Risk Factors for Hearing Loss From Meningitis in Children

The Children’s Hospital Experience

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Objectives: To identify statistically significant risk factors for hearing loss in children with meningitis, determine the overall incidence of hearing loss in a large group of children with confirmed meningitis, and quantify the percentage of children with progressive or fluctuating hearing loss after meningitis.

Design: Retrospective analysis.

Patients and Other Participants: Four hundred thirty-two children admitted to the Children’s Hospital, Birmingham, Ala, from January 1, 1985, to December 31, 1995, with the diagnosis of meningitis.

Results: Of 432 children with meningitis, 59 (13.7%) had the development of hearing loss. Of these 59 children, 46 (78.0%) had stable sensorineural hearing loss and 13 (22.0%) had either progressive or fluctuating hearing loss. Of the variables examined using multiple logistic regression backward-elimination modeling, only 5 appeared to be significantly associated with the development of hearing loss: computed tomographic scan evidence of increased intracranial pressure (estimated odds ratio [OR] = 2.3), male sex (OR = 1.9), the common logarithm of glucose levels in the cerebrospinal fluid (OR = 0.58), Streptococcus pneumoniae as the causative organism (OR = 2.1), and the presence of nuchal rigidity (OR = 1.9). In the children with progressive hearing loss, the time for progression varied from 3 months to 4 years before hearing stabilized.

Conclusions: In this study of children diagnosed as having meningitis, hearing loss developed in 59 (13.7%). Forty-six (78.0%) of these children with hearing loss had stable auditory thresholds over time, and 13 (22.0%) exhibited deterioration or fluctuation of acuity over time. Evidence of increased intracranial pressure by computed tomographic scan, male sex, low glucose levels in the patients’ cerebrospinal fluid, S pneumoniae as the causative organism, and the presence of nuchal rigidity appear to be significant predictors for future hearing loss.


Deafness or some degree of hearing impairment occurs in 3% to 35% of survivors of meningitis.1-4 It is the most common serious complication of bacterial meningitis in children5 and is the leading cause of acquired deafness in infancy and childhood,6 with obvious implications for the development and education of survivors of meningitis. This study was designed as a retrospective review of a large group of children diagnosed as having meningitis. Our objectives were to identify significant risk factors for hearing loss in children with meningitis to determine the overall incidence of hearing loss in this group and to quantify the percentage of children with progressive or fluctuating loss due to meningitis.

Characterization of Hearing Loss

The median age of the children was 7.7 months, with 90.0% of the children being younger than 4.7 years old. Of 432 children, 237 (54.9%) were male. Sensorineural hearing loss was identified in 59 children (13.7%). Of these, the hearing loss was stable in 46 (78.0%) and progressive or fluctuating in 13 (22.0%). Hearing loss was bilateral in 44 (74.6%) of the 59 children and unilateral in 15 (25.4%). Of the 44 children with bilateral loss, loss was more severe in 1 ear in 9 children (20.3%). As a rule, we found that if hearing loss was profound at discharge, no recovery of hearing occurred. In the 13 children with progressive or fluctuating losses, the pe-
PATIENTS AND METHODS

Children admitted to the Children's Hospital, Birmingham, Ala, with a diagnosis of meningitis between January 1, 1985, and December 31, 1995, composed the study participants. Data were obtained by retrospective medical records review and consisted of clinical data from the time of admission to the hospital, during the hospital stay, and limited follow-up data. The follow-up period for these children ranged from 1 year to 5 years. Preliminary statistical analyses included the generation of descriptive statistics and the investigation of pairwise associations among the variables using the Fisher exact test, likelihood-ratio χ² tests for association in 2-way contingency tables, and unpaired Student t tests (with the Satterthwaite approximation for degrees of freedom in the case of unequal variances). Possible risk factors were assessed with regard to the relative importance of their independent contributions for the prediction of hearing loss using multiple logistic regression. Continuous variables with highly right-skewed distributions, such as white blood cell (WBC) count, cerebrospinal fluid (CSF) glucose level, CSF WBC count, and CSF protein levels, were transformed by taking their common logarithms before their inclusion in logistic regression modeling. A final model was selected using the backward-exclusion method and the associated odds ratios with their 95% confidence limits produced for these selected variables.

AUDIOLOGIC TEST METHODS

All children were tested by certified audiologists in the Hearing and Speech Center at Children's Hospital. Standard techniques for testing children of different ages and developmental levels were used, including behavioral observation audiometry, conditioned orientation reflex audiometry, play audiometry, and conventional audiometry.

