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Cranial ultrasound in congenital cytomegalovirus infection.

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Abstract

Cytomegalovirus is the most prevalent agent in congenital infections, causing severe long-term sequelae (sensorineural hearing loss, vision loss). Approximately 11% of newborns born with congenital cytomegalovirus infection are symptomatic at birth. The other newborns do not have clinical findings at birth. Congenital cytomegalovirus infection may cause severe long-term sequelae, in 40%-58% of symptomatic newborns and 5%-15% of the asymptomatic newborns. The aim of our study was to examine the association between cranial ultrasound calcifications and long-term sequelae of a congenital cytomegalovirus infection. We retrospectively evaluated cranial ultrasound findings, hearing test results and ophthalmological findings in two newborns with congenital cytomegalovirus infection. Newborn with thick intracranial calcifications developed hearing loss, while newborn with punctate intracranial calcifications passed the otoacoustic screening. Ophthalmologic findings in both newborns were normal. Cranial ultrasound should be play a significant role in the diagnosis of congenital cytomegalovirus infection and in prediction of outcome, especially sensorineural hearing loss.

Keywords: Cytomegalovirus, Cranial ultrasound, Hearing loss, Infection.

Introduction

Cytomegalovirus (CMV) is the most prevalent agent in congenital infections, causing severe long-term sequelae. The incidence of congenital CMV infection is higher in developing countries (1%-5%) than in developed (0.2%-2.0%) and are most likely driven by non-primary maternal infections. In the developed world, it is the commonest non-genetic cause of childhood hearing loss, and an important cause of neurodevelopmental delay. Approximately 11% of newborns born with congenital CMV infection are symptomatic at birth, resulting in clinical manifestations (jaundice, hepatosplenomegaly, petechiae, microcephaly, chorioretinitis, intrauterine growth restriction and death). The other newborns with congenital CMV infection (approximately 85%-90%) do not have clinical findings at birth (asymptomatic infection) [1].

Congenital CMV infection may cause severe long-term sequelae, including progressive Sensorineural Hearing Loss (SNHL), vision loss, and developmental delay in 40%-58% of symptomatic newborns, and 5%-15% of the asymptomatic newborns. SNHL may be present at birth, progress in severity, or develop later. The risk for SNHL appears to be the highest in newborns born to mothers with primary infection in the first half of pregnancy. About a quarter of newborns (20%-25%) who are congenitally infected after the first-trimester will develop SNHL). Overall, 2% of case-patients developed SNHL that was severe enough for them to be candidates for cochlear implantation. Visual impairment occurs in 22%-58% of symptomatic newborns. Cognitive deficits occur in up to two-thirds, and death in around 4% of children with symptomatic infection. Considerably lower rates of sensory and cognitive sequelae have been reported in asymptomatic children [2].

Recognition of the congenital CMV infection in pregnancy, at birth or in the first 3 weeks of an infant's life is increasingly needed, particularly as therapeutic and preventive interventions expand for delayed-onset SNHL. Without early detection and prompt rehabilitation, it will lead to speech, and language impairment in a significant number. The majority of children with CMV-associated SNHL have normal hearing at birth and develop subsequent late-onset hearing loss. For these children, long-term monitoring for SNHL is needed. Despite these facts, the routine CMV screening of newborns have never been recommended by any public health authority. Ultrasound is valuable tool to assess fetal structural and growth abnormalities. Ultra sound monitoring is currently the only way of monitoring, and assessing the prognosis of a fetus infected by CMV. Studies showed a good correlation between cerebral ultrasound abnormalities and the prediction of outcome in newborns who were congenitally infected with CMV [3].

Cranial calcifications are common ultrasound examination finding in newborns with congenital CMV infection. This study analyzed the different patterns of cranial calcifications, of two newborns with documented congenital CMV infection. The aim was to examine the association between cranial ultrasound abnormalities and sequelae (SNHL, vision function). Also, our study set the question: Could cranial ultrasound findings help us to recognize congenital CMV infection and to predict its long-term sequelae [4].

Case Study

There are presented two newborns with congenital CMV infection. First was symptomatic, and second one was asymptomatic. Congenital CMV infection had been proven with positive Polymerase Chain Reaction (PCR) in blood and urine. We retrospectively evaluated cranial ultrasound findings, hearing test results and oftalmological findings [5].

Female newborn was admitted in hospital at 5 day of life because of weaknesses, physical findings (petechial rash, jaundice and lethargy) and laboratory signs (thrombocytopenia, hyperbilirubinemia). Newborn is second child, from the third pregnancy, complicated by hypertension (1 missed abortion). Term vaginal delivery, APGAR scores were 10 and 10 on 1st and 5th minutes of life, birth weight 2790 g. On inpatient admission newborn was sick, but the clinical course was mild. Thrombocytopenia (40-63 × 109) was maintained during the first week of life [6].

Serological diagnosis of CMV infection (TORCH screening) was performed based on positive serum-CMV specific-IgM and IgG antibodies. Congenital CMV infection was confirmed by a positive PCR in blood and urine. Cranial ultrasound finding: Severe (thick and chunky) intracranial calcifications, mainly in the area of the basal ganglia and brain parenchyma. Ophthalmological screening was normal. Newborn fails the otoacoustic emissions screening. Control OAE (Otoacustic Emission) and BERA (Brainstem Evoked Response Audiometry) confirmed SNHL. Antiviral treatment was not included, because of a stable general condition and a proper eye finding [7-9].

