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A Quiet Disease With Loud Manifestations

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Cytomegalovirus (CMV) is the most common congenital virus passed from mother to fetus in the United States, and the most common acquired cause of sensorineural hearing loss. Neuroimaging in patients with symptomatic congenital CMV demonstrates abnormalities frequently, but many providers are unaware of the extent of these findings. We present a case of a 15-month-old girl with progressive sensorineural hearing loss and developmental delays. Magnetic resonance imaging of her brain was done by her otolaryngologist as part of a routine cochlear implant evaluation where it was found to be drastically abnormal and reported as a likely leukodystrophy. It was subsequently found to be related to congenital CMV on further evaluation. Congenital CMV should be considered in the differential of white matter hyperintensities, especially in the setting of sensorineural hearing loss, developmental delays, or both, and given how common CMV is around the world.
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Introduction

Cytomegalovirus (CMV) is the most common congenital virus passed from mother to fetus in the United States.[1] Of all pregnant women in the United States, 15%-45% are CMV seronegative. Of those who are seronegative, 1%-4% experience a primary maternal infection, and 40% of these women produce a congenitally infected newborn. Of those congenitally infected newborns, 10% will have symptoms at birth, the large majority of which will have permanent disabilities. The other 90% of congenitally infected newborns will have "silent infections," eventually resulting in another 10%-15% experiencing hearing loss and other disabilities over time.[2] This amounts to 4000-8000 new cases of problematic CMV congenital infection each year in the United States. Unfortunately, congenital CMV is one of the least recognized or understood congenitally acquired viruses among women of childbearing age and primary care practitioners while among the most prominent childhood diseases in the United States.[3-5] Neuroimaging in patients with symptomatic congenital CMV demonstrates abnormalities approximately 70% of the time with white matter involvement representing 22%-57% of the abnormalities.[6-8] These white matter changes can be mistaken for a leukodystrophy that typically has a progressive rather than static course, causing much avoidable anguish for the parent and provider.

Case Study

This 15-month-old girl was born at 35 weeks. She had a history of recurrent ear infections and myringostomy tubes, who presented with progressive hearing loss. She was noted initially on her newborn hearing screen to have right-sided sensorineural hearing loss and eventually also developed loss on the left. She presented to otorhinolaryngology for evaluation for cochlear implants where it was noted that she had developed profound hearing loss on the left. The otorhinolaryngologist at that time decided to do magnetic resonance imaging (MRI) scan of the brain to confirm the status of the cochlear nerves for surgical planning. The MRI showed normal cochlear nerves, but incidentally showed diffuse, abnormal, nonenhancing T2 hyperintensities within the white matter of the cerebral hemispheres bilaterally with the signal abnormality being almost confluent within the parietal lobes with sparing of the subcortical U fibers and features consistent with temporal horn vacuolization. This was initially read as being a likely leukodystrophy prompting urgent referral to neurology (Figs. 1-3). Upon neurologic evaluation, she was diagnosed with global developmental delay and almost met criteria for microcephaly (head circumference 42 cm, fourth percentile) but showed no evidence of spasticity or hyperreflexia despite the impressive MRI findings. She also lacked other signs pointing to CMV such as hepatosplenomegaly, petechiae, and

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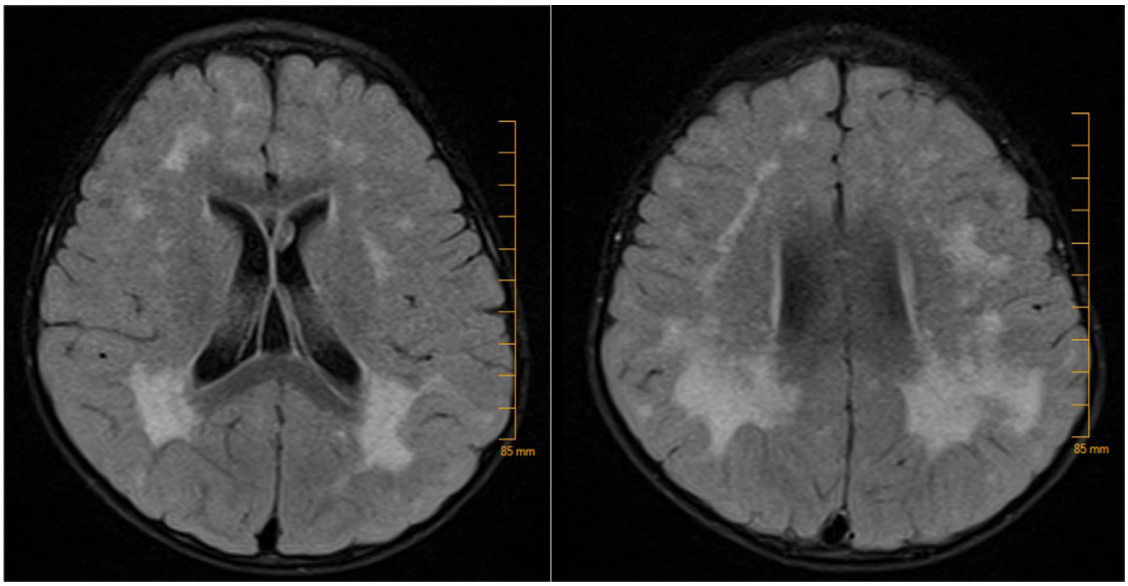

