CLINICAL FEATURES AND COURSE OF BACTERIAL MENINGITIS IN CHILDREN

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(Abstract): \textbf{Aim}: To analyze the clinical features and course of and to define the risk factors for bacterial meningitis in children. \textbf{Material and Methods}: Retrospective study of 100 cases of bacterial meningitis in patients aged 0-18 years admitted to the Iasi Infectious Diseases Hospital between 2005 and 2010. \textbf{Results}: We found a clear prevalence in male children (58\%) from rural area (67\%), with the highest incidence in the age group 2-5 years. A significant percentage of patients (43\%) had previous hospitalization, condition which is known as predisposing factor for bacterial meningitis, the most common being ear infections (20\%) and height and weight deficit (9\%). 71\% of patients were admitted within the first 48 h. The most common onset clinical manifestations were fever (84\%), vomiting (70\%), signs of meningeal irritation (59\%), somnolence (23\%), loss of appetite (19\%), and coma in 5\% of patients. In 36\% of cases CSF was opalescent with moderate pleocytosis (35\%); in 29\% of patients CSF albumin level ranged between 0.7-1.0 g, the majority presenting normal glyco-rahia (71\%). In only 21\% of cases the microbial agent was identified (pneumococcal and meningococcal etiology, 8\% and 6\%, respectively). The course was generally favorable, and mortality rate was low (5\%). Complications occurred in 3\% of patients consisting in hydrocephalus and brain abscess. \textbf{Conclusions}: Bacterial meningitis remains a disease with potentially severe course. Clinical onset, most commonly atypical in children, requires differential diagnosis at the time of admission in order to initiate the most appropriate antibiotic therapy. \textbf{Key words}: CHILDREN, BACTERIAL MENINGITIS, PARTICULARITIES.

The number of bacterial meningitis cases is estimated at over one million per year worldwide, with more than two thirds of these occurring before 5 years of age. Acute bacterial meningitis (ABM) in children continues to be associated with high morbidity and mortality, despite progress in terms of etiological therapy. In all countries, whether industrialized or developing, the risk of epidemics remains a topical issue. Bacterial meningitis in children is, in all cases, a therapeutic emergency, involving allegations of early clinical diagnosis to be confirmed by CSF examination.

The etiologic agent varies with age, immune system, immunization status and the geographical region. \textit{Haemophilus influenzae} type b (Hib), \textit{Streptococcus pneum-
moniae, and Neisseria meningitidis cause most cases of acute bacterial meningitis (ABM) in children, but epidemiological data are changing rapidly because of immunization practices and changing patterns of bacterial resistance.

Before the introduction of an effective vaccine, Haemophilus influenzae (Hi) was the most common etiologic agent before 5 years of age (about 45% of cases). In those countries where Hib vaccine is part of the routine infant immunization, Hib was almost eradicated (1, 2).

Vaccines against pneumococcal and meningococcal diseases have changed significantly the disease profile (3).

Streptococcus pneumoniae (Sp) is involved in about 20% of child MB (about 30% before one year of age, and 40% before 6 months in developed countries). Two features are important to be remembered: a) Sp is common in patients with hemoglobinopathies and splenectomy; b) the increasing rate of penicillin resistance requires rigorous epidemiological surveillance of Sp susceptibility profile. Vaccination at 2 months aims at preventing early infections. In countries where routine pneumococcal immunization was introduced, an increase in invasive pneumococcal disease due to non-vaccine serotypes was not reported (4, 5).

Neisseria meningitidis (Nm) is responsible for severe MB: fulminant meningococcemia and meningitis. The overall incidence of Nm meningitis is approximately 30% of cases (60% over 5 years, 25% before this age) with deadly epidemics reported especially in the "meningitis belt" of sub-Saharan Africa, where Nm serogroup A affects up to 1% of the population. Nm serogroup B predominates in Europe and Nm serogroup C has an increased frequency in France. Effective vaccination against serotypes A and C has reduced the number of secondary cases and epidemics (6).

