

Maternal primary CMV infection with fetal transmission

Fetal geçiş gösteren maternal primer CMV enfeksiyonu

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Summary

The human cytomegalovirus (CMV) is the most common congenital infection in humans. Congenital CMV infection can follow either a primary or recurrent maternal infection, and it can cause one or more of several clinical manifestations such as intrauterine growth restriction, microcephaly, chorioretinitis, sensorineural hearing loss, anemia, thrombocytopenia, jaundice, and hepatosplenomegaly. Seroconversion to cytomegalovirus occurs in 1-4% of pregnant women. We present the case of a pregnant woman with primary congenital cytomegalovirus infection diagnosed by PCR method of amniotic fluid at the 22nd week of pregnancy.

Key Words: CMV, maternal infection, PCR, congenital infection.

Özet

Sitomegalovirus (CMV) insanlardaki en sık konjenital enfeksiyondur. Konjenital CMV enfeksiyonu primer veya tekrarlayan maternal enfeksiyonu takiben gelişebilir ve intrauterin gelişme geriliği, mikrosefali, koryoretinit, sensorinoral işitme kaybı, anemi, trombositopeni, sarılık ve hepatosplenomegali gibi bir veya birden fazla klinik manifestasyona yol açabilir. CMV serokonversiyonu gebe kadınların %1-4'ünde görülür. Olgumuzda, 22. haftada amniotik sıvı PCR analizi ile tanısı konan primer konjenital CMV enfeksiyonunu sunmaktayız.

Anahtar Sözcükler: CMV, maternal enfeksiyon, PCR, konjenital enfeksiyon.

Introduction

Cytomegalovirus (CMV) infection is the most frequent congenital infection worldwide and it is a common cause of hearing impairment and mental retardation (1). The prevalence of CMV antibodies varies widely among different populations depending on socioeconomic status varying 50-85% in adults by the age 40 years. On average, seroconversion occurs in 1-4% of all pregnancies (2,3) and congenital CMV infection occurs in approximately 0.2-2.5% of all live births.

Case

A 24-year-old woman, gravida 2 para 0, with 7 weeks of pregnancy was admitted to the Ege University Hospital for routine pregnancy follow-up. She had a past obstetric history of one tubal ectopic pregnancy which was treated by laparoscopic salpingectomy. At her first visit, after the anamnesis, routine laboratory tests including blood count, blood group, TORCH serology, urine analysis, urine culture were evaluated.

TORCH serology revealed a previous rubella infection with IgM negativity and IgG positivity. By her 7th week, maternal CMV IgM and IgG were both negative. A transvaginal ultrasonography was also performed and revealed a fetus with a crown rump length of 12.5 mm (7⁺³ weeks) with positive cardiac activity. A first trimester trisomy screening test was also normal. At the 16th week of pregnancy, CMV serology was re-evaluated and revealed both IgM and IgG positivity with an IgG avidity of 10%. Low IgG avidity revealed a recent maternal infection. To detect fetal infection, amniocentesis was performed at the 22nd week of pregnancy, and the polymerase chain reaction (PCR) analysis of amniotic fluid was positive with 1500 copy/ml. There were no abnormal ultrasonographic findings supporting the congenital infection. The karyotype was also normal. The couple was counseled about the early neonatal and late childhood risks, and they decided to carry on the pregnancy. The pregnancy follow-ups were performed regularly. Magnetic resonance imaging (MRI) was also performed at the 34th week of pregnancy and no sign of brain abnormality was detected. At the 38th week of pregnancy the patient delivered a 3050 gr baby by cesarean section, without symptomatic infection. The

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CMV specific IgM of the newborn was negative, but IgG was positive suggesting previous CMV infection. The newborn period was uneventful, however the follow-ups will carry on regularly.

Discussion

Primary infection is defined as CMV infection in a seronegative person who has never been infected before and secondary infection is defined as a rise in IgG or IgM antibody titers in a person who had been previously infected. In utero CMV infection results from transplacental transmission of the virus during maternal viremia, and may follow either primary or recurrent infections. The transmission rate after primary infection is about 40%, whereas it is about 1-3% following recurrent infection with the degree of fetal damage being higher in early primary infection than in late infection (4).

10-15% of infants infected with congenital CMV exhibit the clinically apparent or symptomatic form of the disease, characterized by petechiae, hepatomegaly, splenomegaly, jaundice, periventricular calcifications, microcephaly, hearing impairment, and chorioretinitis. As in the present case, the remaining 85% to 90% of infected infants are asymptomatic at birth, however 15% of them may develop delayed sequelae, especially progressive hearing loss (5). Sensorineural hearing loss develops in 30% of symptomatic infants at birth (6). Also intrauterine infection may present with central nervous system abnormalities detected by ultrasonography or MRI such as periventricular calcifications and echogenicity, sulcation and gyral abnormal patterns, hypoplastic corpus callosum, cerebellar and cisterna magna abnormalities, however normal findings do not completely exclude the fetal infection. In this case neither ultrasonography nor MRI showed any abnormality (Figure- 1, 2, 3).

