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CASE SUMMARY

A preterm neonatal male was born at 30 weeks gestation with frequent jerking movements of all extremities and poor responsiveness to stimulation. Physical exam also demonstrated a denuded area of skin anterior to the left ear as well as a number of healed skin lesions on his face. Electroencephalogram (EEG) revealed a markedly abnormal pattern of generalized voltage suppression without definable cortical rhythmicity consistent with marked generalized cortical activity suppression and poor neurological prognosis. Ophthalmologic consult revealed vitreous haze, retinal lipid exudation, and multiple areas of retinal hyperpigmentation. Pertinent laboratory tests revealed the cerebrospinal fluid (CSF) to be clear yellow with elevated lymphocytes, low glucose, and elevated protein. Secretion and blood cultures initially were negative. Additionally, the mother had been admitted at 18 weeks gestation with fever secondary to suspected chorioamnionitis and was treated supportively. Later that same month, the mother described having a nonpruritic rash on her abdomen, buttocks, and upper legs that resolved spontaneously.

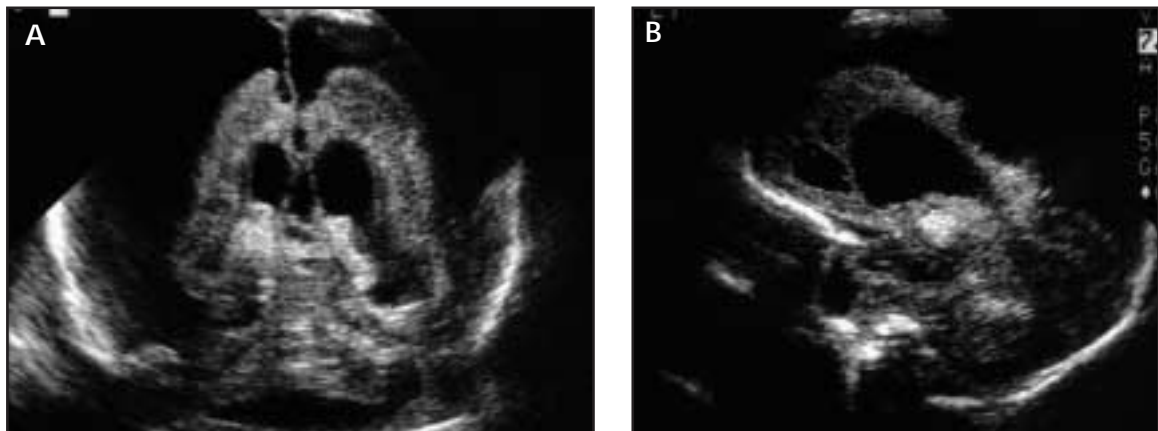


FIGURE 1. Neonatal cranial ultrasound images performed through the anterior fontanel in the (A) coronal plane and (B) sagittal plane demonstrate diffuse parenchymal volume loss with associated ventriculomegaly and large extra-axial fluid collections. Cystic parenchymal changes are also evident on the sagittal image (B).