**MATERIAL AND METHODS**

The present study aims at evaluating the clinical and biological features and the trends in the course of bacterial meningitis in children in order to optimize the first-line antibiotic therapy for this category of patients. Our study is a retrospective analysis which included 100 patients aged 0-18 years diagnosed with bacterial meningitis at the Iasi Infectious Diseases Hospital Iasi between 2005 and 2010.

The diagnosis of bacterial meningitis was based on clinical and laboratory criteria. A t-test, Fisher's exact test, or Pearson chi-square test were used where appropriate, and a p-value of < 0.05 was considered significant.

**RESULTS**

During the 6-year study period, 354 patients with bacterial meningitis, of which 28.24% were children, were admitted to the Iasi Infectious Diseases Hospital. In the interval 2005-2010 the number of pediatric bacterial meningitis cases was relatively constant, peaking in 2008 (24%).

Comparing the incidence of bacterial meningitis in the two genders, a slightly higher value was observed in males (58% vs. 42% in women). Age of patients ranged between 0 and 18 years, with a mean age of 8 years. Bacterial meningitis was more common in the age group 1-5 years (28%), with lower but comparable rates in the age group 6-11 years (27%) and 0-12 months (25%).

Upon admission we noticed that the predisposing factors for bacterial meningitis were ENT infections (20%), height and weight deficit (9%), digestive system infections (5%), trauma (4%), protein-caloric
malnutrition (4%), and ventriculoperitoneal shunt (1%). 71% of patients were admitted within 48 hours after the onset. The most common onset clinical manifestations were fever (84%), vomiting (70%), signs of meningeal irritation (59%), somnolence (23%), loss of appetite (19%), and coma in 5% of patients. CSF examination revealed a turbid macroscopic appearance in 36% of cases, clear CFS in 33%, and in only 13% of cases a typical purulent appearance. 35% of cases had a moderate pleocytosis in CSF, and increased cellularity > 1000/mm³. Glycorrhia was found low (0.2 to 0.3 g / l ) in almost a half of patients (47%).

Of the 100 children diagnosed with bacterial meningitis, in only 21% the infection was microbiologically documented: in 8% of patients the causative agent was pneumococcus, meningococcus was isolated in 6% of patients, and Haemophilus influenzae in 4% of cases. Two (2%) cases of bacterial meningitis with Gram-negative and 1 case (1%) of staphylococcus meningitis were reported. These small positivity rates are most likely due to the fact that more than half of patients received antibiotics prior to admission.

In this study we analyzed the age-related clinical and laboratory features of bacterial meningitis and found significant statistical differences with regard to meningeal irritation syndrome and vomiting at the onset (tab. I, II).

### TABLE I

<table>
<thead>
<tr>
<th>Clinical manifestation</th>
<th>Age group 1-5 Years (n=28)</th>
<th>Age group 6-11 years (n=27)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>27 (96.42%)</td>
<td>25 (92.5%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Meningeal irritation syndrome</td>
<td>11 (39.2%)</td>
<td>22 (81.48%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4 (14.48%)</td>
<td>19 (73.37%)</td>
<td>0.00002</td>
</tr>
<tr>
<td>Anorexia</td>
<td>21 (75%)</td>
<td>16 (59.29%)</td>
<td>0.213</td>
</tr>
<tr>
<td>Somnolence</td>
<td>20 (71.42%)</td>
<td>19 (73.37%)</td>
<td>0.931</td>
</tr>
<tr>
<td>Seizures</td>
<td>14 (50%)</td>
<td>9 (33.33%)</td>
<td>0.210</td>
</tr>
<tr>
<td>Coma</td>
<td>2 (7.14%)</td>
<td>3 (11.11%)</td>
<td>0.608</td>
</tr>
</tbody>
</table>

