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Fetal Brain Magnetic Resonance Imaging Findings In Congenital Cytomegalovirus Infection With Postnatal Imaging Correlation

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Fetal brain magnetic resonance imaging (MRI) is a powerful tool in the diagnosis of symptomatic congenital cytomegalovirus infection, requiring a detailed search for specific features. A combination of anterior temporal lobe abnormalities, white matter lesions, and polymicrogyria is especially predictive. Fetal MRI may provide a unique opportunity to detect anterior temporal cysts and occipital horn septations, as dilation of these areas may decrease later in development. Cortical migration abnormalities, white matter abnormalities, cerebellar dysplasia, and periventricular calcifications are often better depicted on postnatal imaging but can also be detected on fetal MRI. We present the prenatal brain MRI findings seen in congenital cytomegalovirus infection and provide postnatal imaging correlation, highlighting the evolution of findings at different times in prenatal and postnatal developments.
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Introduction

Cytomegalovirus (CMV) is an endemic herpesvirus that is spread by close contact with bodily fluids, with up to 90% of individuals infected by late adulthood.[1] In children and adults, CMV infection is typically asymptomatic or produces a mild, flulike illness. Special groups, though, are susceptible to severe illness caused by the virus, including immunocompromised patients, newborns (especially when premature), and fetuses. Congenital CMV infection occurs through transplacental transmission, most commonly in women who acquire a primary infection during pregnancy, although transmission during secondary infection can also occur.[2] Congenital CMV infection is seen in approximately 0.6%-0.7% of all live births in industrialized countries, with 11%-13% of those being symptomatic at birth.[3,4]

Clinical findings of congenital CMV infection in the newborn are varied, with more severe features associated with first and second trimester infection.[5] Intrauterine growth restriction, hydrops, thrombocytopenic purpura, jaundice, hepatosplenomegaly, hepatitis, pneumonitis, chorioretinitis, microcephaly, poor tone and suck, sensorineural hearing loss, and seizures have all been described.[2] Outcomes for these newborns are varied as well. Long-term neurologic sequelae are seen in approximately 50% of symptomatic newborns including sensorineural hearing loss, visual impairment, cognitive impairment, seizures, cerebral palsy, and developmental delay.[3] An additional 5%-15% of asymptomatic newborns will develop neurodevelopmental sequelae, most commonly hearing loss, although developmental delay and seizures are also seen. Sensorineural hearing loss due to congenital CMV infection can be unilateral or bilateral and may not be detected with routine newborn screening owing to its often progressive or fluctuating course.[6] It is estimated that congenital CMV infection is responsible for 10%-25% of cases of sensorineural hearing loss diagnosed by 4 years of age.[7,8]

Serologic screening for CMV infection is not part of routine prenatal or neonatal care in the United States. If performed, maternal primary infection can be established by conversion from IgG-negative to IgG-positive status, or positive IgM with low IgG. Fetal infection can be confirmed with positive viral culture or polymerase chain reaction (PCR) of amniotic fluid. In the newborn, confirmation of congenital CMV infection with blood, urine, or saliva viral culture or PCR must be

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performed within the first 3 weeks of life to exclude postnatal infection.[2] It is possible to perform PCR testing on the dried blood spot of the newborn screening card later.[9]

Brain abnormalities seen on prenatal ultrasound (US) are often the first indication of congenital CMV infection. Ventriculomegaly is most commonly seen, with microcephaly and periventricular calcification also commonly noted.[10] Other features that can be detected with targeted US include subependymal cysts, intraventricular synechiae, white matter hyperechogenicity, callosal hypoplasia, lenticulostriate vasculopathy, sulcation and gyral abnormalities, and cerebellar and cisterna magna anomalies.[11] When 1 or more of these features is detected, magnetic resonance imaging (MRI) is often pursued for more detailed evaluation, as the addition of MRI increases the sensitivity and positive predictive value for the diagnosis of symptomatic congenital CMV infection.[10,12] New developments in prenatal and postnatal antiviral treatments add to the importance of accurate and timely diagnosis.

In this article, we review the prenatal brain MRI findings seen in congenital CMV infection and provide postnatal imaging correlation, highlighting the evolution of findings at different times in prenatal and postnatal development (Box 1).

Fetal Brain MRI Features of Congenital CMV

As for most fetal MRI examinations, multiplanar T2-weighted images (eg, single-shot fast spin echo or half-fourier acquisition single-shot turbo spin-echo [HASTE]) are the workhorse for structural evaluation of the brain. Steady-state free precession images (eg, fast imaging employing steady-state acquisition [FIESTA] or true fast imaging with steady-state precession [TruFISP]) can be a useful adjunct for structural evaluation. T1-weighted and gradient-recalled echo images aid in detection of hemorrhage or calcification. Fetuses as young as 18 weeks of gestation can be imaged, although the normal lack of sulcation at this point in development limits the ability to detect migration abnormalities associated with congenital CMV infection. On the contrary, a detailed third trimester fetal MRI may obviate the need for immediate postnatal MRI.

Intracranial Calcifications

Periventricular calcification is considered a hallmark of congenital CMV infection and a predictor of developmental delay, seen in 34%-70% of cases.[13] Although more easily depicted with targeted prenatal US,[10] intracranial calcification can be seen on fetal MRI as low T2 or high T1 signal. Careful evaluation is needed to detect subtle, punctate foci of signal abnormality along the ventricular walls. Calcification can also occur in the basal ganglia, as linearly arrayed lenticulostriate vasculopathy or more puncate foci, and in the brain parenchyma, but it is usually more fine and difficult to detect on fetal MRI. The lack of obvious intracranial calcification on fetal MRI, then, should not dissuade the reader from the diagnosis of congenital CMV. Postnatal MRI with high-resolution susceptibility-weighted images, computed tomography, or US can be confirmatory (Figs. 1 and 2).

Cortical Migrational Abnormalities

A spectrum of cortical migration abnormalities can be seen in congenital CMV infection, largely depending on the timing of in utero infection. If the infection occurs before 16-18 weeks of gestation, lissencephaly results.[14] If the infection occurs between 18 and 24 weeks of gestation, polymicrogyria

Box 1–Summary of Fetal and Postnatal MRI Findings in Congenital CMV Infection.

Imaging Feature	Specific Details	Fetal MRI	Postnatal MRI
Microcephaly	Usually detected on prenatal US, which may be an indication for fetal MRI	May detect microencephaly as well	
Calcification	Most often periventricular	Low T2 or high T1 signal, which is often subtle	More easily detected with susceptibility-weighted imaging, or CT or US
Ventriculomegaly	May be only indication on prenatal US for fetal MRI	Often mild to moderate	Variable, often moderate to severe
Periventricular cysts	Especially anterior temporal lobes	Temporal polar lesions highly predictive of CMV infection	Decrease in size and conspicuity with age, consider high-resolution SSFP
Intraventricular septa	Especially occipital horns	Cystic dilation of occipital horns	Decrease in size and conspicuity with age, consider high-resolution SSFP
Cerebellar hypoplasia or dysplasia	Sometimes with cerebellar white matter abnormalities	Difficult to detect unless severe	Mild dysplasia and white matter abnormalities well depicted
Cortical migration anomalies	Frontal or perisylvian polymicrogyria or pachygyria	Smudgy or thickened cortex on T2, better seen in third trimester	More easily seen, especially after myelination has occurred
White matter abnormalities	Periventricular high T2 signal, which may sometimes be cystic	May be extensively involved	High T2 signal may be more conspicuous with age, but appears less extensive

CT, computed tomography; SSFP, steady-state free precession.