Photo Quiz

Intracranial Calcifications Discovered During Prolonged New Seizure

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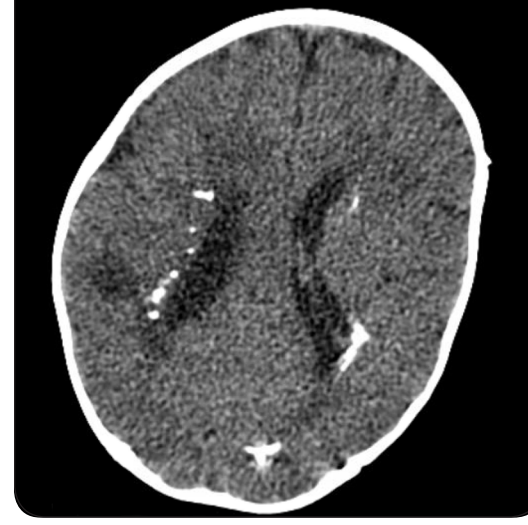
An eight-month-old infant presented to the emergency department with a prolonged episode of left upper and lower extremity shaking and eye deviation. The day before, he had developed nasal congestion and a cough but no fever. The infant was delivered at term, and had thrombocytopenia with facial and chest petechiae at birth that improved without intervention. He was developmentally delayed and unable to sit without support, although he could roll over. The remainder of his medical history was unremarkable.

On physical examination, he was febrile (101.9°F [38.8°C]) and drowsy but nontoxic in appearance. He had diffuse hypotonia, diminished patellar deep tendon reflexes, truncal instability, and head lag. There was no rash. Complete blood count and chemistry panel findings were normal, except for hyponatremia (sodium level of 133 mEq per L [133 mmol per L]). Computed tomography of the head showed periventricular calcifications but no hydrocephalus *(Figure 1)*.

FIGURE 1



Question

Based on the patient's history, physical examination, and imaging findings, which one of the following is the most likely diagnosis?

- ☐ A. Aicardi-Goutières syndrome.
- ☐ B. Congenital cytomegalovirus infection.
- ☐ C. Congenital lymphocytic choriomeningitis virus infection.
- ☐ D. Congenital toxoplasmosis.

See the following page for discussion.

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SUMMARY TABLE

Condition	Clinical features	Imaging findings
Aicardi-Goutières syndrome	Developmental regression, microcephaly, fevers, abnormal movements	Frontotemporal white matter changes, cerebral atrophy, intracranial punctate calcifications of the basal ganglia
Congenital cytomegalovirus infection	Petechiae, purpura, jaundice, hepatosplenomegaly, intrauterine growth restriction, microcephaly, seizures, retinitis, thrombocytopenia, developmental delay, or hypotonia	Periventricular calcifications, white matter atrophy, ventriculomegaly, neuronal migration anomalies
Congenital lymphocytic choriomeningitis virus infection	Chorioretinitis, macrocephaly or microcephaly, cerebral palsy, seizures, intellectual disability	Periventricular calcifications, obstructive hydrocephalus
Congenital toxoplasmosis	Classic triad of hydrocephalus, chorioretinitis, and intracranial calcifications; microcephaly, hepatosplenomegaly, petechiae, jaundice, seizures	Hydrocephalus, randomly distributed parenchymal calcifications

Discussion

The answer is B: congenital cytomegalovirus (CMV) infection. The differential diagnosis for intracranial calcifications is broad. Calcifications associated with congenital CMV infection are predominantly periventricular because of germinal matrix damage, which leads to white matter atrophy, ventriculomegaly, and neuronal migration anomalies.[1-3] Occuring in 0.2% to 2.0% of pregnancies, CMV infection is the most common congenital infection in the United States.[4] Congenital CMV is acquired by transplacental passage of the virus, through the genital tract at birth, or by ingesting infected human milk. Only 10% of neonates with congenital CMV infection are symptomatic at birth, but possible symptoms include petechiae, purpura, jaundice, hepatosplenomegaly, intrauterine growth restriction, microcephaly, seizures, retinitis, thrombocytopenia, developmental delay, or hypotonia.[5]

Congenital CMV infection is confirmed with culture or polymerase chain reaction testing that is positive for the virus in body fluids, typically urine or saliva, within three weeks of birth.[6] Symptomatic infants are treated within the first month of life with oral valganciclovir (Valcyte) for six months.[7] Treatment is not typically indicated for mild or asymptomatic infections with isolated sensorineural hearing loss.[6] Because of hearing loss, audiology testing should be done every six months for the first three years.[6] Children with congenital CMV infection should have an ophthalmologic examination and routine developmental assessments.

Aicardi-Goutières syndrome is an early-onset leukoencephalopathy presenting as developmental regression, microcephaly, fevers, and abnormal muscle movements. Affected newborns may exhibit thrombocytopenia, hepatosplenomegaly, and neurologic abnormalities, which can mimic congenital infections. Neuroimaging reveals frontotemporal white matter changes, cerebral atrophy, and intracranial punctate calcifications of the basal ganglia.[8]

Congenital lymphocytic choriomeningitis virus infection also affects the germinal matrix, leading to periventricular calcifications; however, lymphocytic choriomeningitis virus infection often causes hydrocephalus because of inflammation and obstruction of the cerebral aqueduct.[2,9] The condition can lead to macrocephaly or microcephaly, cerebral palsy, seizures, or intellectual disability. Chorioretinitis occurs in virtually all cases of congenital lymphocytic choriomeningitis virus infection.[9]

Congenital toxoplasmosis infection produces a triad of hydrocephalus, chorioretinitis, and intracranial calcifications. The nodular calcifications seen on computed tomography are randomly distributed throughout the brain parenchyma. Microcephaly, hepatosplenomegaly, petechiae, jaundice, and seizures may occur.

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