Male newborn, 20 days old in good condition at outpatient examination. Outpatient examination is scheduled due to a positive serum CMV specific-IgM and IgG antibodies. Newborn is first child, from the first normal pregnancy. Term vaginal delivery, APGAR scores were 10 and 10 on 1st and 5th minutes of life, birth weight 3350 g. On the third day of life he had a jaundice (hyperbilirubinemia gravis), which was the reason for TORCH screening (CMV specific-IgM and IgG antibodies). Congenital CMV infection has been proven with a positive PCR in urine. Cranial ultrasound finding: Mild (fine and punctate) intracranial calcifications in periventricular area and basal ganglia. Ophthalmological screening was normal. New born has passed the otoacoustic emissions screening. Antiviral treatment was not included [10-13].

Results and Discussion

Congenital CMV infection remains a leading cause of SNHL and a major contributor to permanent neurological disabilities and cognitive deficits in childhood. CMV acquired by the fetus is the most common non-genetic cause of SNHL. Infants with symptomatic CMV infection are more likely to develop SNHL, but studies showed that infants with asymptomatic congenital CMV infection also have SNHL. In addition, many cases of congenital CMV infection are still not diagnosed. We present two newborns with documented congenital CMV infection, with different patterns of ultrasound cranial features and different outcomes. The first newborn (symptomatic) was identified after deterioration (petechial rash, jaundice, lethargy). For the second newborn (asymptomatic) torch screening was made during the stay in the maternity hospital. Cranial calcifications are common ultrasound examination finding in newborns with congenital CMV infection. We showed that first newborn with severe (thick and chunky) intracranial calcifications developed SNHL. The second newborn with mild (fine and punctate) intracranial calcifications did not develop hearing loss. Ophthalmologic findings in both the newborn were normal.

Studies also showed that cranial ultrasound is a readily available screening tool useful in the identification of CMV infected newborns and those intracranial calcifications in asymptomatic case patients were significantly associated with SNHL by age 5 years. Also in patients with SNHL, intracranial calcifications are strongly suggestive of congenital CMV infection. The authors recommend that in newborns with intracranial sonographic findings such as calcification, consideration should be given to congenital CMV infection. Imaging findings such as thick and chunky intracranial calcifications are indicative of poor neurologic outcome. Fine and punctate intracranial calcifications are indicative for better outcome. Normal cranial ultrasound predicts a favorable outcome. There are authors who believe that the diagnosis of congenital CMV infection cannot be established based on ultrasound findings [14].

We consider, based on the presented cases, that cranial ultrasound findings can help both in the diagnosis of congenital CMV infection and in the prediction of its late consequences, especially SNHL. Also, thick and chunky intracranial calcifications predict SNHL, while fine and punctate point to a better outcome. In the case of intracranial calcifications in newborns should be thinking of congenital CMV infection. Because of that cranal ultrasound findings (intracranial calcifications) should be involved in screening for congenital CMV infection. The recent studies confirm that universal CMV screening is still cost-effective as long as the incidence of CMV remains above 0.89%. Cranial ultrasound should be performed in first week of life. A positive finding of intracranial calcification should be an indication for CMV testing. Also, CMV testing should be done in children who do not pass the hearing screen or have any clinical sign of congenital CMV infection (Figures 1 and 2) [15,16].

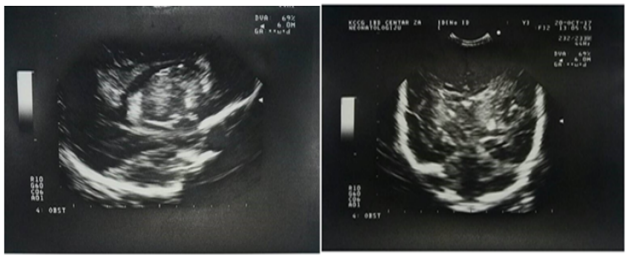

Figure 1. *Cranial ultrasound finding: Severe (thick and chunky) intracranial calcifications, mainly in the area of the basal ganglia and brain parenchyma.*

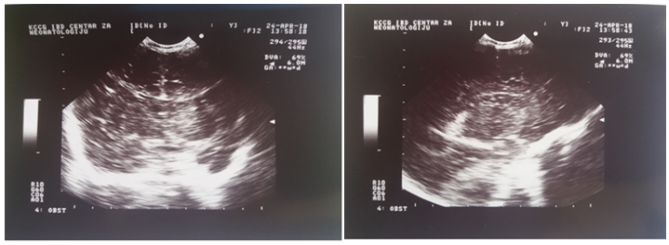

Figure 2. *Cranial ultrasound finding: Mild (fine and punctate) intracranial calcifications in periventricular area and basal ganglia.*

Conclusion

In this way, we will have the opportunity for early intervention (antiviral treatment), and we will reduce risc for late onset and progressive hearing losses. To assess the diagnostic and prognostic value of cranial ultrasound in predicting CMV-related SNHL, studies with a larger sample size could be done. Further research will improve our understanding of the pathogenesis of congenital CMV infection and will be able to identify the other predictors of outcomes.

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