COMMUNITY STAPHYLOCOCCAL MENINGITIS

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Abstract. Aim. This epidemiological retrospective study was aiming to establish the incidence of primitive or secondary staphylococcal meningitis, in community, clinical peculiarities of evolution by the pathogenic mechanism and the associated co-morbidities, population accessibility to health services, the aspects of diagnosis and therapy, the susceptibility of staphylococcal infection to the antibiotics and the efficiency of the therapy.

Materials and methods. The data on the staphylococcal meningitis have been obtained in the Clinical Hospital of Infectious Diseases from Iaşi. In this study there were included all cases from this region (North-East România). There have been investigated 87 hospitalized cases of staphylococcal meningitis between 1977 and 2007.

Results. The incidence by sexes was 3.5/105 for men and 1.9/105 for women. A higher incidence by residence area was registered in rural area (3.8/10 5). The most frequent registered co-morbidities were registered within otorhinolaringology (ORL) pathology (14 cases): oto-mastoiditis 4 cases (4.5%), sinusitis 4 cases (4.5%), otitis 2 cases (2.3%), rhinopharingitis 3 cases (3.4%), amigdalitis 1 case (1.1%). Also, there were registered 6 cases (6.8%) of pulmonary tuberculosis and 5 cases of type II diabetes (5.7%). A proportion of 31% from the examined patients had a primitive meningitis and 69% of them secondary meningitis. The study of cerebrospinal fluid (CSF) helped us to determine the diagnosis of meningitis, as well as the etiology of the meningeal infection.

Conclusions. In the period of 1977-2007 there has been registered a tendency of decreasing of the number of cases with staphylococcal meningitis from 13 patients to one patient per year. The prevalence in males was two times higher than the female one. The frequency of children with staphylococcal meningitis was 35.6% of cases.

Key words: staphylococcal meningitis, co-morbidities, cerebro-spinal fluid, antibiotic resistance, therapeutic strategies

Rezumat. Scop. Acest studiu epidemiologic retrospectiv a avut scopul de a stabili incidenţa meningitei stafilococi primitive sau secundare în comunitate, particularităţi ale aspectelor clinate în evoluţie, prin mecanisme patogene şi comorbidităţile asociate, adresabilitatea populaţiei la serviciile medicale, aspecte de diagnostic şi terapie, sensibilitatea stafilococului la antibioticele şi eficienţa tratamentului. Material şi metodă. Informaţiile referitoare la pacienţii cu meningită stafilococică au fost obţinute de la Spitalul Clinic de Boli Infecţioase Iaşi. În acest studiu au fost incluse toate cazurile din regiune (Nord Estul României). Au fost studiate un număr de 87 cazuri cu meningită stafiilococică comunitară la pacienţii spitalizaţi în perioada 1977-2007. Rezultate. Incidenţa meningitei stafilococice comunitare pe sexe a fost de 3,5/105 la bărbaţi şi 1,9/105 la sexul feminin. Pe medii de provenienţă incidenţa mai mare s-a înregistrat în rural (3,8/105). Cele mai frecvente comorbidităţi asociate au fost: oto-mastoidită 4 cazuri (4,5%), sinusită 4 cazuri (4,5%); otită 2 cazuri (2,3%), rinofaringită 3 cazuri (3,4%), amigdalită 1 caz (1,1%).
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INTRODUCTION
The staphylococcal meningitis has a lower incidence in comparison with other bacterial meningitis. The infection can be seen at any age, without exception, but some authors have reported a higher incidence in children. Lerche has performed a survey in 1995, in Denmark, reporting an incidence of staphylococcal infection of 2.4% (1). Kirchoff reported an incidence of 5% in 1985. Also, according to these findings, the prevalence of staphylococcal meningitis was 20% (2).

In Romania there have not been reported results or data referring on this subject. The meningeal affection is a secondary lesion, in the most frequent situation, after a sepsis, endocarditis or after a staphylococcal localized infection like: oto-mastoiditis, sinusitis, and epiduritis. In some cases the point of primary infection is unknown (3).

