

COMMUNITY STAPHYLOCOCCAL MENINGITIS

Doina Fedulov¹, Doina Mihalache^{2,3}, Setalia Ostapov³

1. District House of Pensions and Social Insurance Galați, România
2. Clinical Hospital of Infectious Diseases Iași, România
3. University of Medicine and Pharmacy „Gr. T. Popa” Iași, România

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 Iași. 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 $3.5/10^5$ for men and $1.9/10^5$ 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 otorhinolaryngology (ORL) pathology (14 cases): oto-mastoiditis 4 cases (4.5%), sinusitis 4 cases (4.5%), otitis 2 cases (2.3%), rhinopharyngitis 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 incidența meningitei stafilococice primitive sau secundare în comunitate, particularități ale aspectelor clinice în evoluție, prin mecanisme patogenice și comorbiditățile asociate, adresabilitatea populației la serviciile medicale, aspecte de diagnostic și terapie, sensibilitatea stafilococului la antibioticele și eficiența tratamentului. **Material și metodă.** Informațiile referitoare la pacienții cu meningită stafilococică au fost obținute de la Spitalul Clinic de Boli Infecțioase Iași. În acest studiu au fost incluse toate cazurile din regiune (Nord Estul României). Au fost studiate un număr de 87 cazuri cu meningită stafilococică comunitară la pacienți spitalizați în perioada 1977-2007. **Rezultate.** Incidența meningitei stafilococice comunitare pe sexe a fost de $3.5/10^5$ la bărbați și $1.9/10^5$ la sexul feminin. Pe medii de proveniență incidența mai mare s-a înregistrat în rural ($3.8/10^5$). Cele mai frecvente comorbidități asociate au fost preponderent reprezentate de patologia ORL (14 cazuri): otomastoidită 4 cazuri (4,5%); sinuzită 4 cazuri (4,5%); otită 2 cazuri (2,3%), rinofaringită 3 cazuri (3,4%), amigdalită 1 caz (1,1%). De

COMMUNITY STAPHYLOCOCCAL MENINGITIS

asemenea s-au înregistrat 6 cazuri de tuberculoză pulmonară (6,8%) și 5 cazuri (5,7%) de diabet zaharat tip II. O proporție de 31% din pacienți au prezentat meningită primară și 69% meningită secundară. Studiul lichidului cefalorahidian (LCR) a ajutat la confirmarea diagnosticului de meningită, dar și la stabilirea etiologiei infecției meningeale. **Concluzii.** În perioada 1977-2007 s-a înregistrat o tendință de scădere a numărului de cazuri de meningită stafilococică de la 13 pacienți/an până la 1 pacient/an. Prevalența la bărbați a fost de aproximativ 2 ori mai mare decât la femei. Frecvența apariției acestei afecțiuni la copii a fost de 35,6% din cazuri.

Cuvinte cheie: meningită stafilococică, comorbidități, lichid cefalorahidian, rezistența la antibiotice, strategii terapeutice

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 linezolid (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

residence area. There have been considered the aspects and treatment strategies of the disease as well as clinical evolution, risk factors and comorbidities.

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).