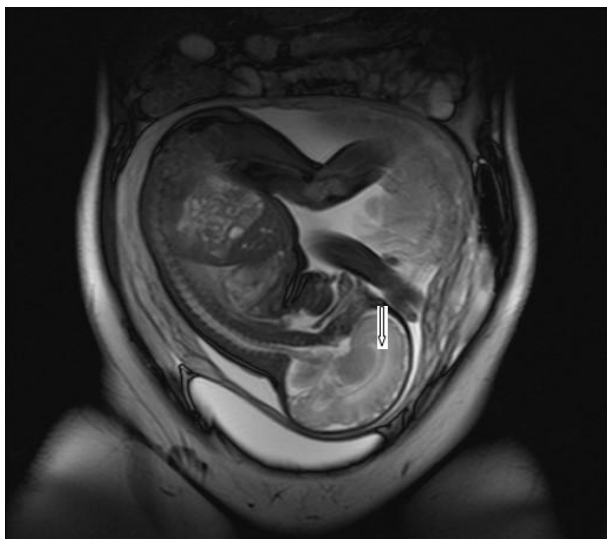


Figure-1. Sagittal view of the fetus with normal spinal cord and brain (MRI) White Arrow: Corpus callosum.

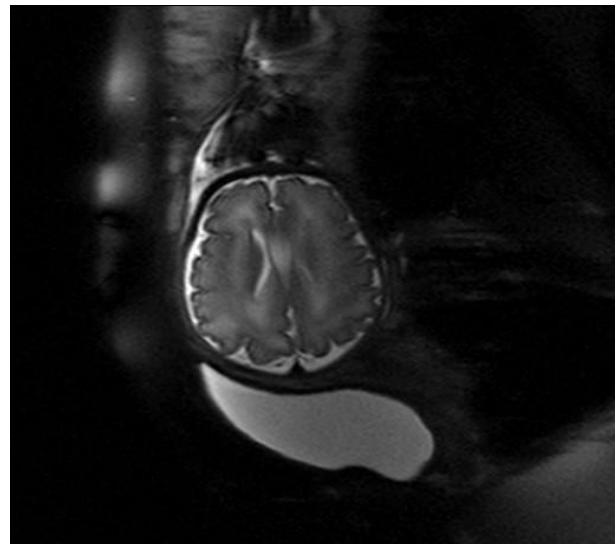


Figure-2. Transvers view of brain with normal lateral ventricles (MRI).

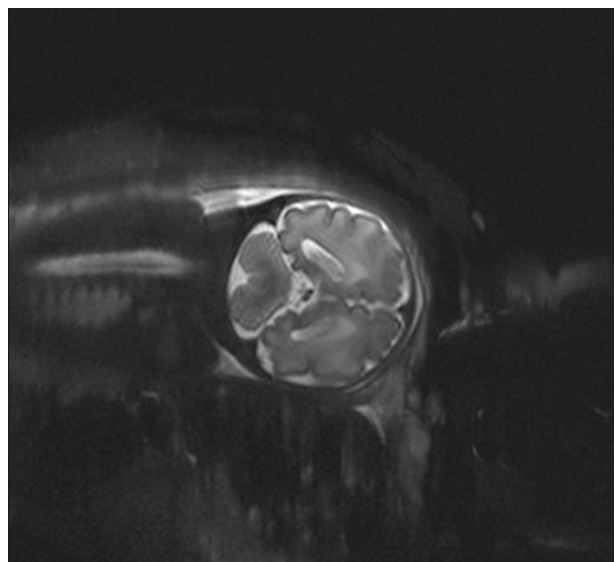


Figure-3. Coronal view of brain with normal cerebellum and vermis (MRI).

CMV can be transmitted from mother to fetus even if the mother had primary infection long before conception apparently up to 6 months (7). The presence of maternal antibody to CMV before conception provides an incomplete protection and congenital CMV infection may follow recurrent maternal infection. Some have suggested that women who transmit CMV to fetuses might have defective immunologic responses and, therefore, are unable to limit replication of the virus (8). In contrast, the studies about twin pregnancies have showed that each fetus may react differently to primary maternal CMV infection, although exposed to the same maternal influences, suggesting that the placenta might have a more important role as a protective factor than maternal immunologic reactivity (9,10) .

The first step for diagnosing primary CMV infection in a pregnant woman is to detect seroconversion. The detection of CMV-specific IgG and IgM antibody during pregnancy as well as during follow-up in a previously seronegative woman, can be used to determine clinically significant primary CMV infection. Further testing by an IgG avidity test may be of great help in both confirming and clarifying the clinical significance of IgM antibody. After a primary CMV infection is either diagnosed or suspected, prenatal diagnosis should be offered to verify whether the infection has been transmitted to the fetus. This can be established by PCR analysis of the amniotic fluid obtained by amniocentesis (11). PCR has a sensitivity of 77.3% and specificity of 100% with a positive predictive value of 100% and negative predictive value of 82.8%. Since it takes 5-7 weeks from fetal infection and replication of the virus in the kidney until a sufficient quantity of the virus is secreted to the amniotic fluid, a negative PCR can not completely exclude fetal infection if the amniocentesis is carried out too early (12). PCR should not be performed before 21st week of pregnancy or at least 6 weeks after maternal infection in cases of

late infection. The sensitivity of amniotic fluid PCR is higher and it is more reliable in such conditions.

Currently there is no approved agent for antiviral therapy for congenital CMV infection. Although recent evidence suggests that ganciclovir may have a beneficial effect in neonates with severe congenital CMV infection, treatment does not seem to induce a significant improvement in the course of disease or neurodevelopmental sequelae. It seems that prevention is much more important and pregnant women should take care of good personal hygiene and avoid urine or saliva of others. Also several candidate vaccines are under development.

In conclusion, after the diagnosis of congenital CMV infection, counseling is important and the couple should be informed that children with congenital CMV infection are at risk for hearing loss, mental retardation, psychomotor delay, cerebral palsy and impaired vision, with some of the cases being late onset. These children should have long term audiologic, neurodevelopmental, and ophthalmic follow-up for early identification of these problems.

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