All subjects aged 6 months and older were evaluated in sound-attenuated test booths (models 402-A and 1203-A; Industrial Acoustics Company, Bronx, NY, and model RE-243; Acoustic Systems, Austin, Tex). Pure-tone thresholds were obtained in the sound field or with the use of earphones (model TCH39; Telephonics, Huntingdon, NY) with a clinical diagnostic audiometer (model GS16; Grason-Stadler, Inc; Mildford, NH) or a clinical audiometer (Orbit 822; Madsen Electronics, Minnetonka, Minn). Testing was completed in at least the sound field; testing with the use of earphones was also conducted whenever the child tolerated headphone placement.

Before mid-1994, testing was completed using auditory brainstem response (ABR) evaluation for children younger than 6 months or whenever behavioral test methods were unsuccessful or yielded questionable results. Two-channel recordings were obtained using an auditory evoked potential system (Navigator; Biologic Systems Corp, Mundelein, Ill). After mid-1994, these children were initially tested using distortion product otoacoustic emissions machine (model GS1 60; Grason-Stadler, Inc). Any child failing the otoacoustic emissions screening was then evaluated using ABRs. The degrees of hearing loss were classified according to the following table.

<table>
<thead>
<tr>
<th>Hearing Level, dB</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;90</td>
<td>Profound</td>
</tr>
<tr>
<td>71-90</td>
<td>Severe</td>
</tr>
<tr>
<td>56-70</td>
<td>Moderately severe</td>
</tr>
<tr>
<td>41-55</td>
<td>Moderate</td>
</tr>
<tr>
<td>26-40</td>
<td>Mild</td>
</tr>
<tr>
<td>&lt;26</td>
<td>Normal hearing</td>
</tr>
</tbody>
</table>

FOLLOW-UP

All children were observed at 6-month intervals for at least 1 year after their bout of meningitis. In addition, all children were observed routinely until hearing acuity in both ears could be assessed. For those children exhibiting hearing loss, whether conductive or sensorineural, recommendations for management and follow-up were based on specific test findings and varied accordingly. For this study, only children with sensorineural hearing loss are included.

CAUSATIVE ORGANISMS

Three organisms were responsible for 66.9% of all cases (Table 2). Streptococcus pneumoniae accounted for 63 of the 432 cases, or 14.6% of the total cases of meningitis. Of the 63 children with S pneumoniae, 15 (23.8%) had resultant hearing loss. Another 177 (41.0%) of the 432 cases during the 11-year period were due to H influenzae type b, with a 14.1% (25/177) incidence of hearing loss. Before the introduction of the Hib vaccine, there were 164 cases of H influenzae type b during a 6-year period, but after 1990 when the Hib vaccine became available, this number decreased to just 13 cases in a 5-year period. In other words, the average annual number of cases dropped from 27.3 to 2.6, a 90.5% reduction. The other organisms that resulted in meningitis during the 11-year period are listed in Table 2.
We selected clinical variables that commonly occur in children with meningitis. These consisted of clinical signs at presentation (sex, age, the presence of fever, serum WBC count, CSF WBC count and protein and glucose levels, and physical findings), complications of the meningitis (evidence of increased intracranial pressure and seizures), and treatment variables (specific pathogens, type[s] of antibiotic used, corticosteroid use, and duration of hospital stay) that might influence the prognosis of hearing loss. For an initial description of those with and without hearing loss, each possible risk factor was individually analyzed to evaluate its marginal association with hearing loss. Then, using multiple logistic regression with a backward-elimination selection procedure, all variables were evaluated as to their independent contributions to the prediction of hearing loss. Five variables were found to contribute independently and significantly to this prediction: ultrasonographic or computed tomographic evidence of increased intracranial pressure \((P = .02)\), male sex \((P = .04)\), a lowered common logarithm of the CSF glucose level \((P = .03)\), \textit{S} \textit{pneumoniae} as the causative organism \((P = .05)\), and the presence of nuchal rigidity \((P = .04)\) (Table 3). For CSF glucose level, an average decrease of 0.54 in the logarithmic odds for hearing loss for every increase of 1 common logarithmic unit of CSF glucose level translates to an odds ratio of 0.58, indicating the negative association of an increased CSF glucose level with hearing loss. So the odds of hearing loss are decreased by a multiplicative factor of 0.58 for each logarithmic unit that the CSF glucose level is increased. None of the other variables analyzed—age, duration of hospital stay, the presence of fever, the level of consciousness, the presence of seizures, the type of pathogen other than \textit{S} \textit{pneumoniae}, the use of steroids, serum WBC count, and CSF protein level and WBC count—were significant risk factors for hearing loss (Table 4).