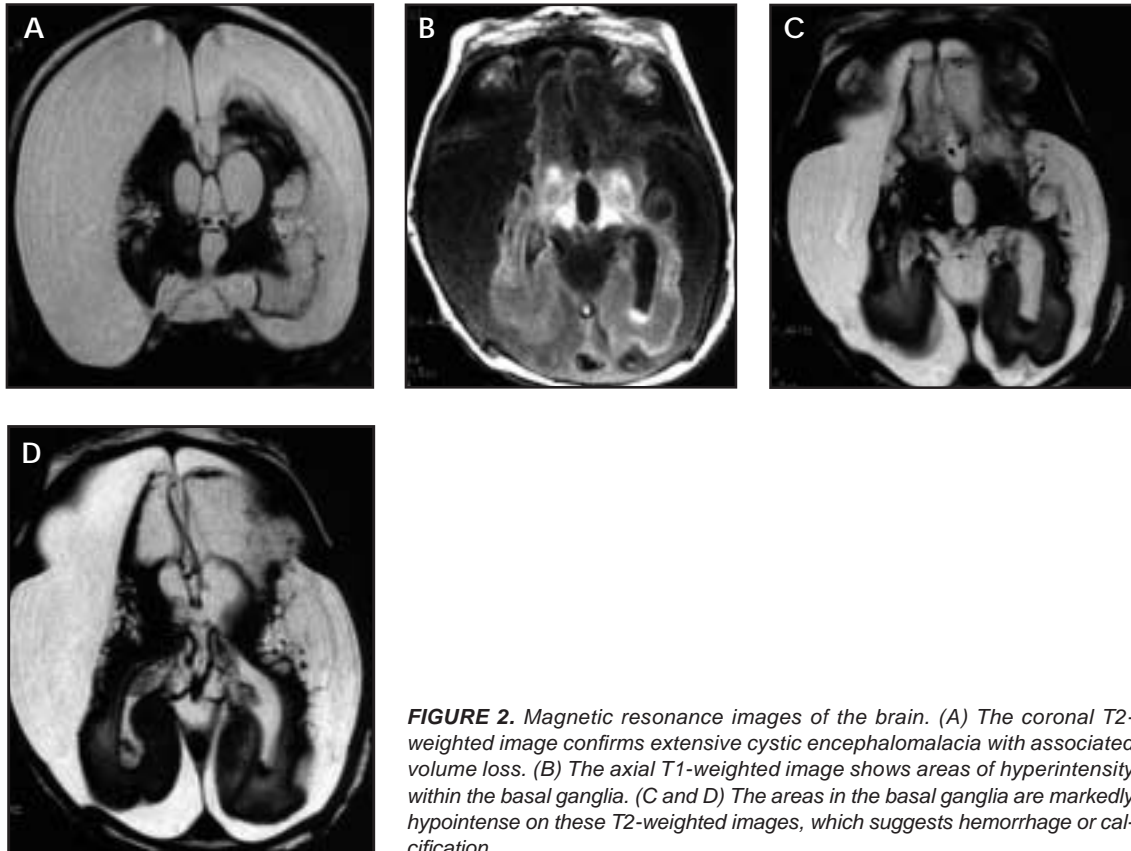


FIGURE 2. Magnetic resonance images of the brain. (A) The coronal T2-weighted image confirms extensive cystic encephalomalacia with associated volume loss. (B) The axial T1-weighted image shows areas of hyperintensity within the basal ganglia. (C and D) The areas in the basal ganglia are markedly hypointense on these T2-weighted images, which suggests hemorrhage or calcification.

DIAGNOSIS

Postinfectious encephalomalacia secondary to herpes simplex type 2 virus

IMAGING FINDINGS

A neonatal neurosonogram (figure 1) and an MRI of the brain following delivery (figure 2) were performed. Neonatal cranial ultrasound performed through the anterior fontanel in the coronal (figure 1A) and sagittal (figure 1B) planes demonstrate diffuse parenchymal volume loss with associated ventriculomegaly and large extra-axial fluid collections. Additionally, cystic parenchymal changes are evident on the sagittal image.

A coronal T2-weighted image confirms extensive cystic encephalomalacia with associated volume loss (figure 2A). Also, note the areas of hyperintensity on the axial T1 image (figure 2B) within the basal ganglia, which are markedly hypointense on the T2 images (figures 2C and 2D), suggestive of hemorrhage or calcification.

