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Congenital CMV Infection: A Complex Case of Neurological Complications and Therapeutic Approaches in Infancy

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ABSTRACT

Introduction and purpose

Congenital Cytomegalovirus (CMV) infection stands as the prevalent infection among newborns and it may be associated with later complications such as progressive sensorineural hearing loss or neurological diseases. Infection occurs during pregnancy or during childbirth. Congenital CMV infections manifest in various ways, ranging from asymptomatic cases to severe complications such as microcephaly, hepatosplenomegaly, and chorioretinitis. Routine antibody screenings for pregnant women are not common, underlining the significance of early infection detection to minimize the risks of transmission to the fetus and potential complications in the child.

The aim of this case report is to present the course of congenital CMV infection and its complication. This case report explores the challenges of managing an infant with congenital CMV infection complicated by hydrocephalus and viral co-infections. The infant underwent various treatments, including antiviral therapy, highlighting the need for multidisciplinary approaches.

Conclusion

With no available vaccine, prevention of congenital CMV infection relies on educating reproductive-age women and expectant mothers about infection risks. Early detection, frequent medical check-ups, and preventive education are crucial due to the absence of vaccines. Ongoing exploration of antiviral treatments and prompt interventions is imperative to improve outcomes for infants and families affected by the virus.

**Key words:** Cytomegalovirus, CMV, congenital CMV infection, hydrocephalus
INTRODUCTION

Congenital CMV (cytomegalovirus – CMV) (cCMV) infection is the most common congenital infection and affects approximately 0.2 - 2% children. [1] Cytomegalovirus (CMV) infection is a widespread and potentially serious viral condition that affects people of all ages, but it can be particularly concerning when contracted during pregnancy. The main complications of the infection are neurological disorder and sensorineural hearing loss (SNHL). [2] Infection occurs as a result of transmission of the virus from the infected mother by the transplacental route, during and after childbirth. Fetal infection may occur after a primary maternal infection, or after a reinfection or a reactivation of the virus in a previously immunised pregnant woman. [3] Intrauterine infection has the highest risk of severe neurological complications. 90% infection may be asymptomatic and about 10% infants may show symptoms such as IUGR, ventricular dilatation or asymmetry, calcifications, microcephaly, hepatosplenomegaly and chorioretinitis. [4] Asymptomatic cases further complicate early detection, necessitating a nuanced understanding of diverse symptoms for timely intervention. Laboratory tests may reveal hemolytic anemia, thrombocytopenia, increased conjugated bilirubin level and increased transaminase activity.

We present a case of an infant born with congenital CMV infection, complicated by hydrocephalus and other neurological issues. The infant underwent various treatments, including antiviral therapy and regular medical evaluations.

CASE REPORT

The female infant born from the third pregnancy at 37 weeks of gestational age, delivered by a C-section, with a body weight of 2980 g, Apgar 7/8/9 points. The pregnancy complicated by COVID-19 infection from 33 weeks of pregnancy, mother tested positive for HSV IgM. After birth, previously detected hydrocephalus (at 33 gestational age) was confirmed by transfontanellar ultrasound and cerebrospinal fluid was collected for virological examination. One day after birth, the newborn was transferred from the Neonate Department (the part of Obstetrics Clinic) to the Department of Neonate and Infant Pathology. At
the time of admission the patient was in average condition with spontaneously breathing and periodic circulatory problems, and a head circumference of 30,5 cm (<3rd percentile) and anterior fontanelle 1,5cm x 2cm. Acyclovir was prescribed due to mothers HSV infection. Brain CT revealed multiple calcifications, reduced volume of cerebral lobes and dilated lateral ventricles with asymmetry, the Evans index was 0.63. The surgeon performed a puncture of the brain's ventricles through the anterior fontanelle. The cerebrospinal fluid was bloody, with a protein level of 497.0 mg/dl. Cytosis was observed at a level of 110 cells per microliter, with 72% of them being lymphocytes. The cerebrospinal fluid analysis showed a positive result for CMV DNA and negative for HSV DNA. The CMV test using the PCR method in urine showed a positive result with a level of 9.8 x 10^7 IU/ml. The treatment was changed to ganciclovir at a dose of 6mg/kg every 12 hours. On the tenth day after birth, according to the neurologist's consultation the Rickham reservoir was inserted on the left side. Following the procedure, the infant was transferred to the Department of Anesthesiology and Intensive Care for the next two weeks. After stabilizing the overall condition, the girl with diagnosed respiratory failure, congenital hydrocephalus, congenital cytomegalovirus infection, microcephaly, and an atrial septal defect, was transferred back to the Department of Neonate and Infant Pathology. The child was in fair overall condition, pale, without obvious circulatory failure, breathing spontaneously with visible retractions of the lower ribcage. The body weight at that time was 3040 grams, and the body length was 52 centimeters. Consulted by an ophthalmologist, without any deviations from the norm. The patient was placed in an incubator with oxygen therapy, monitored closely, and continued the pharmacotherapy. The baby's condition deteriorated, loose stools were observed and due to this condition the viral tests was performed (positive results for rotavirus and adenovirus). Laboratory tests showed elevated levels of GGTP, ALP, CRP (16,93 mg/dl from 3,04 mg/dl), while platelet count (33,000 from 158,000 a day before) and hemoglobin level (7,6 mg/dl from 10,6 mg/dl a day before) were decreased. Antibiotic therapy and oxygen therapy were intensified and ganciclovir was discontinued. Due to temporary leukopenia and anemia, the baby was treated with immunoglobulins and received blood. Under the influence of the administered treatment, the child's condition gradually improved, and inflammatory markers decreased. Blood and cerebrospinal fluid cultures showed no bacterial growth.
When the condition improved, a drug against CMV infection - valganciclovir was initiated. Regular checks of Rickham’s reservoir and cerebrospinal fluid were conducted. The CMV DNA level increased from 4.7 x 10^4 IU/ml to 9.8 x 10^7 IU/ml, and ganciclovir (instead of valganciclovir) resumed. Control tests did not show any deviations from the norm. The level of CRP dropped to 0.1 mg/dl from 16.93 mg/dl. After consultation with the Children's Health Center in Warsaw, the patient was transferred there. MRI of the brain revealed - microcephaly, generalized significant cortical-subcortical atrophy of the cerebral hemispheres, asymmetric biventricular hydrocephalus and numerous small calcifications in the lining of the lateral ventricles. The baby was regularly monitored on an outpatient basis by cardiologist, neurologist and audiologist. Due to increased muscle tone in the upper limbs, the girl also underwent rehabilitation. The girl remained under the observation of a neurologist to monitor the occurring tremors in the upper limbs, epilepsy and the possibility of cortical visual impairment. Further diagnostics were carried out also for hearing loss (treated with hearing aids) and cardiac defect (PFO detected in the ECHO examination of the heart).