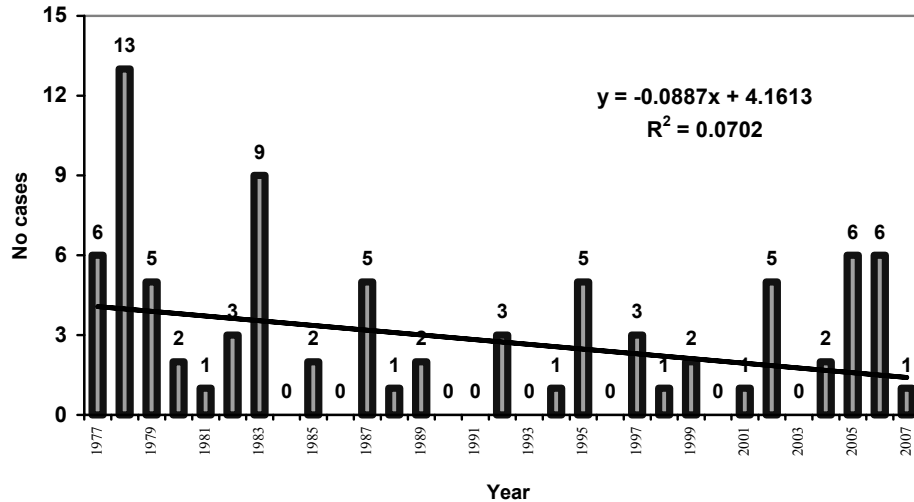


Fig. 1. Distribution of the cases with meningitis over studied period

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).

COMMUNITY STAPHYLOCOCCAL MENINGITIS

Table 1. Structure of the studied batch of patients with meningitis by sex and age group

| Age (Years) | Sex | | Total cases | |
|-------------|------|--------|-------------|------|
| | Male | Female | n | % |
| 0-11 months | 7 | 5 | 12 | 13.8 |
| 1 - 3 | 2 | 2 | 4 | 4.6 |
| 4 - 7 | 2 | 3 | 5 | 5.7 |
| 8-14 | 10 | 1 | 11 | 12.6 |
| 15-19 | 7 | 1 | 8 | 9.2 |
| 20-29 | 8 | 7 | 15 | 17.2 |
| 30-39 | 6 | 2 | 8 | 9.2 |
| 40-49 | 7 | - | 7 | 8.0 |
| 50-59 | 5 | 6 | 11 | 12.6 |
| > 60 | 3 | 3 | 6 | 6.9 |
| Total | 57 | 31 | 87 | 100 |

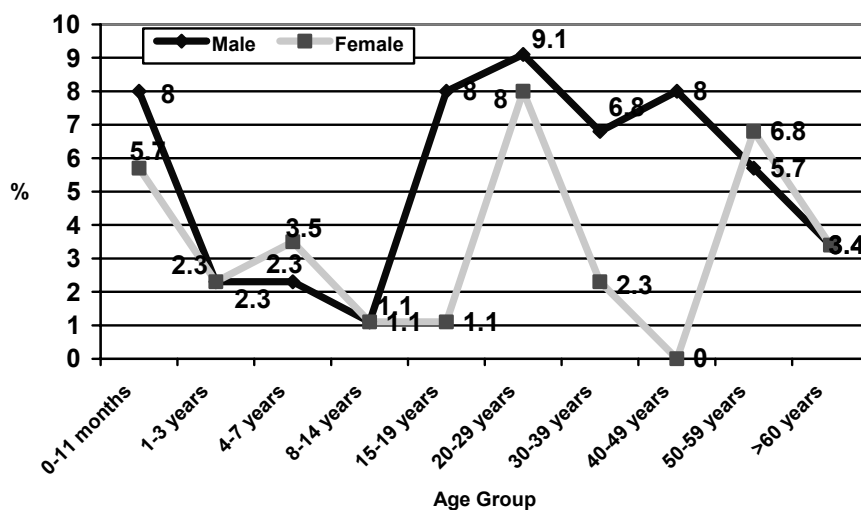


Fig. 2. Distribution of the subjects from the batch by sex and age group

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).

