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Characteristics of nosocomial bacterial meningitis in children

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Nosocomial meningitis is uncommon in children. We reviewed the medical records of all children who developed bacterial meningitis at least 72 hours after admission to Mackay Memorial Hospital for the period July 1992 through June 2000. Clinical manifestations, predisposing factors, pathogens, and outcomes were analyzed. Twenty-two cases of nosocomial meningitis were identified, comprising 9.2% (22/239) of all pediatric cases of bacterial meningitis during the study period. The male-to-female ratio was 14:8. All patients were younger than 6 months of age except for one, who was 7 years old. The mean duration between admission and onset of meningitis was 15.3 days (range, 3 to 58 days). Twenty-two organisms were isolated, including 13 Gram-negative bacteria (59%) and 9 Gram-positive bacteria (41%). The most common pathogen was *Escherichia coli* (5 cases), followed by *Enterobacter cloacae* (3), *Staphylococcus aureus* (3), and *Chryseobacterium meningosepticum* (3). Seventeen patients (77%) had concomitant bacteremia. Predisposing factors for acquisition of nosocomial meningitis included previous treatment with broad-spectrum antibiotics (68%), prematurity with very low birth weight (41%), and total parenteral nutrition (32%). Two patients (9%) had previous neurosurgical intervention. Four patients (18%) died, 3 of whom were low birth weight premature infants. Nine patients (41%) had sequelae, including developmental delay, hydrocephalus, hearing impairment, and epilepsy. Neurosurgery was not a significant risk factor for the development of nosocomial meningitis, while very low birth weight played an important role. Previous intraventricular hemorrhage or hydrocephalus, prematurity with very low birth weight, infection with Gram-negative bacteria, and prior broad-spectrum antibiotic administration were associated with poor outcome.

Key words: Bacterial meningitis, cross infection, infant

Nosocomial infection increases hospital stay and medical costs. Among the various types of hospital-acquired infections, bacterial meningitis is the most severe. Nosocomial bacterial meningitis is uncommon in children, accounting for only 0.64% to 4% of all nosocomial infections [1,2]. It may result in significant complications, including mental and motor disabilities, convulsive disorders, hydrocephalus, hearing loss, and abnormal speech patterns [3,4]. Although many studies have investigated nosocomial infection in general [1,2,5-7], fewer have focused specifically on meningitis [8,9]. The purpose of this study was to delineate the predisposing factors, pathogens, clinical features, and prognosis of nosocomial bacterial meningitis in children.

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Materials and Methods

Mackay Memorial Hospital (MMH) is a 2000-bed referral center, with a total of 213 pediatric beds. At the time of this report, there were 26 beds in the neonatal intensive care unit (NICU), 14 in the pediatric intensive care unit, 70 in the newborn center, with the remaining 103 beds in the general pediatric wards.

Patients with nosocomial bacterial meningitis during the period from July 1992 to June 2000 at MMH were identified from the logbooks of the infection control committee. We reviewed the records of patients younger than 18 years old who developed nosocomial bacterial meningitis, defined as the appearance of culture-positive bacterial meningitis developing at least 72 hours after hospital admission. Clinical information collected included age, length of time from admission to the onset of meningitis, underlying diseases, clinical manifestations, predisposing factors, pathogens,

laboratory data, and outcome. Neurological sequelae were defined as any neurological abnormality found at follow-up. Mortality was defined as death directly related to nosocomial meningitis. Prematurity was defined as birth before 36 weeks of gestational age. Very low birth weight (VLBW) was defined as a birth weight less than 1500 grams. Other predisposing factors assessed included endotracheal intubation, central line insertion, start of total parenteral nutrition when meningitis developed, broad-spectrum antibiotics used in the previous 1 month, previous neurosurgical intervention, and lumbar puncture during hospitalization prior to the onset of meningitis.

The association between risk factors and outcome was analyzed by Fisher's exact test. A two-tailed test was used with a $p<0.05$ considered to be significant.