In the original marginal (univariate) comparisons for these 5 variables, 66 of the 432 children were confirmed to have evidence of increased intracranial pressure on ultrasonography or computed tomographic scan. Of those 66 children, 27 (28.8%) had hearing loss compared with 42 (11.5%) of the 366 children lacking evidence of increased intracranial pressure \((P = .004)\). Of the 59 children identified with hearing loss, 40 (67.8%) were male compared with 197 (52.8%) of the group \((n = 373)\) without hearing loss \((P = .03)\). Nuchal rigidity was present in 206 children. Of these, 34 (16.5%) had the development of hearing loss compared with 25 (11.1%) of those \((n = 226)\) without nuchal rigidity \((P = .10)\). The mean ± SD common logarithm of CSF glucose level was 1.37 ± 0.54 for the 350 children for whom that was recorded in the no-hearing-loss group compared with 1.15 ± 0.57 for the 54 children having these data in the hearing-loss group \((P = .006)\). These translate into a geometric mean ± SE of 23.5 ± 1.56 mg/dL \((1.30 ± 0.09 \text{ mmol/L})\) and 14.1 ± 2.5 mg/dL \((0.78 ± 0.14 \text{ mmol/L})\) for these 2 groups, respectively. With regard to the 63 chil-

### Table 1. Progressive Fluctuating Hearing Losses

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age at Onset, mo</th>
<th>Discharge From Hospital Hearing Level</th>
<th>Time of Progression, mo</th>
<th>Stabilized Hearing Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7</td>
<td>Bilateral: normal</td>
<td>6</td>
<td>Bilateral: moderate to severe loss</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>Left: mild to moderate loss; right: severe loss</td>
<td>18</td>
<td>Bilateral: profound loss</td>
</tr>
<tr>
<td>3</td>
<td>11</td>
<td>Bilateral: mild to moderate loss</td>
<td>3</td>
<td>Bilateral: moderate to severe loss</td>
</tr>
<tr>
<td>4</td>
<td>6</td>
<td>Left: moderate to severe loss; right: normal</td>
<td>36</td>
<td>Bilateral: moderate to severe loss</td>
</tr>
<tr>
<td>5</td>
<td>7</td>
<td>Left: severe to profound loss; right: mild loss</td>
<td>12</td>
<td>Left: severe to profound loss; right: moderate to severe loss</td>
</tr>
<tr>
<td>6</td>
<td>14</td>
<td>Left: normal; right: severe loss</td>
<td>5</td>
<td>Left: normal; right: mild to moderate loss</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>Bilateral: severe loss</td>
<td>24</td>
<td>Large fluctuations before stabilizing; left: profound loss; right: mild to moderate to severe loss</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>Left: moderate to severe loss; right: normal</td>
<td>36</td>
<td>Left: profound loss; right: normal</td>
</tr>
<tr>
<td>9</td>
<td>12</td>
<td>Left: moderate to severe loss; right: severe loss</td>
<td>6</td>
<td>Left: severe to profound loss; right: profound loss</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>Bilateral: moderate loss</td>
<td>24</td>
<td>Left: moderate to mild to severe loss; right: severe loss</td>
</tr>
<tr>
<td>11</td>
<td>11</td>
<td>Bilateral: moderate to severe loss</td>
<td>12</td>
<td>Bilateral: moderate to severe to profound loss</td>
</tr>
<tr>
<td>12</td>
<td>36</td>
<td>Bilateral: mild to moderate loss</td>
<td>72</td>
<td>Fluctuating loss or improvement before stabilizing; left: moderate loss; right: mild to moderate to severe loss</td>
</tr>
<tr>
<td>13</td>
<td>7</td>
<td>Bilateral: mild loss</td>
<td>8</td>
<td>Bilateral: profound loss</td>
</tr>
</tbody>
</table>

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This figure is consistent with past reports.

The main incidence of hearing loss due to meningitis to be 13.7%.

Of the 369 with another causative organism (Pneumococci) developing in 15 (23.8%) compared with 44 (11.9%) of the 369 with another causative organism.

Streptococcus pneumoniae has now become the leading cause of bacterial meningitis.

The introduction of the Hib vaccine appears to have been the single biggest clinical advance in the treatment of meningitis in the past 10 years. Although other organisms were identified as etiologic agents of meningitis, this group of pathogens was small, and few caused substantial hearing loss. The variable "Log10" is the common logarithm of the cerebrospinal fluid glucose level. "Nuchal rigidity" and "Streptococcus pneumoniae" were scored as no (absent) = 0 and yes (present) = 1. "Sex" is scored as female = 0 and male = 1. Ellipses indicate not applicable.

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of bacteria in the CSF appears to have a great effect on the prognosis.

Although boys have been shown to outnumber girls in the overall incidence of meningitis,² ⁶ ⁷ this is the first study to show that being male is a significant independent risk factor for hearing loss.