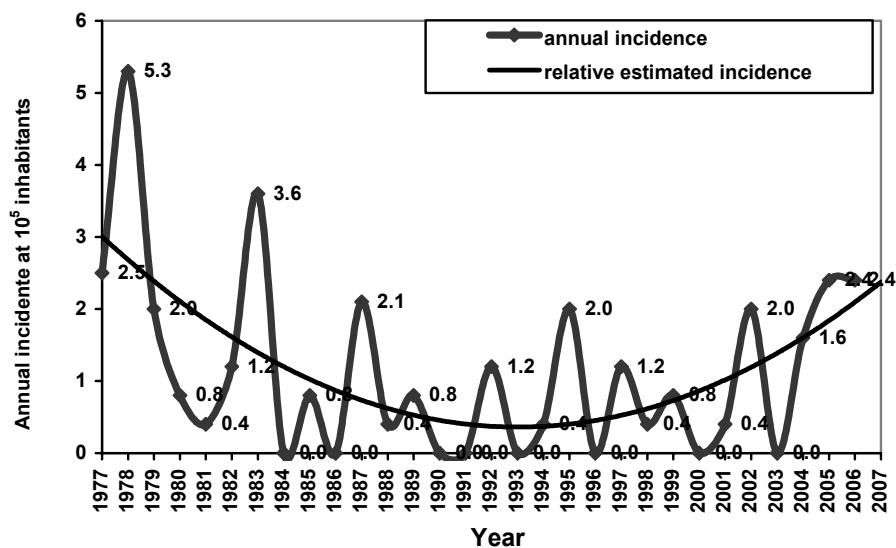


Fig. 3. The annual incidence of the cases of meningitis between 1977 and 2007

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).

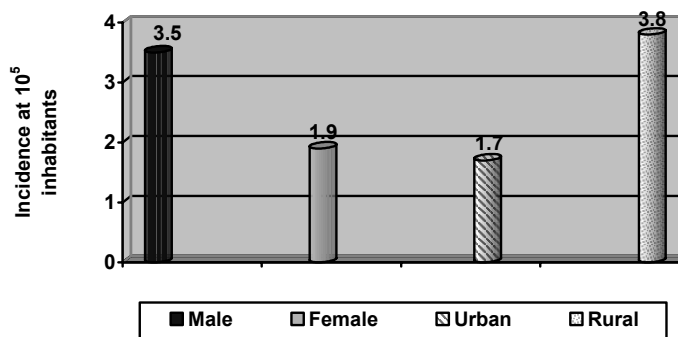


Fig. 4. Incidence of meningitis by sex and residence

COMMUNITY STAPHYLOCOCCAL MENINGITIS

Our study was also aimed to evaluate the frequency of the associated diseases. The most frequent registered comorbidities of staphylococcal meningitis were:

1. Otorhinolaryngology (ORL) pathology- 14 cases (15.9%);
 - oto-mastoiditis - 4 cases (4.5%),
 - sinusitis - 4 cases (4.5%),

- otitis - 2 cases (2.3%),
 - 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

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

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‰ 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 *intravital* 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

COMMUNITY STAPHYLOCOCCAL MENINGITIS

injection. After that there have been applied new antibiotics like: pefloxacin, ciprofloxacin, vancomycin, ceftriaxone, linezolid.

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 arachnoid space that was associated with a high penetrability one at the place of located infection. There were used cloramfenicol, ciprofloxacin, rifampicin, vancomycin, linezolid. 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 vancomycin with rifampicin and an aminoglycoside or vancomycin with ciprofloxacin, and an aminoglycoside. Two from deceased cases had an infection associated with oxacillin resistance staphylococcus. Another patient had hydrocephalus, 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

1. Lerche A, Rasmussen N, Wandall JH: *Staphylococcus aureus meningitis. A review of 28 consecutive community-acquired cases*. Scand J Infect Dis 1995, 27: 569-573.
2. Kichoff LV, Sheagren JN: *Epidemiology and clinical significance of blood culture positive for coagulase-negative staphylococcus*. Infect Control 1985, 6: 476-486.
3. Bruno Mourvillier, Michel Wolff: *Méningites infectieuses et méningo-encéphalites*. Rev Prat 2006, 56: 1927-1932.
4. Feigin RD, Mc Craken GH, Klein JO: *Dagnosis and management of meningitis*. Pediatr Infect Dis 1992; 11: 785-814.
5. Doina Mihalache, Cătălina Logigan, Doina Fedulov, Olga Filip, Tatiana Turcu: *Nosocomial staphylococcal meningitis*, 13th Panhellenic Pharmaceutical Congress, Athena, mai, 2007, p. 363.
6. Doina Mihalache, Cătălina Logigan, Tatiana Turcu, Olivia Dorneanu, Doina Fedulov: *Vancomicina utilizată în tratamentul meningitei nosocomiale stafilococice*, Zilele „Gh. Năstase”, Dermato, Iași, iulie, 2007, p. 60.