Results

During the 8-year study period, 22 patients with nosocomial bacterial meningitis were identified out of a total of 239 children with bacterial meningitis. Hospital-acquired infection thus accounted for 9.2% of the total cases. There were 14 males and 8 females. Twenty patients (91%) were younger than 3 months old, 1 was 6 months old, and the other was 7 years old. Eleven episodes (50%) occurred in the NICU and 5 (23%) occurred in the neonatal nursery. Nosocomial meningitis accounted for 1.3% (11/862) of nosocomial infections in the NICU during this period. Nine cases (41%) were diagnosed in July and August.

The clinical manifestations are shown in Table 1. The most common symptom or sign was fever, followed by poor activity, apnea, and cyanosis. The mean duration between admission and the onset of meningitis was 15.3 days (range, 3 to 58 days).

Twenty-two organisms were isolated (Table 2). Thirteen (59%) were Gram-negative bacteria and 9 (41%) were Gram-positive. The most common pathogen was *Escherichia coli* (5 cases), followed by *Enterobacter cloacae* (3), *Staphylococcus aureus* (3), and *Chryseobacterium meningosepticum* (3). Seventeen patients (77%) had concomitant bacteremia.

Predisposing factors for development of nosocomial meningitis included prematurity (16 patients), previous broad-spectrum antibiotic treatment (15), total parenteral nutrition (7), central catheter insertion (5), and endotracheal intubation (4). Among the premature babies, 9 had very low birth weight. Two patients had had previous neurosurgical intervention and 1 had acute lymphoblastic leukemia. Four patients had undergone lumbar puncture prior to the development of infection.

Table 1. Clinical manifestations of nosocomial bacterial meningitis in children (n = 22)

Symptom/sign	No. of cases (%)
Fever	14 (64)
Poor activity	14 (64)
Apnea	8 (36)
Cyanosis	8 (36)
Bradycardia	6 (27)
Irritability	3 (14)
Convulsion	3 (14)
Respiratory distress	2 (9)
Change in consciousness	1 (5)

Table 2. Pathogens causing nosocomial bacterial meningitis in children

Microorganism	No.of isolates (%)
Gram-positive	9 (41)
Staphylococcus aureus	3 (14)
Gemella morbillorum	2 (9)
Enterococcus faecalis	2 (9)
Streptococcus bovis	1 (5)
Streptococcus sangius	1 (5)
Gram-negative	13 (59)
Escherichia coli	5 (22)
Enterobacter cloacae	3 (14)
Chryseobacterium meningosepticum	3 (14)
Klebsiella pneumoniae	1 (5)
Pseudomonas aeruginosa	1 (5)

Four patients (18%) died directly due to meningitis, 3 of whom were VLBW premature infants. Three patients died within 3 days of symptom onset and 1 patient died within 1 week. Nine patients (41%) had neurological sequelae, including developmental delay (5), hydrocephalus (5), hearing impairment (4) and epilepsy (3). Of these 9 patients, 2 subsequently died, both due to complications of the meningitis and another episode of infection. Previous intraventricular hemorrhage or hydrocephalus, prematurity with VLBW, infection with Gram-negative bacteria, and prior use of broad-spectrum antibiotics were significantly associated with a worse outcome (Table 3).

Discussion

Hemming et al [1] conducted a 41-month surveillance of nosocomial infection in an NICU and found a 24.6% nosocomial infection rate, with meningitis accounting for 4.0% of cases. In this study, nosocomial meningitis

Table 3. Underlying diseases and predisposing factors in pediatric patients with nosocomial bacterial meningitis

	No. of patients	Death/ neurological sequelae (n)	Cured (n)	*p*
Birth body weight				
>1500 g	13	5	8	0.018
<1500 g	9	8	1	
Previous IVH or hydrocephalus				
Yes	6	6	0	0.017
No	16	7	9	
Gender				
Male	14	8	6	0.806
Female	8	5	3	
Fever				
Yes	14	7	7	0.251
No	8	6	2	
Convulsion				
Yes	3	2	1	0.774
No	19	11	8	
Prior antibiotic use				
Yes	15	11	4	0.047
No	7	2	5	
Prior central line insertion				
Yes	5	4	1	0.279
No	17	9	8	
Prior ETT intubation				
Yes	4	4	0	0.066
No	18	9	9	
Prior TPN support				
Yes	7	6	1	0.083
No	15	7	8	
Prior neurosurgical intervention or lumbar puncture				
Yes	6	4	2	0.658
No	16	9	7	
Pathogens				
Gram-negative	13	10	3	0.041
Gram-positive	9	3	6	
Serum Na <130 mmol/L				
Yes	5	3	2	0.533
No	10	7	3	
Glucose CSF/serum <0.5				
Yes	13	7	6	0.552
No	4	2	2	

Abbreviations: CSF = cerebrospinal fluid; ETT = endotracheal tube; IVH = intraventricular hemorrhage; TPN = total parenteral nutrition

accounted for only 1.3% of the nosocomial infections in the NICU.

