view of chronic leaking. The baby developed severe hypoxemia, and persistent pulmonary hypertension after delivery, with progressive deterioration and minimal effect of advanced ventilation, antibiotics, and pulmonary vasodilators. Sepsis screen and cultures for bacteria and fungi were negative. The baby was having enlarged liver and spleen which was noticed on day 15 of life. TORCH titer of the baby revealed CMV IgM and subsequently, CMV was isolated in the urine and in the blood plasma by polymerase chain reaction. Oral valganciclovir improved hematological parameters of the baby and respiratory support could be weaned. CMV being the most common intrauterine infection should be considered in differential diagnosis in unusual presentation of suspected sepsis and oral valganciclovir can be considered as good option for treatment.

Keywords: Cytomegalovirus, persistent pulmonary hypertension, preterm, valganciclovir

Introduction

Human cytomegalovirus (CMV) is member of herpes family and the most common congenital viral infection in neonates.[1,2] About 10%–15% are symptomatic and clinical features include intrauterine growth restriction, rash, microcephaly, intracranial calcifications, chorioretinitis, thrombocytopenia, neutropenia, and hepatosplenomegaly.[2] CMV disease in postnatal period is uncommon in full-term infants, presumably because of protection from passive transfer of maternal antibodies that occur mostly in the third trimester, and the infant's more mature immune system.[3,4] However, preterm may be at higher risk of developing symptomatic postnatal CMV disease.[4,5] As we know, there are many complications related to CMV in a preterm baby and persistent pulmonary hypertension (PPHN) is a rare one, and moreover, generally regarded as disease of term babies. Hence, we report a first of its kind in literature as per our knowledge, an association of CMV infection in preterm neonate as persistent pulmonary hypertension with mechanical ventilation dependence and dramatic recovery after start of oral valganciclovir in sick ventilated patient.

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Case Report

A 26-year-old woman in her third normal pregnancy delivered vaginally a 1200 g male infant with a head circumference of 26 cm at 30 weeks' gestation. Chronic leaking for 5 months of gestational age complicated the pregnancy. Prenatal abnormal ultrasonograph showed oligohydramnios. Perinatal events included low Apgar score of 4/10 at 1 min and 6/10 at 5 min and the baby was started on supportive care, mechanical ventilation mode and antibiotic therapy with amikacin (as per unit policy) on the suspicion of early-onset sepsis and congenital pneumonia due to chronic leak. Despite mechanical ventilation, refractory hypoxemia developed within 2 h of life. Chest X-ray showed bilateral whiteout of the lungs. The baby was treated with high-frequency ventilation (HFV), inotropic support (dobutamine 10 μg/kg/min), and surfactant therapy (Neosurf 5 ml/kg) but the infant's condition did not

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improve and was struggling with severe hypoxemic respiratory failure. Echocardiogram showed a structurally normal heart and was diagnosed with severe pulmonary hypertension with a pulmonary pressure of 50 mm Hg and right to the left shunt on Doppler study. Baby was started on milrinone, sildenafil intravenous (IV) therapy along with adrenaline at low dose to enhance systemic blood flow. At 58 h of life, pulmonary hemorrhage complicated the ongoing critical nemesis, antibiotic dose stepped up, and symptomatic care continued. Severe hypoxemia persisted with progressive hypercapnia with minimal effect of pulmonary vasodilators and also signs on echocardiography persisted. Subsequently, antibiotics were further stepped up in view of nonresolving chest X-ray findings such as alveolar interstial pneumonia and suspected sepsis. Hematological parameters included high total leukocyte count and dropping hemoglobin, platelets (2.64 lakhs to 90,000 cells/cumm) and normal C-reactive protein (2.8 mg/L), normal cerebrospinal fluid screen, elevated conjugated bilirubinemia (total serum bilirubin 15 mg/dl and direct bilirubin 2.8 mg/dl), and aspartate aminotransferase (534 UI/L). Cultures for bacteria and fungi were negative. Hepatosplenomegaly noticed on day 15 of life, baby torch titer, urine, and blood plasma by polymerase chain reaction (PCR) showed CMV. Despite stormy course, the baby continued with and tolerated minimal orogastric feeds, and so oral valganciclovir was started on day 32 of life along with supportive care. Baby improved with initial improvement in hematological and echocardiographic parameters. There was improvement in pulmonary and tricuspid regurgitation (TR) jet. Ventilation was tapered after 36 days of life and stopped by 39 days of life. The baby was discharged and was clinically stable.

Discussion

Routine physical examinations in newborn fail to identify CMV infection in the majority of the cases. In this baby, due to chronic leakage, bacterial sepsis leading to secondary PPHN was suspected on initial assessment. Hepatomegaly presented at 15 days of life and so, CMV infection could not be suspected earlier. A very peculiar feature about the diagnosis of the congenital infection is that it should be made before the 3rd week of life since, after this period, it is not possible to assess whether viral transmission occurred through the placenta or through breast milk, birth canal, or saliva.[6,7] Culture-based testing of urine and saliva specimens has been the standard method to diagnose congenital CMV infection.[8,9] We diagnosed with the help of urine PCR but since this needed a long period, i.e., more than 3 weeks, we were not able to differentiate between congenital or acquired infection. Infants with CMV infection may benefit from antiviral therapy especially if the treatment is initiated within the 1st month of life. The antiviral of choice is IV Ganciclovir. However, since the duration of treatment required was long, we opted for oral therapy with Valganciclovir (16 mg/kg BD). Studies have shown that is equally efficacious to IV ganciclovir. Our literature search showed that there is a paucity of literature regarding CMV infection presenting as PPHN, ventilatory dependence and treatment with oral valganciclovir and we reported it.

Conclusion

In developing countries, neonatal sepsis is very common and rampant and can lead to different manifestations. In view of nonresponse to standard treatment in cases of suspected sepsis, viral markers screen should be sent and CMV infection should be considered. Orally valganciclovir can be used as a best suited drug therapy for treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's mother has given her consent for her baby's images and other clinical information to be reported in the journal. The patient's mother understands that name and initial will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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