Post-natally acquired cytomegalovirus infection in a pre-term infant

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ABSTRACT

Cytomegalovirus (CMV) infection is the most common intra-uterine and peri-natal viral infection. CMV infections in neonates are acquired by aspiration of cervico-vaginal secretions during birth, through breast milk and from exposure to blood products. Most of the infections in neonates are asymptomatic. Pre-term infants tend to show higher susceptibility to peri-natal and post-natal infections. We report CMV infection in a pre-term low birth weight infant who presented with fever, and respiratory distress due to pneumonitis and was successfully treated with Ganciclovir.

Key words: Blood transfusion, cytomegalovirus infection, Ganciclovir, low birth weight pre-mature infant, post-natal

INTRODUCTION

Cytomegalovirus (CMV) is a DNA virus and a member of the human herpes virus family. Human cytomegalovirus (HCMV) is one of the most common causes of congenital, peri-natal and post-natal viral infection in developed countries. CMV infects nearly 1% of all newborns, 40,000 infants per year, in the United States.[1] In India, 2.1% of neonates are affected.[2] Infection with CMV is the most common cause of non-hereditary sensorineural hearing loss. It may be acquired *in utero*, at the time of delivery through contact with or aspiration of infected cervical secretions[3] or after birth. Important sources of post-natal infection include breast milk[4] close contact with individuals shedding virus and transfusion of seropositive blood products.[5] In pre-mature neonates, post-natal CMV infection can lead to potentially life-threatening problems.[6] CMV infection in pre-mature infants can result in sepsis like syndrome, protracted interstitial pneumonitis, hepatosplenomegaly, thrombocytopenia, atypical lymphocytosis or hemolytic anaemia.

Serologic assays that measure CMV IgG or IgM are not recommended for the diagnosis of CMV infection in neonates.[7] Polymerase chain reaction (PCR) is preferred for detection of CMV in blood specimens, and the finding of CMV DNA in blood is supportive of active infection. The best utility of blood CMV PCR in neonates is in diagnosis of CMV disease acquired natally or post-natally.

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CASE REPORT

A 29-week-old male baby was referred to the Neonatal ICU of Institute of Maternal and Child Health of Govt Medical College, Kozhikode with respiratory distress after one week of delivery. The baby was delivered at 28 weeks of gestation in a private hospital through caesarean section and weighed 790 g. The mother had severe Pregnancy induced hypertension (PIH) and abruptio placenta. His Apgar scores were 6 at 1 and 5 min. The chest X-ray of the baby was suggestive of hyaline membrane disease. He was put on continuous oxygen support and treated with surfactants. As the symptoms persisted he was referred to our hospital.

Investigations

Blood R/E–TC–35,700, Hb–5 g, Platelets–2.5 lakhs CRP-33.2 mg, total Bilirubin–8.9 SGPT – 65.

Peripheral smear–Few atypical lymphocytes present.

Computed tomography (CT) scan–Ground glass opacities of both lung fields with patchy cystic foci in posterior segment of both lower lobes.

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USG abdomen–Mild hepatosplenomegaly Neurosonogram–Normal, Echo–Normal.

He was given six units of packed red blood cells for anaemia in the first 2 months of life. He developed fever in the third month of life and he could not be weaned from oxygen support. Suspecting sepsis he was treated with antibiotics Cloxacillin, Piperacillin Tazobactum and Amikacin. As he showed features of failure to thrive and as fever persisted, an anti-fungal Fluconazole was also started. All cultures taken before initiation of antibiotic treatment were sterile. As the clinical deterioration persisted and as he could not be weaned from oxygen support, he was investigated for CMV infection and tested positive for CMV IgM and IgG antibodies. His blood and urine were sent for quantitative estimation of CMV viral load by PCR to our laboratory.

CMV viral load was detected by real-time PCR system (BIORAD-California, USA). DNA was extracted using Quiagen's DNA extraction kit (Netherland) according to the manufacturer's instructions. CMV primers containing the major immediate early antigen procured from Genome Diagnostics were added to the extracted nucleic acid. CMV DNA copy numbers per millilitres in serum and urine samples were 1.2×10^4 copies, and 1.4×10^7 copies, respectively. As the copies were high in both blood and urine, a diagnosis of CMV disease was made. He was treated with IV Ganciclovir 6 mg/kg body weight 12th hourly and his respiratory symptoms and fever resolved in a week. He was discharged after 2 weeks of IV Ganciclovir. A 4-week therapy with oral Valganciclovir was advised. Neither any side effect due to Ganciclovir nor relapse of the infection after treatment was observed in this patient. His blood and urine were sent for CMV DNA load determination after 2 weeks of IV Ganciclovir therapy. The DNA copies were < 100 copies in blood and not detected in urine, thereby showing his response to treatment. The baby was asymptomatic on review after 4 weeks of oral Valganciclovir.

DISCUSSION

This pre-term low birth weight baby developed symptomatic CMV infection with fever and pneumonia probably following a CMV antibody-positive transfusion. Mother was negative for CMV antibodies. Her antenatal period had been uneventful.