The clinical aspect, evolution and the prognosis of staphylococcal meningitis depend, in a great part, on the severity of the septicemic process (like the localization of septicemic metastases in vital organs) as well as age (newborn, child and elder), co morbidities, time of diagnosis and therapy, and the resistance of staphylococcus at methicillin (4).

It usually develops as a complication of a diagnosis or surgical procedure, or as infection spread by the blood from another site (5).

The therapy of meningitis with methicillin-resistant staphylococcus represents a particular situation. An alternative therapeutic strategy is represented by association of antibiotics like: vancomycine, rifampicine, fosfomicine, systemic fluoroquinolones, and linezolide (6). The preventive treatment strategies consist in the use of antibiotics in high risk population before diagnosis or surgical procedure.

MATERIAL AND METHOD
This study has included 87 cases of staphylococcal meningitis, hospitalized in Clinic of Infectious Diseases from Iași (România), in the period of 1.01.1977–1.03.2007. All of these cases represented 1.25% from the all of bacterial meningitis hospitalized in this period of time.

There has been estimated the tendency of the evolution of the disease and the distribution by sex, age group and...
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residence area. There have been considered the aspects and treatment strategies of the disease as well as clinical evolution, risk factors and co-morbidities. The applied statistical analyze to this study was one-dimensional, considering the frequency calculated of some variables. There have been used statistical instruments like: incidence, morbidity, T-Student test, Chi-squared test, coefficient of correlation and linear trend. The values have been registered and processed into EXCEL and EPIINFO files.

RESULTS
As figure 1 shows, the tendency of evolution of the phenomenon was the decreasing of the number of cases from 13 cases in 1998 to one case in 2007 (fig. 1).

![Graph showing the distribution of case numbers from 1977 to 2007.](image-url)

**Fig. 1. Distribution of the cases with meningitis over studied period**

Analyzing the batch of patients, on age group and sex, there can be observed that the distribution registered a statistical significance: \( \chi^2 = 15.68, p < 0.05 \) (tab. 1).

The number of cases in males was sensible higher in all age groups than in females, except those with ages between 4-7 years and 50-59 years.

The mode of the batch (the higher frequency) was, for both males and females between 20-29 years, 9.1% and 8% respectively (fig. 2).

The lowest levels for women have been registered in the group aged 40-49 years (0%) and for men within the group age of 8-14 years (1.1%) (fig. 2).
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Table 1. Structure of the studied batch of patients with meningitis by sex and age group

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Male</th>
<th>Female</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-11 months</td>
<td>7</td>
<td>5</td>
<td>12</td>
<td>13.8</td>
</tr>
<tr>
<td>1 - 3</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>4.6</td>
</tr>
<tr>
<td>4 - 7</td>
<td>2</td>
<td>3</td>
<td>5</td>
<td>5.7</td>
</tr>
<tr>
<td>8-14</td>
<td>10</td>
<td>1</td>
<td>11</td>
<td>12.6</td>
</tr>
<tr>
<td>15-19</td>
<td>7</td>
<td>1</td>
<td>8</td>
<td>9.2</td>
</tr>
<tr>
<td>20-29</td>
<td>8</td>
<td>7</td>
<td>15</td>
<td>17.2</td>
</tr>
<tr>
<td>30-39</td>
<td>6</td>
<td>2</td>
<td>8</td>
<td>9.2</td>
</tr>
<tr>
<td>40-49</td>
<td>7</td>
<td>-</td>
<td>7</td>
<td>8.0</td>
</tr>
<tr>
<td>50-59</td>
<td>5</td>
<td>6</td>
<td>11</td>
<td>12.6</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>3</td>
<td>3</td>
<td>6</td>
<td>6.9</td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>31</td>
<td>87</td>
<td>100</td>
</tr>
</tbody>
</table>