**DISCUSSION**

Congenital CMV infection can result in various complications, such as progressive hearing loss and neurological disorders. Hearing impairment can even develop in asymptomatic children. In severe cases, the infection can lead to significant neurological complications, cardiopulmonary failure, and, tragically, death. Newborns are at higher risk of infection if the mother experiences a primary infection during pregnancy as observed in the described case. [3;5] The case brings attention to the significance of prenatal and postnatal diagnostics. The mother's CMV infection can present as a mild illness, including symptoms such as mild fever, rhinitis, pharyngitis, headache, fatigue, and hepatic disorders, or it can be completely asymptomatic. [6] Since anti-CMV antibodies are not routinely screened in pregnant women, early detection of CMV infection becomes crucial to minimize the risk of transmission to the fetus. It is estimated that in Poland over 80% of women of reproductive age have serological evidence of CMV infection. [7] Diagnosis of CMV infection in pregnant women involves detecting specific IgM
antibodies and low avidity IgG antibodies. [17;20] If an infection is suspected in the fetus, the virus or its genetic material (DNA) should be identified in the amniotic fluid collected during amniocentesis. [8;18] During the prenatal period, intraamniotic treatment with specific immunoglobulins against CMV can be administered. In the diagnostic process for CMV, both fetal and newborn ultrasounds are routinely conducted. To confirm congenital CMV infection in infants, CMV DNA testing is conducted using PCR technique on blood, urine, cerebrospinal fluid, or saliva within the first 21 days of life. [4;16] It is crucial to analyze both the mother's and the newborn's antibody results. For asymptomatic and mild cases, it is advisable to monitor the infant regularly and conduct routine eye and hearing examinations. There is no evidence of the benefit of antiviral therapy in asymptomatic cases. [22] In severe cases, antiviral treatment is initiated, involving intravenous (i.v) ganciclovir or oral (p.o) valganciclovir, typically administered for an average of 6 weeks or even longer, depending on the severity of the infection. [9;15;19;21] It is necessary to check the morphology, AST, ALT and the level of the medication due to severe side effects. [8;10;22]

Educating parents about this topic is crucial. It is advisable for children with congenital CMV infection to undergo regular check-ups. The challenges in management are underscored by the necessity of multidisciplinary approaches. Neurological complications, hydrocephalus, and visual impairments necessitate close collaboration between neurologists, neurosurgeons, ophthalmologists, and other specialists. Complications, such as sensorineural hearing loss, may develop in later stages of life. [11;14] Currently, there are no available vaccinations against CMV infection. Therefore, prevention strategies primarily rely on educating women of reproductive age and pregnant women about infection prevention. [12;13;23]

CONCLUSION

Congenital CMV infection poses significant risks to newborns, potentially leading to severe complications such as sensorineural hearing loss and neurological disorders. Understanding the diverse symptoms of congenital CMV infections is paramount for early identification and intervention. This case report
highlights the challenges and complexities involved in managing infants with congenital CMV infection, particularly when complicated by additional health issues like hydrocephalus and viral co-infections. Postnatal care demands multidisciplinary approaches, including antiviral treatments and regular medical evaluations by audiologists, ophthalmologists, neurologists and other specialists. As there are currently no available vaccines against CMV, preventive strategies rely heavily on education, early detection, and meticulous medical management. Furthermore, continued research into antiviral therapies and early intervention strategies is essential to improve the outcomes for infants born with congenital CMV infection. By raising awareness, enhancing medical protocols, and fostering a supportive environment, we can collectively work towards bettering the lives of infants and families impacted by this significant health concern.

**Author's contribution**

Conceptualization: Sylwia Koziej, and Emilia Kowalczyk; methodology, Sylwia Koziej, Martyna Niemczuk; software, Sylwia Koziej, Mateusz Wiekiera; check, Emilia Kowalczyk, Martyna Niemczuk and Adrianna Jasiuk; formal analysis, Sylwia Koziej, Emilia Kowalczyk, Martyna Niemczuk, Adrianna Jasiuk; Mateusz Wiekiera; investigation, Sylwia Koziej, Martyna Niemczuk, Adrianna Jasiuk; resources, Emilia Kowalczyk, Martyna Niemczuk, Adrianna Jasiuk; writing - rough preparation, Sylwia Koziej, Adrianna Jasiuk, Mateusz Wiekiera; writing - review and editing, Sylwia Koziej, Emilia Kowalczyk; visualization, Sylwia Koziej; supervision, Sylwia Koziej; project administration, Sylwia Koziej, Martyna Niemczuk.

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