

Fulminant *Citrobacter* Meningitis With Multiple Periventricular Abscesses in a Three-Month-Old Infant

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Citrobacter, a Gram-negative enteric bacillus, is a rare cause of septicemia and meningitis, seldom reported beyond the neonatal period. It is characterized by a fulminant clinical course and a high incidence of complications, including brain abscesses. We studied a three-month-old infant with *Citrobacter meningitis*, who developed acute communicating hydrocephalus and multiple periventricular brain abscesses while on treatment. The patient died, despite intensive antibiotic treatment directed towards the causative organism, *C. diversus*.

Key Words: *Citrobacter*, meningitis, brain abscess.

Despite considerable advances in antimicrobial therapy, bacterial meningitis continues to be a major cause of pediatric morbidity and mortality, particularly in infants. The substantial reduction in cases of *Haemophilus influenzae* meningitis, following successful immunization campaigns, has helped focus attention on other, less frequent causative agents. Rarely diagnosed organisms are known to produce meningitis in vulnerable groups and can confound standard therapeutic approaches.

Citrobacter is a normal inhabitant of the human intestine. The generic term was proposed by Werkman and Gillen in 1931. The genus consists of three different species. One of them, *C. diversus* (*C. koseri*), is a rare cause of sporadic and epidemic meningitis, with a high incidence of brain abscesses. There are occasional reports of *Citrobacter* meningitis in neonates, though it has seldom been reported from the tropics. We report an older infant with *Citrobacter* meningitis, who had a fulminant course of disease, complicated by hydrocephalus and multiple brain abscesses.

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Case Report

A 92-day-old male infant was admitted with a history of fever, vomiting and incessant crying since three days of age. He was feeding poorly and was lethargic, with two episodes of generalized tonic clonic seizures on the day of admission. Delivered at term, with a birth weight of 3,200 grams, he had been asymptomatic till this illness began.

Clinical evaluation revealed a sick febrile infant, with a bulging anterior fontanel and no sutural separation. There were no obvious congenital anomalies, infection foci, or focal neurological deficits. A lumbar puncture was made and two drops of thick pus were obtained. A Gram stain of the specimen revealed Gram-negative bacilli. He was immediately started on an initial empirical antimeningitis treatment of ampicillin 400mg/kg/day and ceftriaxone 100mg/kg/day, as per standard institutional protocols, pending the results of blood and cerebrospinal fluid (CSF) cultures. A full blood count gave a leukocyte count of 4,600 cells/mm³, with a differential of 40% neutrophils and 54% lymphocytes. The erythrocyte sedimentation rate was 80mm/1st hour and the C-reactive protein was elevated.

The bacterial culture of CSF produced smooth, convex colonies of Gram-negative bacilli on nutrient agar. The bacilli were motile, gas producing and late lactose fermenting. The citrate utilization test was

positive. These characteristic features pointed to *Citrobacter* as the etiological agent. The species identification of *C. diversus* was made on the basis of indole and adonitol positivity, hydrogen sulphide negativity and utilization of malonate. The antibiogram revealed sensitivity to gentamicin, cefotaxime and ceftriaxone, with resistance to ampicillin and trimethoprim. The blood culture was sterile.

The patient deteriorated during the first two days, with deep coma and occasional decerebrate posturing. On receiving the bacterial sensitivity report, ampicillin was substituted by gentamicin, and ceftriaxone was continued. A computed tomography (CT) scan of the head revealed a grossly dilated ventricular system, with ventriculitis, multiple (six) brain abscesses and a thinned out cortical mantle (Figure 1). Four of the abscesses communicated with the ventricles. Because of the fulminant clinical course, and the lack of adequate response to therapy, lumbar puncture was repeated on the fourth day. Turbid CSF was tapped, with a leukocyte count of 3,600/mm³, of which 70% were neutrophils; CSF protein was elevated to 900 mg/dl and the CSF sugar was 50 mg/dl, while the concurrent blood sugar was 110 mg/dl. Cultures were sterile.

The sensorium improved over the next few days and seizures were partially controlled. But the head circumference increased by one centimeter during the first week in the hospital. Antibiotics and supportive measures were continued, along with decompression of the abscesses and serial ventricular taps. Intraventricular gentamicin was administered at a dose of 5mg/kg on the 10th and 12th days. Despite these measures he succumbed to the illness on the 13th. Tests to detect any underlying immunodeficiency, including HIV screening of the mother and estimation of serum complement levels of the infant, were non-contributory.