Fig. 2. Distribution of the subjects from the batch by sex and age group

The relative estimated incidence trend of meningitis cases showed the lowest values of the phenomenon in the years of 1992, 1993 and 1994 (fig. 3).
As the figure 3 shows, the higher incidence values of meningitis have been registered in 1978 (5.3/10^5) and 1983 (3.6/10^5). In 1987, 1995 and 2002 the incidence values have had almost the same values 2.0/10^5. In the period of 1999-2007 there was noticed an increasing tendency of the incidence rates up to the value of 2.4/10^5. The incidence by sexes has registered values of 3.5/10^5 for men and 1.9/10^5 for women. Most cases have been registered in rural area (3.8/10^5) (fig. 4).
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Our study was also aimed to evaluate the frequency of the associated diseases. The most frequent registered co-morbidities of staphylococcal meningitis were:

1. Otorhinolaryngology (ORL) pathology - 14 cases (15.9%);
   - oto-mastoiditis - 4 cases (4.5%);
   - sinusitis - 4 cases (4.5%);
   - rhinopharyngitis - 3 cases (3.4%);
   - amigdalitis - 1 case (1.1%);

2. Pulmonary tuberculosis - 6 cases (6.8%);

3. Diabetes mellitus type II - 5 cases (5.7%).

Table 2. Co-morbidities in staphylococcal meningitis

<table>
<thead>
<tr>
<th>Pathology</th>
<th>No. cases</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type II diabetes</td>
<td>5</td>
<td>5.7</td>
</tr>
<tr>
<td>Toxic chronic hepatitis</td>
<td>2</td>
<td>2.3</td>
</tr>
<tr>
<td>Viral chronic hepatitis (with B, C virus)</td>
<td>2</td>
<td>2.3</td>
</tr>
<tr>
<td>ORL chronic pathology</td>
<td>14</td>
<td>15.9</td>
</tr>
<tr>
<td>Pulmonary tuberculosis</td>
<td>6</td>
<td>6.8</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>4</td>
<td>4.5</td>
</tr>
<tr>
<td>Bronchopneumonia</td>
<td>1</td>
<td>1.1</td>
</tr>
<tr>
<td>Urinary infection</td>
<td>4</td>
<td>4.5</td>
</tr>
<tr>
<td>Cardiac pathology</td>
<td>3</td>
<td>3.4</td>
</tr>
<tr>
<td>Total</td>
<td>41</td>
<td>46.6</td>
</tr>
</tbody>
</table>

The studied batch was classified in two groups that try to define the evolution, pathogenic and therapeutic aspects of the cases:

- primary staphylococcal meningitis - 27 cases (30.7%) and
- secondary staphylococcal meningitis:
  - septicemic infection - 46 cases (52.9%);
  - ORL localized infection - 7 cases (11.7%);
  - spinal abscess - 7 cases (11.7%).

The clinical symptomatology of primary staphylococcal meningitis was represented by presence of infectious and meningeal syndromes in 77.8% and 90% respectively from all cases. In 44.4% of cases the encephalitis and intracranial hypertension have been associated in 40.7% and the presence of the neurological syndrome was noted in 14.8% of cases.

In the secondary septicemic meningitis 23.9% from patients had a meningeal implication in the same time with the beginning of a systemic infection. In other 18 patients (39.1%) the meningeal affection was noticed in the first week of pathological evolution, when the febrile syndrome was associated with encephalitic symptoms like convulsion, encephalitic cry and drowsiness.

The last 17 patients (37%) have been diagnosed after 2 or 3 weeks. Their
symptoms have been represented by a discrete nervous component like headache and agitation. In the first two cases of secondary meningitis with an ORL infection the start of clinical symptoms was acute, patients presenting in the same time oto-mastoiditis. In the other 5 cases the start of the clinical symptomatology was after 10-21 days from the localized infection.

The meningitis secondary to a spinal abscess has started in the first week from the moment of diagnosis of the infection in the subdural space (6 cases). In one case, the meningitis started in the second week. Three patients presented a cephalalgic and meningeal syndrome and in 4 patients the meningeal affection was confirmed with the help of a spinal puncture under and over suspected lesion.

The diagnosis of staphylococcal meningitis was based on clinical arguments which varied with the pathogenic mechanism of meningeal affection. The confirmation of the pathology was based on micro and macroscopical aspect of cerebro-spinal fluid (CSF), and the presence of an inflammatory reaction that was detected by the CSF analysis. A positive bacteriologic exam and in the same time more impregnation in the CSF and positive culture like hemoculture or other positive cultures from septic location, helped us to confirm the diagnosis of secondary meningitis.

