Brain Magnetic Resonance Imaging of Infants with Bacterial Meningitis

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Objectives To describe the results of brain magnetic resonance imaging (MRI) of infants with bacterial meningitis and how the findings affected clinical management.

Study design This retrospective study included all infants <12 months of age who were hospitalized at Children's Medical Center, Dallas and had culture-confirmed bacterial meningitis and a brain MRI from January 1, 2001 to December 1, 2011. Infants were identified by review of all positive bacterial cultures of cerebrospinal fluid (CSF) from the Children's Medical Center Microbiology Laboratory. Demographic, clinical, laboratory, and neuroimaging data were reviewed. Infants with ventriculoperitoneal shunt or whose CSF culture yielded skin commensals were excluded. A neuroradiologist blinded to clinical information reviewed all MRI studies.

Results Of the 440 infants who had a positive CSF culture result, 111 (25%) had a pathogen isolated from CSF and were enrolled in the study. Of these, 68% (75/111) had a brain MRI performed during the hospitalization; abnormalities included leptomeningeal enhancement (57%), cerebral infarct (43%), subdural empyema (52%), cerebritis (26%), hydrocephalus (20%), and abscess (11%). By multiple logistic regression analysis, infants with late seizures and an abnormal neurologic examination were more likely to have an abnormal MRI ($P < .05$). MRI results led to neurosurgical intervention in 23% of infants; a positive bacterial culture of CSF obtained >48 hours after initiation of antibiotic therapy was associated with neurosurgical intervention ($P = .01$). Fourteen (19%) infants with bacterial meningitis had a normal brain MRI.

Conclusions Brain MRIs were performed frequently and often were abnormal in infants with bacterial meningitis, leading to changes in clinical management. *(J Pediatr 2014;165:134-9)*.

Bacterial meningitis occurs in approximately 0.2 infants per 1000 live births.[1,2] Although mortality in neonates has decreased from 70% to 14%,[3] morbidity persists with as many as 47% of survivors experiencing intellectual and academic impairment.[4] Neuroimaging may detect central nervous system abnormalities that have been associated with worse neurodevelopmental outcomes, but the frequency and characteristics of such findings by magnetic resonance imaging (MRI) have not been well characterized. Studies have suggested obtaining neuroimaging if infants have persistent fever, positive cerebrospinal fluid (CSF) cultures despite treatment, focal neurologic signs, late seizures, or decreasing level of consciousness.[4,5] However, correlation of these clinical characteristics with MRI findings has not been performed, and whether the results of brain MRI leads to changes in clinical management has not been documented. Bacterial meningitis can be a diagnostic challenge when the lumbar puncture is traumatic or unsuccessful, and it is not known whether a normal brain MRI can exclude a diagnosis of bacterial meningitis.

The objectives of this study were to characterize the brain MRI findings of infants with bacterial meningitis and to identify clinical features and pathogens that are associated with brain MRI findings that lead to changes in clinical management, and specifically with neurosurgical intervention.

Methods

This retrospective study included all infants less than 12 months of age who had culture-confirmed bacterial meningitis and were hospitalized at Children's Medical Center (CMC), Dallas, Texas from January 1, 2001 to December 1, 2011. Infants were identified by review of all positive CSF cultures results performed by the Microbiology Laboratory at CMC. Infants were excluded if they had a ventriculoperitoneal shunt at the time of diagnosis. In addition, positive CSF culture that yielded coagulase-negative staphylococci or other skin commensals were assessed as contaminants and were excluded. The study was approved by the Institutional Review Board of the University of Texas Southwestern Medical Center.

CMC	Children's Medical Center
CSF	Cerebrospinal fluid
MRI	Magnetic resonance imaging

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The authors declare no conflicts of interest.

Portions of the study were presented at ID Week, San Diego, CA, October 7-21, 2012 and at St Jude/Pediatric Infectious Diseases Society's Pediatric Infectious Diseases Research Conference, Memphis, TN, February 24-25, 2012.

0022-3476/$ - see front matter.
http://dx.doi.org/10.1016/j.jpeds.2014.02.061

Pertinent demographic, clinical, laboratory, and neuroimaging data from all infants were reviewed. When multiple test results were available, the most abnormal one was used. Prematurity was defined as a gestational age <37 weeks, and low birth weight was <2500 g. Persistent fever was defined as a temperature >38.0°C for ≥4 days after initiation of intravenous antibiotic therapy, and secondary fever was new onset of fever after initial defervescence for ≥24 hours. Late seizure activity was epileptic activity ≥4 days after initiation of antibiotic therapy. Abnormal neurologic examination was defined as the presence of any of the following chart notations: persistent meningismus ≥2 days after initiation of therapy, or altered level of consciousness in the absence of sedation, unequal pupils, clonus, hypertonia, hyperreflexia, paralysis, increased frontal-occipital-circumference, or cranial nerve palsy any time during hospitalization. Leukopenia was defined as a white blood cell count of ≤5000 mm^3. CSF that had a red blood cell count of >100 000/mm^3 was excluded from analysis; otherwise, the CSF white blood cell count was adjusted for blood contamination by dividing the red blood cell count by 500 and subtracting this value from the white blood cell count.[6] Infants were assessed as having hearing impairment if they did not pass automated auditory brainstem response or evoked otoacoustic emissions tests (with confirmation by a diagnostic auditory brainstem response test) that were performed during the hospitalization for meningitis. Neurosurgical interventions consisted of ventriculoperitoneal shunt placement, performance of burr hole surgery, drainage of subdural empyema or abscess, or ventricular tap through the anterior fontanel.