The administration of seropositive blood products to neonates in the post-natal period has been associated with the development of CMV disease, which can be fatal in up to 20% of infants.[8] Pre-term infants weighing less than 2 kg are at the highest risk for complications from post-natally acquired CMV infection.[9] The serious or fatal problems described include pneumonia, hepatitis, haemolytic anaemia and long-term neurological sequelae.[10] Hence in pre-term babies who require blood transfusion, efforts should be made to transfuse these infants with only CMV-negative blood or components or to use blood that has been filtered to remove leucocytes (leukoreduced).[11]

Post-transfusion CMV infections have an incubation period ranging from 20 to 60 days. Transfusion of whole blood or certain blood products containing viable leukocytes may transmit CMV with a frequency of 4-10%/unit transfused.[12] The total volume of transfused blood is an important risk factor for the development of significant transfusion-transmitted CMV disease.[13] Although documented, little information is available regarding post-transfusion associated CMV infection in neonates in India. One study has reported that 11.5% babies developed CMV infection following blood transfusion but they did not exhibit any clinical manifestations.[14]

Ganciclovir and its pro-drug Valganciclovir, Foscarnet and Cidofovir are the agents that are active against CMV. Our patient was treated with IV Ganciclovir for 2 weeks. The baby showed signs of improvement in 2 days. Successful treatment of post-natal CMV infection with Ganciclovir have been described.[15] Those with persistent viraemia and end organ damage or haematological manifestations are treated with Ganciclovir, which causes viral load reduction and reversal of manifestations.[16] Commonly reported side effects of Ganciclovir include myelosuppression, and long-term side effects such as gonadal toxicity. The baby did not develop any adverse effects during therapy. He was discharged after 2 weeks of IV Ganciclovir followed with oral Valganciclovir for 4 weeks. There was no relapse of the infection after treatment. Anti-viral treatment should be considered in the sick preterm infant. A 10- to 14-day course of Ganciclovir may be beneficial in most pre-term, critically ill infants who acquire the infection post-natally.

Our patient is among the few cases with CMV infection acquired post-nally, most likely due to blood transfusion with CMV-infected blood, treated successfully with intravenous Ganciclovir. The risk of symptomatic transfusion transmitted CMV is high in multi-transfused pre-term infants weighing less than 1200 g who are born to sero-negative mothers. Transfusion-acquired CMV can be prevented by administration of

CMV antibody-negative blood products and filtration of blood to remove white blood cells.[17]

REFERENCES

1. Plosa EJ, Esbenshade JC, Fuller MP, Weitkamp JH. Cytomegalovirus infection. Paediatr Rev 2012;33:156-63.
2. Dar L, Pati SK, Patro AR, Deorari AK, Rai S, Kant S, *et al*. Congenital cytomegalovirus infection in a highly seropositive semi-urban population in India. Pediatr Infect Dis J 2008;27:841-3.
3. Schleiss MR, Steele RW, Barton LL, Windle ML, Tolan RW. Paediatric Cytomegalovirus infection (available form http://www.emedicine.medscape.com/article/963090-overview#a0199).
4. Stagno S, Reynolds DW, Pas RF, Alford CA. Breast milk and the risk of cytomegalovirus infection. N Engl J Med 1980;302:1073-6.
5. Adler SP, Chandrika T, Lawrence L, Baggett J. Cytomegalovirus infections in neonates acquired by blood transfusions. Pediatr Infect Dis 1983;2:114-8.
6. Okulu E, Akin İM, Atasay B, Ciftci E, Arsan S, Türmen T. Severe postnatal cytomegalovirus infection with multisystem involvement in an extremely low birth weight infant. J Perinatol 2012;32:72-4.
7. Stehel EK, Sanchez PJ. Cytomegalovirus infection in the fetus and neonate. Neo Rev 2005;6:e38-45.
8. Yeager AS. Transfusion-acquired cytomegalovirus infection in newborn infants. Am J Dis Child 1974;128:478-83.
9. Paryani SG, Yeager AS, Hosford-Dunn H, Johnson SJ, Malachowski N, Ariagno RL, *et al*. Sequelae of acquired cytomegalovirus infection in premature and sick term infants. J Pediatr 1985;107:451-6.
10. Amin H, Jadavji T, Sauve R, Gill J. Use of ganciclovir in the treatment of acquired cytomegalovirus disease in a preterm infant. Can J Infect Dis 1990;1:28-30.
11. Caserta MT. Congenital and perinatal cytomegalovirus infection (available form: http://www.merckmanuals.com/professional/pediatrics/infections_in_neonates/congenital_and_perinatal_cytomegalovirus_infection_cmv.html). Merck Man Health Care Prof; 2009.
12. Hirsch MS in Cytomegalovirus and Human herpes Virus Types 6, 7 and 8. From Harrison's Principles of Internal Medicine. Vol. 1, 16th ed. 2005. p. 1049-52.
13. Kim AR, Lee YK, Kim KA, Chu YK, Baik BY, Kim ES, *et al*. Transfusion-related cytomegalovirus infection among very low birth weight infants in an endemic area. J Korean Med Sci 2006;21:5-10.
14. Kothari A, Ramachandran VG, Gupta P. Cytomegalovirus infection in neonates following exchange transfusion. Indian J Pediatr 2006;73:519-21.
15. Fischer C, Meylan P, Bickle Graz M, Gudinchet F, Vaudaux B, Berger C, *et al*. Severe postnatally acquired cytomegalovirus infection presenting with colitis, pneumonitis and sepsis-like syndrome in an extremely low birthweight infant. Neonatology 2010;97:339-45.
16. Tanaka-Kitajima N, Sugaya N, Futatani T, Kanegane H, Suzuki C, Oshiro M, *et al*. Ganciclovir therapy for congenital cytomegalovirus infection in six infants. Pediatr Infect Dis J 2005;24:782-5.
17. Kim CS. Congenital and perinatal cytomegalovirus infection. Korean J Pediatr 2010;53:14-20.

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