Discussion

The genus *Citrobacter* consists of three species, namely *C. freundii*, *C. amalonaticus* and *C. diversus* (*C. koseri*). Among these, *C. diversus* is a particularly devastating, albeit rare, cause of neonatal meningitis. Central nervous system infection with this organism

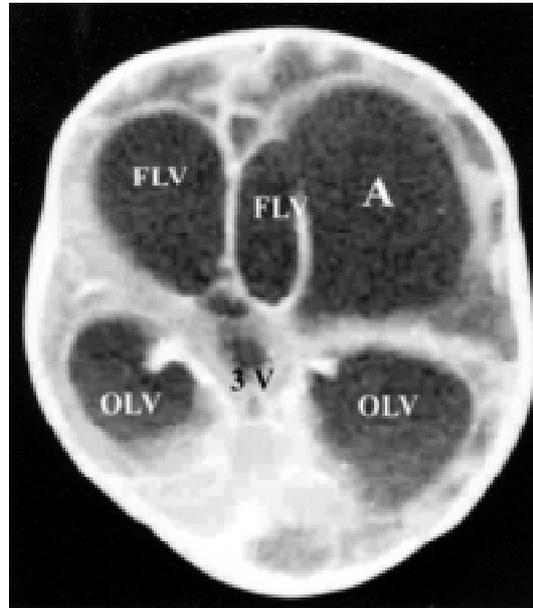
produces multiple brain abscesses, at an unusually high frequency [1]. Whereas it is almost exclusively an opportunistic pathogen in older children, the reasons for the enhanced virulence of *Citrobacter* in early infancy and its propensity to produce multiple brain abscesses are unexplained [2]. Pathogenic mechanisms, like cerebral vasculitis, infarction and invasion of the necrotic tissue by the bacteria, are believed to be responsible for the frequent complications [3].

Citrobacter meningitis is unique in that its course is characterized by a high incidence of periventricular brain abscesses, which occurred in this infant as well [4]. In an extensive review by Graham and Band, 77% of the cases of *Citrobacter* meningitis were found to result in intracerebral abscesses [1]. This is in striking contrast to non-*Citrobacter* Gram-negative meningitis, the incidence of which was found to be as low as 10% [1]. There have been several documented instances of epidemic, sporadic and nosocomial neonatal sepsis by this organism. In 1973, four cases of neonatal *Citrobacter* meningitis were reported from a single premature baby unit within a period of six months [5]. There is evidence that *C. diversus* can persist in the brain, as suggested by a case report of recovery of this organism from the CSF during a neurosurgical procedure four years after an episode of neonatal meningitis [6].

Generic and specific identification is based on the typical morphology, growth pattern and biochemical reactions. An antigenic scheme comprised of 14 different subtypes, with serological and biochemical characterization of each subtype, has been attempted [7].

Most *Citrobacter* strains are reported to be resistant to ampicillin, reaching as high as 97% in one series [8]. However, almost all were sensitive to aminoglycosides and third generation cephalosporins. Such was the case with this infant also. Once the organism is identified, the standard treatment is an intravenously administered third or fourth generation cephalosporin, with or without an aminoglycoside [9]. The suggested alternative drugs are meropenem and trimethoprim/sulfamethoxazole [9]. Due to the poor meningeal penetration of aminoglycosides, intrathecal

Figure 1. A large abscess (A) in the right parietal lobe, communicating with the dilated frontal horn of the lateral ventricle (FLV). Also note the dilated third ventricle (3V) and the occipital horns of the lateral ventricles (OLV).



and intraventricular gentamicin have been tried in individual cases, but this is not routinely recommended [10]. Considering the paucity of definitive data in this regard, the unusual etiology and the fulminant clinical course in our patient, this modality of treatment was administered to make sure that the antibiotics reached the affected area.

As brain abscesses occur frequently, a high index of suspicion and an early CT scan of head may help with management. Recommendations vary regarding the treatment of brain abscesses in infancy. Multiple abscesses and inadequate response to medical measures require repeated aspiration and drainage [11]. These procedures were used in our patient, along with continued medical management. However, even with these aggressive measures, the morbidity of this disease remains high, and mortality is about 30% to 50% [1].

Isolation of an atypical organism should alert the physician to carefully evaluate the patient for predisposing factors, like presacral sinuses, spinal defects, immunodeficiencies and CSF leaks. Prompt epidemiological surveillance and ensuring strict adherence to aseptic techniques are essential to control the source and prevent epidemics. Non-availability of appropriate bacteriological techniques, coupled with

probable under-reporting by clinicians, have led to a lack of credible data regarding the diagnosis and management of meningitis caused by atypical organisms in the developing countries.

Acknowledgements

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