Figure 1 Axial T2 FLAIR-weighted brain MRI images showing the prominent diffuse and patchy white matter hyperintensities. FLAIR, fluid-attenuated inversion recovery. (Color version of figure is available online.)

periventricular calcifications. We performed multiple investigations to work up this leukodystrophy, which included serum amino acids, lactate level, pyruvate level, urine organic acids, complete metabolic panel, serum creatine kinase, very long-chain fatty acids and peroxisomal profile, and lysosomal enzyme screen. She also saw ophthalmology and findings of the eye examination were normal. The results of all of these tests were normal. Further testing for CMV antibodies returned positive (CMV IgG index 4.21). Although we are unable to tell for certain if this is congenital or acquired, given her age, the clinical scenario, MRI findings, and hearing loss, congenital CMV is the most likely diagnosis. Making the diagnosis of congenital CMV after 12 months of age is difficult, as CMV testing then often reflects community acquired rather than congenital CMV. She completed her cochlear implant placement at 22 months and speech has already begun to improve.

Discussion

According to the CDC (Centers for Disease Control and Prevention), 1 in 691 births are affected by Down syndrome, 1 in 2858 births are affected by spina bifida, and 1 in 150 births are affected by congenital CMV infection.[5] Unfortunately, congenital CMV remains one of the least recognized or understood congenitally acquired viruses among women of childbearing age and primary care practitioners while among the most prominent childhood diseases in the United States.[3-5]

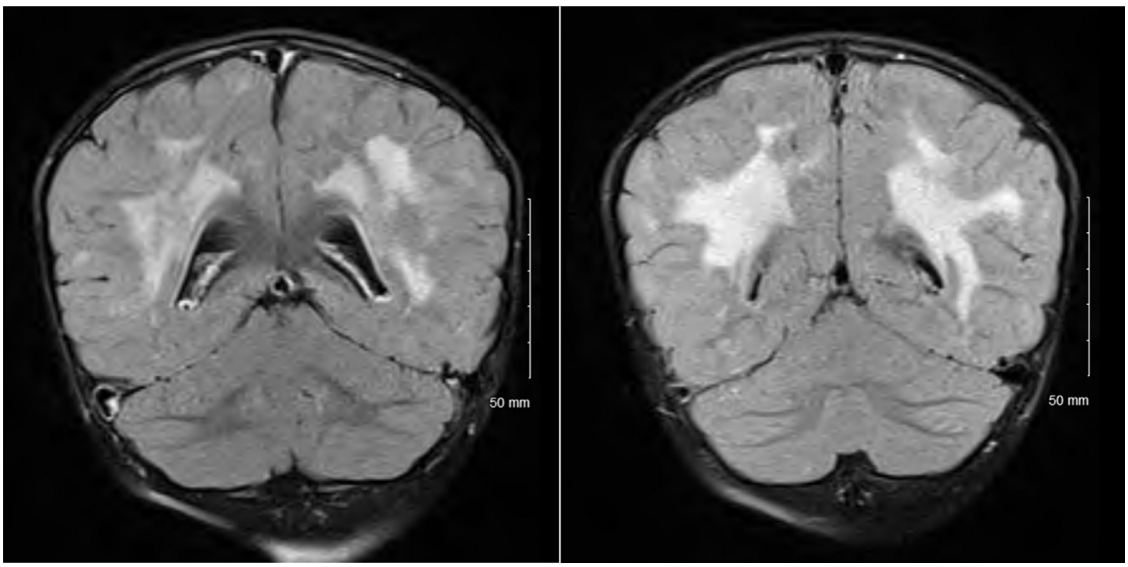

Figure 2 Coronal T2 FLAIR-weighted brain MRI scan with diffuse periventricular white matter hyperintensities. FLAIR, fluid-attenuated inversion recovery.