Cytomegalovirus Congenital iInfection: It is Time for Early Diagnosis and Treatment during Gestation

Infeção Congénita por Citomegalovírus: É Hora para o seu Diagnóstico e Tratamento Precoce durante a Gestação

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Congenital cytomegalovirus (CMV) infection is still a public health concern as the major non-genetic cause of sensorineural hearing loss and an important contributory factor to cerebral palsy and other child neurodisabilities.[1-5] Unfortunately, vaccination has proven to be ineffective.[1]

This condition has a global incidence ranging from 0.2% to 2%. In Portugal, it is estimated to be around 1%, resulting in approximately 900 infected newborns per year.[6] Most of the neonates infected with CMV in the prenatal period are asymptomatic (around 87%), and approximately 80% to 95% of the asymptomatic babies have no sequelae.[1-5] Nevertheless, symptomatic congenital CMV infection can be serious.

Although congenital CMV infection may affect many fetal organs, the most significant lesions occur in the central nervous system due to the virus preferential tropism for both neural stem and progenitor cells.[7,8] Pathological brain findings comprise necrosis, microglial nodules, microglial activation, astrocytosis, and vascular changes.[8] These anomalies will result in variable degrees of cerebral affection, including abnormal neuronal migration, brain atrophy, white matter lesion, ventriculomegaly, calcifications, hemorrhage and cysts. Consequently, CMV congenital infection can cause neurodevelopmental delay, cognitive impairment, neuromuscular dysfunction, epilepsy as well as impaired visual function. It has also been related to the autism spectrum disorder.[1] Concerning hearing loss, the mechanisms through which CMV infection leads to deafness are not fully understood but they seem to be related to immune response, which would result in the destruction of the inner ear structure.

It is well known that the risk of vertical transmission raises as pregnancy advances.[1-5] However, until recently, it was not clear that, although less likely to occur, first trimester infection is the only one related to higher clinical risks for the fetus. It is now known that congenital CMV infection is severe almost exclusively when the virus hits the fetus in the embryonic or early fetal period, before 14 weeks gestation. After this stage of pregnancy, serious fetal impairment is very rare.[1,5] Several reports show that the risk of neurodevelopmental disability in infected liveborn fetuses decrease from 20%-25% in infections occurring during the first trimester to 0.1% when they take place in the second trimester, and to 0% when vertical transmission happens in the last three months of the gestation. Sensorineural hearing loss was also reported to be much less

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severe in infections that occurred after the first trimester, and significative deafness has been reported only in first trimester insults.[5,7] This relatively new concept implies that all efforts to diagnose a CMV congenital infection should be focused on the first 14 weeks of gestation.

Universal maternal screening for CMV is still controversial. The main argument against it is that there is no treatment to offer the parents. Nonetheless, a recent randomized controlled study revealed that the administration of high-dose oral valacyclovir following first-trimester maternal primary infection led to a significantly decreased rate of fetal infection.[1] In the last 2 years, this therapeutic option started being offered in many countries for women whose infection was detected in the first 14 weeks of gestation, including Portugal. The management and treatment of maternal CMV infection must be carried out in referral centres, for better results and notification.

In view of recent knowledge on the diagnosis and management of prenatal CMV infection, it is mandatory that healthcare providers reassess universal CMV screening programs in the first trimester of pregnancy. It is more than time for CMV congenital infection early diagnosis and treatment!

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