Meningitis caused by gram-negative enteric bacteria usually is limited in children to the neonatal period. Among neonates, the disease is severe, with a mortality of up to 80%. The most common etiologic agent in this type of meningitis is *Escherichia coli*. Meningitis due to *Citrobacter diversus* has occurred in sporadic small outbreaks throughout the United States. This devastating disease frequently results in death, brain abscess, or white matter necrosis.¹⁻³

Central nervous system infection with *Citrobacter diversus* seems to have a unusual propensity for producing massive white matter necrosis, liquefaction, cavitation, and brain abscesses. The morbid anatomy, possible pathophysiologic events, and neurosonographic findings of *Citrobacter diversus* meningitis are distinct from the findings in meningitis from more common bacterial agents and are described here.

CASE REPORT

The patient was a 7 day old white male infant born by vaginal delivery at 30 weeks’ gestation. There was a history of premature rupture of amniotic membranes, for which the mother received ampicillin. The patient was discharged to home and appeared well for 3 days. On the day of admission, the neonate had stopped feeding and became irritable and less active. He was brought to the emergency room for evaluation and was lethargic with appearance of sepsis. White blood cell count was 9,500, platelets, 339,000 differential count, 39 polymorphonuclear leukocytes, 23 band cells, 14 lymphocytes, and 11 monocytes per cc. Chest radiograph showed minimal bilateral interstitial lung parenchymal abnormality. The patient was admitted and a regimen of cefotaxime and ampicillin was started. Bloody cerebrospinal fluid was obtained on lumbar puncture, possibly from a traumatic tap, and was sent for cultures. The child was intubated because of apnea. Gentamicin was added to the antibiotic regimen. A neurosonogram was performed and showed normal ventricles without extraxial fluid. The white matter was extremely echogenic (Fig. 1). Blood and cerebrospinal fluid cultures from the day of admission grew *Citrobacter diversus*.

The patient’s condition worsened clinically over the next 10 days. He had poor muscle tone, decreased peripheral spinal reflexes, no rooting or sucking reflexes, and no response to voice or touch. He had intermittent seizures, despite anticonvulsant therapy. On hospital day 10, a neurosonogram showed normal ventricles without extraxial fluid. The white matter of this brain was diffusely necrotic.
Echogenic. Cranial computed tomographic examination with intravenous contrast agent showed normal cerebral cortex and deep gray matter without abscess formation. No enhancing abnormality was seen. The white matter was hypodense, nearly equal to the cerebrospinal fluid density of the ventricles (Fig. 2A, B). The patient died on the eleventh hospital day.

**DISCUSSION**

Meningitis is the most common form of central nervous system infection in children. Imaging studies are not routinely obtained to evaluate patients with meningitis. They are indicated if the clinical diagnosis is undetermined, if neurologic deterioration has occurred, or if a complication of meningitis is suspected. Imaging studies also are used in diagnosed cases of meningitis when the patient has seizure activity, focal neurologic deficit, or extremely slow recovery.

Bacterial inoculation of the meninges can occur in five ways: (1) by hematogenous spread, (2) via the blood supply of the choroid plexus, (3) by direct extension from an adjacent cortical abscess, (4) as a complication of trauma, (5) by contiguous spread from infection of the mastoid, sinus, or middle ear. Once the infection becomes established, it extends along the leptomeninges of the small cortical vessels in the Virchow-Robin spaces, often obstructing them and producing cerebral infarction. In arteries, inflammation can result in vascular necrosis; in veins, thrombosis is more common. An increased prevalence of venous thrombosis occurs when meningitis is associated with an epidural empyema; the thrombus forms in the lumen of the vein as it courses through infected extraaxial spaces. Abscesses and cerebritis occur from the extension of the infectious process through the wall of the obstructed vessel into the brain parenchyma. Obstructive hydrocephalus can occur if the inflammatory response is intense and exudate accumulates in the foramina of Luschka.