Nuchal rigidity as a predictor of hearing loss was surprising, and this may be explained by an error in data collecting. Only 206 children were documented as having nuchal rigidity, which is a surprisingly low number because this physical finding is almost universally found in conscious children with meningitis in whom this finding can be documented. Nuchal rigidity may not have been recorded or tested for in all children, and therein lies 1 flaw of a retrospective study. If this variable had been tested for in all children, it may not have been found to be predictive of hearing loss. We report this value but realize the potential error in the data recording of this variable.

Surprisingly, we did not find a correlation between hearing loss and seizures or hearing loss and altered level of consciousness. Seizures are a common complication of meningitis, occurring in 20% to 30% of patients,⁸ but the cause of hearing loss in meningitis may be a different pathogenic process than the one that results in neurologic deficits. In our study, 110 (25.5%) of the 432 children had seizures. Of the 59 children with hearing loss, 19 (32.2%) had seizures compared with 91 (24.2%) of those without hearing loss, but this slight tendency failed to reach statistical significance (P = .21). Hearing loss during meningitis occurs due to the spread of bacteria or bacterial toxins through the internal auditory canal or cochlear aqueduct, causing a suppurative labyrinthitis or perineuritis of the eighth nerve;¹⁰ or both, and may occur independent of damage to the central nervous system. Other mechanisms of hearing loss that have been described include septic thrombophlebitis or embolization of the small blood vessels supplying the inner ear and hypoxic damage to the eighth nerve or central auditory pathways related to infection or an associated increased intracranial pressure.¹¹ This may explain the large number of children with hearing loss who had evidence of hydrocephalus.

The onset of hearing loss associated with bacterial meningitis most likely occurs early in the illness, perhaps even during the bacteremic phase before other symptoms and signs are evident. The role of corticosteroid use is controversial. Giving dexamethasone as an adjuvant measure is beneficial in decreasing hearing loss in association with H influenzae but may not be effective in patients with pneumococcal or meningococcal meningitis.⁷ ¹⁰ In our study, we did not separate out therapy according to different organisms, but the overall effect of corticosteroid use in 151 children did not appear to be protective against hearing loss, which occurred in 21 (13.9%).

Thirteen children had progressive or fluctuating hearing loss. Unfortunately, we could find no variable that was predictive of which children would incur this progressive loss, and that was one of the goals of our study. A past study¹¹ has shown that postmeningitic sensorineural hearing loss can lessen, fluctuate, or progress over a period as short as several months or as long as 12 years.

In our study, the time of the progression of hearing loss varied from 2 months to 4 years. We observed a trend in that children who had initial improvement during periods of fluctuation had mild to moderate hearing losses. Children with severe to profound losses did not improve. This is consistent with data reported by Brokhouser et al¹¹ in a larger series of children with fluctuating hearing loss.

Regarding treatment, any damage to hearing appears to occur early in the infection; therefore, early diagnosis and early appropriate treatment is important and will most likely decrease the risk of hearing loss. The rules of management remain prompt diagnosis and intravenous antibiotic therapy.

All children recovering from bacterial meningitis should be referred for audiologic assessment before discharge from the hospital. The time that is best for testing a child for hearing loss following meningitis is controversial but appears to be just before discharge. Conductive losses are frequently documented early in the acute phase of meningitis when the patient’s condition is fluctuating. They can be ruled out with otoscopy and tympanometry. In young children, the best test battery appears to be otoacoustic emissions combined with tympanometry and followed by ABR testing should otoacoustic emissions suggest a hearing loss. Normal results on an ABR test can be misleading because the test reflects the presence of normal thresholds only in the frequency range of 2000 to 4000 Hz. So behavioral audiometry is recommended as soon as possible to determine sensitivity for the complete range of test frequencies from 250 to 8000 Hz.¹¹ Reassurance can be provided if the initial hearing studies suggest normal hearing because children who do not have early hearing impairment are unlikely to have hearing losses later.

Patients with a fluctuating hearing loss should be monitored long term. Thresholds in patients who demonstrate improvement, deterioration, or fluctuation of auditory function often require a year or more to stabilize following meningitis. If their initial test results are normal with ABR, they need to be tested with the use of earphones in 6 months with behavioral audiometry to determine sensitivity to the complete range of tests from 250 to 8000 Hz. If these test results indicate hearing loss, audiologic reevaluations need to be performed every month until thresholds are stabilized. The child should be observed every 3 months or no less than annually, depending on the age and frequency of fluctuations. These children should also be observed closely for functional disabilities. Twenty-one percent of school-aged survivors of meningitis have functionally important disabilities, including neurologic or central auditory perceptual dysfunction, that adversely affect learning ability, academic performance, and behavior.¹² Careful follow-up is warranted for all children after meningitis, especially to detect
learning disabilities and ensure that they receive the appropriate educational assistance, which may help to compensate for these difficulties.

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REFERENCES