In this study, 91% of patients were younger than 3 months old and 50% of the cases occurred in the NICU. Neonates and young infants were more susceptible to nosocomial infections than older children, as has been reported in previous studies [5,6]. Factors including low birth weight, length of hospital stay, invasive procedures, and frequent use of antibiotics may put infants at increased risk of nosocomial infection [7].

The incidence of nosocomial bacterial meningitis peaked in July and August. This finding might have been due to new medical and nursing staff beginning their work during this period. This observation suggests that infection control measures must be emphasized during training programs.

The clinical manifestations of nosocomial meningitis were non-specific. Most of our patients were young infants who presented with sepsis. Seventeen patients (77%) had concomitant bacteremia, a higher percentage than in previous reports [8,9]. This finding suggests that most of these cases resulted from bacteremia rather than direct invasion. The earliest signs of bacterial meningitis in newborns are often subtle and non-specific [10,11]. If newborns have any signs of sepsis, early lumbar puncture should be performed to rule out meningitis.

Krcmery and Paradisi [9] reported 101 cases of nosocomial bacterial and fungal meningitis. In their study, the most common pathogen was coagulase-negative staphylococci (48.5%), followed by *Enterobacteriaceae* (12.9%), *Pseudomonas aeruginosa* and *Acinetobacter calcoaceticus* (12.9%).The most common pathogen in this series was *Enterobacteriaceae* (41%); there were no cases caused by coagulase-negative staphylococci. The difference may be explained by the fact that most of our patients were in the NICU and central venous catheterization or neurosurgical intervention were less frequent. Gram-negative organisms were significantly related to a poor outcome, as has been previously reported [9].

Three patients acquired *Chryseobacterium meningosepticum* meningitis. All were being treated in the NICU and developed sequelae, and 2 subsequently died. Neonatal meningitis caused by *C. meningosepticum* is fatal in over one-half of cases, and severe sequelae are common [12].

Previous broad-spectrum antibiotics were given in 15 cases (68%), and this history was significantly related to a poor outcome. Systemic antimicrobial agents provide selective pressure, with extensive use leading to elimination of sensitive strains and allowing proliferation of resistant strains [13,14]. Siegman-Igra et al [15] suggested prior lumbar puncture as a possible portal for infection. In this series, 4 patients (18%) had undergone lumbar puncture prior to the development of infection.

According to previous reports, neurosurgical intervention, such as insertion of a ventriculoperitoneal

shunt, ventriculostomy, and craniotomy plays an important role in nosocomial meningitis [3,8,15]. An indwelling ventricular catheter left in place for more than 5 days has been found to be an important risk factor [15]. Filka et al reported that the incidence of ventriculoperitoneal shunt meningitis was 6.3% per insertion [8]. In this study, only 2 patients had undergone neurosurgical intervention prior to the development of infection.

In this series, patients with a VLBW or who had a prior history of intraventricular hemorrhage or hydrocephalus had a poor prognosis. VLBW infants, compared with full-term babies and older children, are relatively immunodeficient and more vulnerable to infections. Once they acquire infection, they often have more invasive disease and a poor outcome [7]. Similarly, patients with a prior history of intraventricular hemorrhage or hydrocephalus are at increased risk for neurological sequelae. Whether the complications were caused by the underlying diseases or by the meningitis could not be determined in this study.

Although nosocomial bacterial meningitis is a rare disease in children, it has significant morbidity and mortality, especially in high-risk patients. Therefore, attention must be paid to strict aseptic practice and judicious use of antibiotics in order to prevent this potentially devastating nosocomial infection.

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