A board-certified pediatric neuroradiologist (M.M.) who was blinded to the clinical data and had not been involved in the original reading of the MRIs reviewed all brain MRIs for this study using a template of a priori findings that he had generated. If multiple MRI studies were performed during the same hospitalization, the initial study at the time of diagnosis of meningitis was assessed, and subsequent studies were reviewed for the development of progressive or new complications. MRI studies were performed on 1.5 and 3.0 Tesla MR units (Philips Healthcare System, Best, The Netherlands) and included T1-weighted sagittal and axial images, T2-weighted axial and coronal images, diffusion-weighted axial imaging, and postintravenous contrast T1-weighted imaging in the axial and sagittal planes and postcontrast fluid-attenuated inversion recovery axial imaging. In 71 (95%) of the studies, intravenous gadolinium enhanced images were available. MRI studies were evaluated for leptomeningeal enhancement, cerebritis, choroid plexitis, ventriculitis, hydrocephalus, empyema, abscess, infarct, venous thrombosis, and hemorrhage. Leptomeningeal enhancement, ventriculitis, cerebritis, and choroid plexitis were diagnosed based on abnormal enhancement of the meninges, ventricular ependymal margins, subcortical parenchyma, and choroid plexus, respectively. Hydrocephalus was diagnosed if ventricles were enlarged outside the normal limits for age (ie, the third ventricle having a width greater than 0.3 cm in a neonate). Edema was defined as abnormally increased T2 signal in the parenchyma. Abscess was noted if there was a fluid collection with enhancing margins, and cortical infarction was diagnosed if there was cortical diffusion restriction and edema.

Statistical Analyses

Data analysis was performed using Statistical Analysis System (SAS-PC; SAS Institute Inc, Cary, North Carolina) with results reported as the mean ± SD, median with IQR, or as the number and percentage. Student *t* test (2-sided), χ^2 or Fisher exact tests, and Mann-Whitney U tests were used where appropriate. A *P* value of <.05 was considered to be statistically significant.

A multiple logistic regression model was used to ascertain variables that were predictive of an infant having an abnormal brain MRI or required neurosurgical intervention. All of the variables that had a *P* value of <.1 in the simple logistic regression were included in the multiple logistic model. A stepwise method was used to select the final group of predictors, and adjusted *P* values were obtained. The variables included were age at presentation, gestational age, birth weight, temperature, heart rate, blood pressure, and respiratory rate at presentation. Also included were duration of illness prior to hospitalization, bulging fontanel, total days of antibiotics, days in the intensive care unit, days in hospital, white blood cell count, hemoglobin, platelets, urinalysis, CSF, liver enzyme tests, serum creatinine concentration, clinical signs at presentation (tachypnea, grunting, apnea, lethargy, diarrhea, emesis, seizures, and irritability), vasopressor therapy, endotracheal intubation, and coexisting bacteremia, urinary tract infection, or pneumonia.

Results

Of the 440 infants who had a positive CSF culture, 111 (25%) had a pathogen isolated from CSF and were enrolled in the study. Excluded infants were 237 (54%) whose positive CSF culture was assessed as a contaminant, and 92 (21%) who had a ventriculoperitoneal shunt at the time that meningitis was diagnosed. The 111 enrolled infants had a median age of 78 ± 79 days, 57% (n = 63) were male, and 77% (n = 86) were full term (**Table I**). None had a cochlear implant before developing meningitis.

The results of the CSF cultures by age of diagnosis are provided in **Table II**. The majority of infants (68%; 76/111) had Gram-positive bacteria isolated from CSF. Among infants ≤59 days of age, the most common bacterial isolates were *Streptococcus agalactiae* (46%; 30/65) and *Escherichia coli* (20%; 13/65). Among infants of 60-179 days of age, *Streptococcus pneumoniae* (45%; 13/29) was the most common, but *S agalactiae* (24%; 7/29) and *E coli* (14%; 4/29) also were seen. After 6 months of age, *S pneumoniae* (71%; 12/17) was the predominant pathogen. *Neisseria meningitidis* accounted for only 1 case in an infant 9 months of age. There was no case of meningitis because of *Haemophilus influenzae type b*, and 4 infants who were older than 2 months of age had nontypeable *H influenzae* isolated from CSF. Overall, only 50% of infants with culture-confirmed meningitis had a positive blood culture at the time of diagnosis.