Case Report

A Perinatal Cytomegalovirus Infection in an Immunocompetent Patient with Chorioretinitis

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Summary

Cytomegalovirus (CMV) infection is the most common viral infection of newborns in all periods worldwide. Perinatal form of infection is usually less severe than the congenital form because of having a lower rate for serious organ involvement like central nervous system. In this article, we report a 3-month-old immunocompetent patient who was diagnosed as having perinatal CMV infection with a scar of chorioretinitis after presenting with gastroenteritis and hepatitis.

Key words: cytomegalovirus, chorioretinitis, perinatal.

Introduction

Cytomegalovirus (CMV) infection is the most common viral infection of the newborn, affecting ~1% of all live births [1]. Acquired CMV infection may be as a result of intrauterine infection known as congenital infection, perinatal infection due to contact with infected genital secretions during delivery or postpartum transmission through breast feeding [2]. Clinical symptoms occur in a wide spectrum of abnormalities including microcephaly, chorioretinitis, periventricular calcification and sensorineural hearing loss [3]. Chorioretinitis, strabismus and optic atrophy are the most common abnormalities due to congenital CMV infection [4]. Perinatal form of the disease usually does not contain any neurological sequelae. Treatment is controversial except congenital CMV infection and CMV infection in immunosuppressed patients [5]. In this article, we presented a case of a 3-month-old boy with perinatal CMV infection associated with chorioretinitis not encountered in the literature.

Case Report

A 3-month-old boy was admitted to our hospital with 39°C fever and diarrhea with no history of the disease. Patient was born term in the hospital with spontaneous vaginal delivery weighing 3320 g, to the third pregnancy of the mother with no perinatal problems. On physical examination, patient's height, weight and head circumference measurements were within normal percentiles. Physical examination results of all systems were normal. In the laboratory studies, hemoglobin was 8.9 g/dl, consistent with a prolonged physiological anemia. Erythrocyte sedimentation rate was 52 mm/h (0–20), and C-reactive protein level was 2.9 mg/dl (0–0.8). The results of blood biochemistry were as follows: alanine aminotransferase, 323 U/l (0–41); aspartate aminotransferase, 634 U/l (0–37); lactate dehydrogenase, 3988 U/l (266–500); gamma-glutamyl transferase, 122 U/l (8–61); and alkaline phosphatase, 181 U/l (0–400); other tests were within normal limits. The patient had mild hematuria in urine examination, and coagulation test results were normal. Urine, stool and blood studies did not yield any pathological microorganisms. Hepatitis markers for hepatitis A, B and C viruses were negative. The results of human immunodeficiency virus (HIV), Toxoplasma and Rubella were negative serologically, but CMV immunoglobulin M (IgM) and immunoglobulin G (IgG) were positive. The patient's humoral immunodeficiency was ruled out with normal absolute lymphocyte count and normal values of the IgG, IgA, IgM and IgE, and cellular immunodeficiency was excluded with normal absolute neutrophil count and lymphocyte subsets. Active CMV infection was suspected in the patient because of positive CMV

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doi:10.1093/tropej/fmu024 Advance Access published on 25 April 2014

IgM antibody detection and concomitant increase in the transaminase levels. Blood CMV DNA [polymerase chain reaction (PCR) method] level of the patient was 2017 copies/ml, and CMV IgG avidity level was 0.13 (<0.5 = low and >0.5 = high). Anti-CMV serology of the mother was negative for IgM and positive for IgG. The lateral ventricles were asymmetric in favor of the left, as shown on cranial computed tomography (CT) imaging, and there was a benign external hydrocephalus simultaneously without calcification. These findings were interpreted as a normal variational finding associated with infantile period due to the lack of an additional concomitant central nervous system (CNS) pathology. Abdominal ultrasonography was normal. On examination of the eyes, non-active non-confluent peripheral chorioretinal scar involving the fovea without retinal detachment was found at the right eye despite normal left eye structure. This finding was evaluated as a chorioretinal scar associated with CMV infection by the Department of Ophthalmology. The hearing test was normal bilaterally. There was no fever and diarrhea after the hospitalization in our department. At the clinical follow-up of the patient, liver function tests decreased spontaneously within a week after the initiation of ganciclovir. Because of the presence of CMV-associated chorioretinitis in the patient, 10 mg/kg/day of ganciclovir treatment was started. CMV DNA was negative after the first week of treatment, and repeated tests remained negative. No side effects due to ganciclovir therapy were identified on follow-up. Ganciclovir therapy was continued for 21 days. The patient followed by the Department of Ophthalmology was reevaluated after the completion of treatment with ganciclovir. Intravitreal ganciclovir disc placing for chorioretinitis was recommended by ophthalmologists because of persistent scar, but the operation was not accepted by the family. The CMV IgG avidity level was noted to be 0.25; and was repeated after 1 month. Ganciclovir treatment was not continued any more because of the lack of improvement in the eye findings.