The purulent and opal aspect was obtained in most cases of primary staphylococcal meningitis (88.7%). In the secondary meningitis the CSF showed a clear aspect in almost 50% of cases.

The elevated CSF albumin values over 1.1 g/l were noticed in 66.7% from patients with primary meningitis and in only 35% of those with secondary meningitis.

The bacteriological examination of the CSF is of a great importance and specific implication for an adequate treatment as well as a favourable evolution of meningitis. The analysis of cellularity, protein, glucose and lactate can be very helpful to a differential diagnosis. Staphylococcal etiology was noticed intravitam in 73 cases (83.9%) and postmortem in 14 patients (16.1%). In 58% of cases the culture of CSF was positive. *Staphylococcus aureus* was the determining agent present in the most cases (65 cases; 74.7%). The coagulase-negative staphylococci infections have been detected in 22 cases (25.3%). *Staphylococcus aureus* haemolytic type was isolated in primary meningitis and in the meningitis secondary to sepsis and spinal abscess (63 cases – 74.2%); coagulase-negative staphylococci strains were present in the secondary form to otitis meningitis (in 5 cases from 7).

The sensitivity to anti staphylococcal antibiotics is of a great importance being an indicator of etiology and prognosis. We studied the sensitivity to classical and new anti staphylococcal antibiotics, over 3 decades.

To the etiological treatment strategies for the staphylococcal infection of the meninges there was given more therapeutical schemes. It was initiated with classical anti staphylococcal like: cloramfenicol, rifampicine, gentamicine, in systemic administration or intrathecal...
injection. After that there have been applied new antibiotics like: pefloxacine, ciprofloxacin, vancomycine, ceftriaxone, linezolide.

In the batch of primary staphylococcal meningitis, the deaths were registered in the patients who have been treated with classical antibiotics.

There was chosen an associated therapy in meningitis secondary to a spinal abscess and ORL infection. It was administered a medication with a high penetrability in sub arachnidan space that was associated with a high penetrability one at the place of located infection. There were used cloramfenicol, ciprofloxacine, rifampicine, vancomycine, linezolide. There was registered only one death caused by to the tardy administration of the treatment.

A number of 3 antibiotics have been associated in meningitis secondary to a sepsis, because of severity and septic dissemination. The most effective schemes of treatment were vancomycine with rifampicine and an aminoglicozide or vancomycine with ciprofloxacine, and an aminoglicozide. Two from deceased cases had an infection associated with oxacillin resistance staphylococcus. Another patient had hidrocefalia, a mechanical complication like.

To the etiological therapy it was associated a pathogenic one (which included anti inflammatory treatment or one for treatment of peripheral circulatory insufficiency), associated with a treatment for disseminated intravascular coagulation (DIC).

The lethality of meningitis ranged between 14.3% and 63%, due to pathogenic mechanism. The mortality rate within the staphylococcal meningitis was 39.1%.

The identified causes of death were:
- meningitis coma (5 cases);
- cerebral complications (9 cases);
- toxico-septic shock (13 cases);
- DIC (4 cases);
- refractory cardiac insufficiency (1 case);
- bronchopneumonia (3 cases).

There have been registered 17 deaths (50%) caused by toxico-septic shock and/or DIC, or a coma induced by meningitis, in the first 72 hours from the therapy initiation point. The others 50% of deaths were caused by cerebral complications, heart rhythm disorders, decompensated heart failure, brain abscess, or inadequate therapy caused by the impossibility to administrate an antibiotic.

CONCLUSIONS
In the period of 1977-2007 there has been registered a tendency of decreasing of the number of cases with staphylococcal meningitis from 13 patients to one patient per year.

The prevalence in males was two times higher than the female one.

The frequency of children with staphylococcal meningitis was 35.6% of cases.

Staphylococcal meningitis is rare registered in community, but it can have clinical and therapeutical complications due of the process of resistance of staphylococcus at classical and new antibiotics.
REFERENCES