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**Figure 1** Coronal neurosonogram shows intensely echogenic white matter without any other structural abnormality. No extraaxial fluid is present.

**Figure 2 A** Coronal neurosonogram shows diffusely echogenic white matter that had increased in intensity from the initial study. The ventricles also have enlarged. **B** Contrast-enhanced cranial CT scan shows hypodense white matter without enhancing lesions or other structural abnormality. This hypodense white matter represents liquefaction.
and Magendie and the aqueduct of Sylvius. Communicating hydrocephalus can develop if exudate accumulates in the basal cisterns or over the cerebral convexity, interfering with normal cerebrospinal fluid resorption. Ventriculitis as a complication of meningitis is not uncommon in neonates and may occur in as many as 90% of patients. Early changes in the lining of the ventricles are minimal. However, in prolonged or severe meningitis, occlusion of subependymal vascular spaces and pial proliferation may occur. This eventually leads to obliteration of the cerebral aqueduct and hydrocephalus. The complications of meningitis are listed in Table 1.

In uncomplicated cases of meningitis, the findings on neurosonography, computed tomography, and magnetic resonance imaging usually are normal. Except on rare occasions, the diagnosis of meningitis is made from clinical signs and symptoms combined with positive lumbar puncture results. Imaging is best reserved to evaluate complications of meningitis in patients with an atypical course.

The neurosonographic findings in Citrobacter diversus meningitis are quite different than those found with meningitis from more usual causes. This difference results from the usual pathophysiology of this infection. In early series of cases of Citrobacter meningitis, postmortem examination revealed widespread necrosis of white matter with preservation of overlying cerebral cortex. It was believed that the necrosis began in the ventricular wall and extended peripherally in the cerebral white matter. Subsequent studies suggested that the necrosis of the subcortical white matter was the result instead of occlusive inflammation of small blood vessels within the white matter.4–6

This pattern of acute inflammatory changes in the cerebral white matter is similar to the distribution of periventricular leukomalacia. In the latter condition, regions of white matter involvement correspond to the vascular distribution of small penetrating vessels of the cerebrum, which are highly susceptible to alterations in cerebral blood flow. Hypotension produced by exsanguination or the injection of endotoxin has been shown to produce a decrease in blood flow to the white matter while maintaining blood flow to the cerebral cortex. Epidemiologic studies suggest that endotoxin plays a significant role in the pathogenesis of lesions of periventricular white matter. Cerebral necrosis as a prominent feature of neonatal meningitis has been described only in cases of meningitis caused by organisms that produce endotoxin: E. coli, Proteus, and Citrobacter. The ultrasonographic and CT findings in our case also suggest the initial insult involves the small penetrating vessels of the cerebral white matter. From the pathologic data in the literature, it is known that Citrobacter meningitis produces cerebral necrosis as a very early finding. In the premature infant or in the infant with brief survival, the major pathologic feature of Citrobacter meningitis is vasculitis, followed by infarction with necrosis and liquefaction of large regions of white matter.4–7

In Citrobacter meningitis, the prominent finding on neurosonography is extensive abnormally increased echogenicity within the white matter, with subsequent excavation. Whether or not these excavated areas represent true abscesses with early wall formation or tissue necrosis may not be distinguishable with neurosonography. Our patient was not autopsied. However, this particular finding of neurosonography strongly suggests Citrobacter as the etiologic agent in an infant with meningitis and may be useful in selecting antibiotic therapy and judging prognosis.

### Table 1: Complications of Meningitis

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<tr>
<th>Hydrocephalus</th>
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<tr>
<td>Deep vein, cortical vein, and sinus thrombosis</td>
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<td>Venous infarction</td>
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<td>Periarteritis</td>
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<td>Subdural effusions or subdural empyema</td>
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<td>Cerebritis or abscess</td>
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<td>Ventriculitis</td>
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**REFERENCES**