Discussion

Congenital CMV infection can result from maternal primary and reactivated infection or reinfection of different strains of CMV during pregnancy, whereas perinatal infection transmitted by aspiration of genital secretions or maternal blood occurs during the intrapartum period or intake of breast milk after birth. Although ~90% of infected children have no evidence of clinical disease, congenital CMV infection causes multiorgan affection. Up to 2 years of age, 10–15% of asymptomatic children develop neurological sequelae, such as mental retardation, cerebral palsy, sensorineural hearing loss, chorioretinitis and seizures [6, 7]. As opposed to intrauterine infection, perinatally acquired CMV infection is not typically associated with long-term sequelae. Most term infants with perinatal CMV infection are asymptomatic because the babies have maternal-transmitted CMV IgG antibody [8]. Patients may present with signs such as pneumonia, hepatosplenomegaly, lymphadenopathy, hepatitis and hemolytic anemia [9]. Because of the combination of fever, diarrhea and hematuria on admission, and also laboratory support of viral infection hematologically, with positive serology for CMV, we suspected an acute symptomatic CMV infection with the involvement of gastroenteritis, hepatitis and hematuria in the patient.

The presence of CMV IgM at birth is highly suggestive of a congenital infection, although its absence does not rule out congenital infection. Diagnosis of congenital CMV infection is based on testing positive for IgM at first 3 weeks of age. So it is difficult to differentiate whether CMV infection was acquired congenitally or perinatally in infants >3 weeks of age. Serologic tests are not recommended for diagnosis of CMV infection in neonates because anti-CMV IgG detected in newborn infants reflects transplacentally acquired maternal antibody that can persist for up to 18 months of age [10, 11]. In the case of IgM and IgG positivity for CMV, CMV IgG avidity test can be used for the interpretation of the infection time. Although low avidity test indicates infection that happened in a short time such as within 2–4 months, the higher values show previously acquired infection. The best test for diagnosis of congenital or perinatal CMV infection is virus isolation or demonstration of CMV genetic material by PCR from urine or saliva of infants [3, 12]. In our case, we could not precisely differentiate between congenital and perinatal infection because the patient was discharged at the age of 3 weeks, and anti-CMV IgM and IgG were positive together on admission. Also, the mother was only positive for CMV IgG. With these results, IgG avidity test was required for the interpretation of the infection time. The patient's IgG avidity test result suggests that infection occurred in the last 3–4 months. So, avidity test supported that the infection did not occur *in utero*. Active CMV viremia was proven in the patient with both sensitive and specific PCR method as 2017 copies/ml. The child was delivered vaginally; therefore, he might have acquired CMV infection from vaginal secretions during birth process. The baby received breast milk for a short period after the birth, and also the infection can be transmitted via breast milk. Mother was not breastfeeding the baby actively on admission, so the examination of the milk was not possible for CMV.

Ganciclovir is the first-step antiviral agent for the management of CMV infection and indicated only in limited conditions, notably in immunocompromised patients. However, in immunocompetent patients with an unstable or clinically deteriorating condition,

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ganciclovir might be considered as a treatment option [13]. A 2–3-week course of ganciclovir may be beneficial in critically ill infants with perinatal CMV infection. Because most common adverse effects of ganciclovir treatment include nephrotoxicity, hepatotoxicity and dose-dependent neutropenia, patients should be monitored closely during the treatment [14]. In our case, there was a perinatal CMV infection with chorioretinal involvement, which is a rare finding in the literature. Although our patient was immunocompetent, chorioretinitis was a serious finding of CMV infection, so ganciclovir treatment was given for 3 weeks without any side effects. However, there was no improvement in chorioretinitis of the right eye; this might be due to developed scar lesions before treatment. In conclusion, we suggest that patients with accompanying chorioretinitis should be evaluated in aspect of perinatal CMV infection, and these patients should be followed closely because of the risk of scarring.

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