KLİNİKİ HADİSƏ КЛИНИЧЕСКИЙ СЛУЧАЙ CLINICAL CASE

A CASE OF CONGENITAL CYTOMEGALOVIRUS INFECTION

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ABSTRACT

Cytomegalovirus is a virus responsible of the majority of intrauterine infections. It may cause hearing loss, microcephaly, cerebral gyral malformations and white matter abnormalities in the fetus. In this paper, a case with congenital cytomegalovirus infection is presented and the current approach is reviewed.

Congenital cytomegalovirus (CMV) infection is the most common congenital viral infection worldwide. It can cause neurological sequelae, of which the most frequent is hearing impairment affecting approximately one out of five infants congenitally infected [1].

The virus is very commonly found in the environment and encountered by most children in the first few years of life. Acquired CMV disease does not cause significant morbidity: except for immunocompromised individuals, acquired CMV infection usually presents as a nonspecific viral disease with lymphadenopathy. On the other hand congenital CMV infection can have major consequences.

A case of congenital CMV infection is reported and discussed in the light of recent literature.

CASE REPORT

This 5 month old girl was referred for small head circumference and seizures from birth. She was born after 37 weeks gestation with a birth weight of 2400 grams. On examination head circumference was 35 cm (< 5 percentile), she was not able to lift her head in the prone position, she was blinking to light but not following objects. No reaction was observed in response to the sound of a bell. EEG showed hypsarrhythmia, MRI showed gyrus abnormalities and small signal intensity changes which were confirmed on CT as periventricular calcifications (Fig. 1).

Figure 1. Lissencephaly, reduced white matter signal intensity and punctate calcifications around lateral ventricles.

Clinical and epidemiological features of congenital CMV infection:

Human CMV is a double-stranded DNA virus of the herpesviridae family. Congenital infection can be due to the pregnant mother becoming infected for the first time during pregnancy (primary infection), or a repeated infection (secondary infection). The fetus is much more likely to be affected in primary (30-40%) than secondary (1.5%) maternal infections, and symptoms are more severe in primary infection. However maternal re-infection during pregnancy is still the most frequent

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cause of congenital CMV infection, because the majority of the adult population is seropositive: in Turkey, 98% of about 6000 pregnant women tested for CMV IgG were seropositive and IgM positivity was 0.18%. IgM positivity after the 20th week of pregnancy indicated infection during the current pregnancy [2].

Most fetuses born with congenital CMV infection are asymptomatic [3]. A study in Slovenia showed a rate of congenital CMV infection as 0.14% of all births. All newborns with congenital CMV infection had detectable CMV DNA in plasma taken at birth and two out of four had detectable CMV DNA in dried blood specimens obtained for newborn metabolic screening. However none of the four newborns with confirmed congenital CMV infection was symptomatic, as frequently reported [4]. Those who are symptomatic have hepatitis, jaundice, splenomegaly; petechiae, purpura due to thrombocytopenia, and findings of neurological involvement: microcephaly, and sensorineural hearing loss [5].

Hearing loss is the most common neurological consequence of congenital CMV infection. It is due to cochlear and neural infection. It may not be apparent at birth and therefore the newborn hearing screening can be normal. The hearing may be progressively lost during the first 6 months or even the first years of life [6]. Congenital CMV is the second most common cause of sensorineural hearing loss in children after hereditary deafness [7].

In symptomatic congenital CMV infection, eye abnormalities such as chorioretinitis, microphthalmos, and cataract can be observed. In the developing CNS tissue, CMV can produce microcephaly with neuronal migration defects such as lissencephaly or schizencephaly. In addition, cerebral calcifications and white matter changes (leukodystrophy) are characteristic for CMV (Figure 1). Clinically, these children can have mental retardation, seizures, abnormal tone or movements, or hydrocephalus. In a recent series, microcephaly, cerebral palsy and epilepsy were the most common neurolog-

ical findings, and some other children later developed sensory-neural hearing loss. White matter abnormalities were common (11/12 patients). Anterior temporal lobe abnormalities were found in 13/14: migration disorders like polymicrogyria and pachygyria-lissencephaly, ventriculomegaly, hippocampal dysplasia correlated with severe neurological sequelae while the presence of white matter abnormalities, periventricular cysts, and cerebellar hypoplasia did not predict the outcome [8].

The timing of the maternal infection affects the outcome: infection in early pregnancy results in severe neurological sequelae, while later infection has less prominent signs: lissencephaly and cerebellar hypoplasia indicate an early (first half of pregnancy) onset of infection while less severe cortical dysplasia (pachy/polymicrogyria) suggest an infection later in pregnancy [9].

Congenital CMV is a persistent chronic infection: the child can have viremia for months, and excrete virus from saliva and urine for several years.

LABORATORY TESTS

The serum IgM positivity in the first month after birth or in cord blood strongly indicates congenital CMV infection. The most reliable method for diagnosis is viral isolation from newborn babies' urine, saliva, or conjunctiva early after birth, but PCR from these body fluids is the most widely used diagnostic test: The tests should be done within 2 weeks after birth because the baby may encounter CMV soon after birth and the tests will not differentiate congenital versus acquired infection. Quantitative PCR can distinguish babies with high viral load, who also are more likely to have symptomatic disease [10]. PCR assays of dried blood spots from newborns are not sufficiently sensitive for universal screening. However, saliva PCR assays are currently being assessed as a useful screening method for congenital CMV infection [11].