### TABLE II

<table>
<thead>
<tr>
<th>CSF parameters</th>
<th>Age group 1-5 years</th>
<th>Age group 6-11 years</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purulent</td>
<td>8 (28.57%)</td>
<td>5 (18.51%)</td>
<td>0.380</td>
</tr>
<tr>
<td>Opalescent</td>
<td>11 (39.28%)</td>
<td>12 (44.4%)</td>
<td>0.698</td>
</tr>
<tr>
<td>clear</td>
<td>9 (32.14%)</td>
<td>10 (30.07%)</td>
<td>0.702,</td>
</tr>
<tr>
<td>100-500 cel/mm³</td>
<td>7 (25%)</td>
<td>8 (29.6%)</td>
<td>0.699</td>
</tr>
<tr>
<td>500-1000 cel/mm³</td>
<td>6 (21.4%)</td>
<td>4 (14.81%)</td>
<td>0.524</td>
</tr>
<tr>
<td>&gt;2000 cel/mm³</td>
<td>10 (35.71%)</td>
<td>8 (29.6%)</td>
<td>0.630</td>
</tr>
<tr>
<td>Protein 0.7-1g/l</td>
<td>5 (17.85%)</td>
<td>7 (25.92%)</td>
<td>0.468</td>
</tr>
<tr>
<td>1-3 g/l</td>
<td>4 (14.28%)</td>
<td>7 (25.92%)</td>
<td>0.28</td>
</tr>
<tr>
<td>3-5 g/l</td>
<td>11 (39.28%)</td>
<td>12 (44.4%)</td>
<td>0.698</td>
</tr>
<tr>
<td>Normal CSF glucose</td>
<td>13 (46.42%)</td>
<td>8 (29.6%)</td>
<td>0.199</td>
</tr>
<tr>
<td>Low CSG glucose</td>
<td>10 (35.71%)</td>
<td>12 (44.44%)</td>
<td>0.508</td>
</tr>
</tbody>
</table>
Clinical features and course of bacterial meningitis in children

To be effective, the etiological treatment must have a rapid microbicidal effect. The majority of patients (60%) received a single beta-lactam antibiotic (ampicillin, ceftriaxone or meronem). 26% of cases were treated with an association of two antibiotics, the most commonly used as first-line being ampicillin + ciprofloxacin, ceftriaxone + ciprofloxacin, or vancomycin + ciprofloxacin (fig. 1). A small number of patients (14%) required a combination of more than two antibiotics, based on CSF culture results, sensitivity testing, and subsequent clinical course.

![Fig.1. Etiological treatment of bacterial meningitis in children](image)

The course of bacterial meningitis in the studied group was generally favorable; only few cases developed neurological complications (3%) consisting of hydrocephalus and brain abscess. Mortality rate was low - 5%. Unfavorable course was associated with severe general status and age at onset (all children in coma upon admission and those belonging to the age group 1-5 years).

**DISCUSSION**

Although it includes only 100 cases of bacterial meningitis, compared with multicenter studies our study brings microbiologically documented data sufficient to support the epidemiological features in our geographic area, taking into account that the Iasi Infectious Diseases Hospital serves patients from most districts of North-Eastern Romania. *S. pneumoniae* was the most common cause of bacterial meningitis in children (8%), followed by *N. meningitidis* (6%) and *H. influenzae* (4%).

As in previous studies, the distribution of etiologies was age-dependent. *S. pneumoniae* was the most frequently isolated pathogen in children <1 year, with a peak of incidence in children 4-6 months, while *N. meningitidis* was the most common pathogen in older children. Mortality rate (5%) was lower than that reported in other industrialized countries (9.2%). Mortality rates associated with *N. meningitidis* and *S. pneumoniae* were 3% and 2%, respectively, lower than those reported in recent studies (7, 8).

The high frequency of *S. pneumoniae* strains with diminished susceptibility to penicillin (53.4% of isolates), supports the use of vancomycin associated with a third
CONCLUSIONS

Bacterial meningitis remains an important public health issue, not just when it occurs in epidemics, but mostly because of its complications and high mortality. The low mortality rate in our hospital was due to an early CSF examination even in children with subtle signs of meningitis.

Bacterial meningitis should be considered in any case of acute fever in infants and children since the clinical picture in young children is less specific.

The high frequency of S. pneumoniae strains with diminished susceptibility to penicillin (53.4%) is an alarm signal that recommends the use of a third-generation cephalosporin or vancomycin as first-line therapy.

A good knowledge of the epidemiology of bacterial meningitis in children may serve as a guide for empirical antibiotic treatment, and also justifies the introduction of new conjugate vaccines into national vaccination scheme.

REFERENCES