DISCUSSION

Herpes virus is included in the congenital TORCH infections (toxoplasmosis, other agents, rubella, cytomegalovirus, herpes simplex), which affect the central nervous system (CNS) in the fetal or neonatal period. Herpes is a DNA virus with two known serotypes, types 1 and 2. Approximately 75% or more of neonatal infections are caused by type 2.¹⁻³ The most common mode of transmission is parturitional, with infection caused by direct contact of the infants' eyes, skin, or oral cavity in the cervix or vagina. In these more typical cases, clinical onset and CNS manifestations are seen 2 to 4 weeks after birth. Infection in the fetal period is extremely rare with virus transmission through the hematogenous-transplacental route. The overall risk of intrauterine infection with herpes virus has been estimated at 1 in 200,000 pregnancies.⁴ Also, the frequency of viral manifestation with intrauterine infection has been estimated at 3 for every 100 infected infants⁵; the protective effects of the placenta mitigate

against transmission of viral agents in most episodes of maternal viremia.³ The rarity of infected fetuses carried to term may be secondary to the severe encephaloclastic destructive effects occurring earlier in the gestational period, possibly due to defective macrophage function or impaired production of antiherpes antibody.⁶ Thus, infections that occur within the first half of pregnancy are associated with an increased frequency of spontaneous abortions and stillbirths.^{3,7}

The neuropathic and radiological findings vary upon the time of gestation/age of infection. Imaging performed early in the infection may demonstrate widespread areas of white matter signal and attenuation abnormality reflecting edema, which eventually evolves into encephalomalacic change.⁸ Hemorrhagic infarction and meningeal enhancement can be seen in some cases.^{1,2,6,8} Further progression reveals cortical gray matter laminar changes with increased attenuation on CT and shortened T1 and T2 signal on MR.⁸ Regardless of the specific radiologic findings, fetal and neonatal meningoencephalitis is usually diffuse and overwhelming, resulting in widespread brain destruction.⁹ Late imaging in the disease process demonstrates volume loss diffusely throughout the cerebral hemispheres, hydrocephalus, and multicystic encephalomalacia.^{1-3,6,8-10} Cerebellar involvement is seen in approximately 50% of cases.^{1,8-10} Calcifications may be seen in the periventricular white matter and the basal ganglia.¹⁻⁷ Occasionally, gyriform-type cortical calcifications are demonstrated.^{1,9}

Pathologically, astrogliosis with multifocal gray and white matter involvement with cystic infarction and demyelination leads to cystic encephalomalacia.⁶ Microglial nodules with intranuclear inclusion-bearing cells are seen under the microscope.⁶ Herpes virus has a predilection for endothelial cells, which

explains the resulting vascular thrombosis and hemorrhagic infarctions.^{1-3,6}

The imaging findings in the fetal form of herpes infection differ from the more commonly described findings seen in the older child/adult form. The more localized manifestations of the infection afflicting the frontal and temporal regions are seen in older children and adults, usually a result of the herpes simplex type 1 virus.^{1,2,8} The parturitional neonatal type of infection is similar to the fetal form in that there is also a diffuse involvement.

Associated clinical findings can include skin, eye, and mouth lesions. These are the most common manifestations of herpes infection. Herpes can cause a chorioretinitis as was seen in this patient. Disseminated infections have a high mortality rate, as do the early gestational CNS infections.^{1,3,4} Cerebrospinal fluid in these infants typically demonstrates at least a partial elevation of protein, some pleocytosis, and mild reduction of glucose.^{4,9} Cerebrospinal fluid evaluation with PCR to detect the viral DNA has become a major diagnostic tool.⁴ Electroencephalography findings can help characterize the infection manifestations by demonstrating characteristic, repetitive sharp-slow wave complexes or spike activity.¹

Long-term sequelae of survivors can be markedly debilitating, with major neurological problems, including mental retardation, blindness, and spastic quadraparesis.^{1,4,11}

Congenital type 2 herpes infection in the fetal period is exceedingly rare in contrast to the more typical neonatal form of the disease. The radiological/pathological findings reflect the diffuse, destructive CNS sequelae the virus can manifest as a result of intrauterine infection. These sequelae typically result in early fetal demise or long-term neurological impairment. The patient in this case expired 4 days following delivery.

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