Other laboratory findings include the pre-

sence of atypical lymphocytes in peripheral blood, thrombocytopenia, anemia, and increased liver enzymes. Neuroimaging may show intracranial (particularly periventricular) calcifications in 25% to 50%, multicentric encephalomalacia, ventriculomegaly, cerebellar hypoplasia, or migration abnormalities such as pachygyria and lissencephaly. CT is superior to MRI in detecting the calcifications that may be present at birth or develop in the first year.

Prevention and Management of prenatal infection:

In the absence of an effective vaccine at present, preventive measures include assessing young women for CMV IgG serology to identify those at risk for primary infection and recommend avoidance of viral exposure during pregnancy to those who are seronegative. For instance, teachers are at high risk for cytomegalovirus exposure. Children who go to school can carry CMV: washing hands when coming from school is very important when there is a pregnant woman at home [12]. Congenitally infected infants actively excrete virus. Awareness of this fact, with appropriate contact isolation and proper hygiene measures, minimizes risk of CMV transmission to any pregnant women.

There is no consensus for measures to be taken when a pregnant woman acquires a primary CMV infection. Pregnant women who experience primary infection during the first trimester should be offered termination. When this is not possible, treatment with ganciclovir and human cytomegalovirus IgG have been used to reduce the risk and degree of mother-to-fetal transmission and fetal infection although there is controversy about the effect [13-15]. Serologic follow-up of the mother, including the CMV avidity test which allows differentiation between recent or past infection, and when there is a change in serum titers, PCR from the amniotic fluid is useful in indicating whether the fetus became infected.

Of pregnant women who acquire a primary CMV infection, about 30-40% transmit infection to their fetuses. Between 10 and 15% of co-

ngenitally infected infants are acutely symptomatic at birth and most of the survivors have serious long-term complications. As most maternal infections are asymptomatic, the only way to disclose primary infection is to implement specific serological testing as early in pregnancy as possible (before week 12-16 of gestation). Appropriate counseling by a physician experienced in the interpretation of serological and PCR test results will reduce the number of unnecessary pregnancy terminations [16]. The fetus can be followed-up by ultrasonography for the pattern of periventricular echogenicity, ventriculomegaly, parenchymal and periventricular abnormalities, and serological tests and PCR can be done when there is a suspicion.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis includes other congenital infections: rubella, toxoplasmosis, syphilis, Herpes simplex, hepatitis, varicella zoster, parvovirus B19. The presence of associated findings, the location of cerebral calcifications, the presence or absence of bone involvement, and microbiological studies: CMV IgM, serial IgG titers, and PCR allow diagnosis.

Metabolic disorders causing neonatal liver disease (like galactosemia, Niemann-Pick disease, cystic fibrosis, tyrosinemia, ...), sepsis, hemolytic anemias, should also be considered in the differential diagnosis.

OUTCOME

This depends on the severity of symptoms at birth, like the presence of multiorgan disease. Only 10% of infected infants have symptoms at birth, and 10% of them end fatally from liver disease or secondary bacterial infections. The presence of microcephaly at birth is the most significant indicator of neurological outcome [17].

TREATMENT

The infant with congenital CMV infection should be examined for neurologic, ophthalmologic, and hearing impairment. Ganciclovir

may reduce the neurologic problem and hearing loss. More recently valganciclovir has been suggested [18]. Certain authors recommend combination of antiviral drugs with anti-CMV IgG.

Although results are mixed, the highest level of evidence suggests that antiviral therapy confers a protective benefit on neonates with hearing loss and symptomatic CMV. Cochlear implantation can result in advancement of speech and language skills, but there are mi-

xed results compared with non-CMV-infected patients [19].

Treatment of the neurological condition includes antiepileptic therapy and rehabilitation with special education as needed. If the child has infantile spasms, adrenocorticotrophic hormone (ACTH) should not be used because it may result in disseminated infection. Infants require multidisciplinary follow-up and special education and rehabilitation.

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XÜLASƏ

ANADANGƏLMƏ SİTOMEQALOVİRUS İNFEKSİYASI HADİSƏSİ

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Sitomeqalovirus bir çox uşaqlıqdaxili infeksiyalara səbəb olan virusdur. Bu virus eşitmənin itirilməsinə, mikrocefaliyaya, beyin şırımlarının anomaliyasına və dölün beyninin ağ maddəsinin zədələnmələrinə səbəb ola bilər. Bu məqalədə anadangəlmə sitomeqalovirus infeksiyası hadisəsi təqdim edilmişdir.

РЕЗЮМЕ

СЛУЧАЙ ВРОЖДЕННОЙ ЦИТОМЕГАЛОВИРУСНОЙ ИНФЕКЦИИ

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Цитомегаловирус - вирус ответственный за большинство внутриматочных инфекций. Этот вирус может вызвать потерю слуха, микроцефалию, мальформацию мозговых извилин и патологии белого вещества мозга зародыша. В этой статье представлен случай врожденной цитомегаловирусной инфекции.

Redaksiyaya daxil olub: 04.07.2012

Çapa tövsiyə olunub: 20.07.2012

Rəyçi: R.K.Şirəliyeva, t.e.d. prof.