

MENINGEAL SYNDROME IN THE PRACTICE OF INFECTIOUS DISEASES SPECIALISTS

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Central nervous system (CNS) infections are among the most dramatic medical conditions, not just because of their clinical presentations, possible ultimate consequences, but also because of the complexity of their diagnosis and treatment, and clinically they are manifested with meningeal syndrome, regardless of the type of causative agent. The aim of the study was to determine the correlation between certain clinical signs of meningeal syndrome and results of lumbar puncture which is used to diagnose the central nervous system infection. The study included a group of 54 patients who were treated at the Clinic for Infectious Diseases Clinical Centre Niš, with a clinical picture of bacterial meningitis.

The diagnosis of the disease was based on a clinical picture, findings of lumbar puncture and isolation of the causative agent out of the cerebrospinal fluid. In all patients, there was pleocytosis in the cerebrospinal fluid with predomination of polymorphonuclears. There were 20 (37.0%) females and 34 (63.0%) males, with mean age 52.37 ± 18.10 years. The most dominant clinical symptoms in patients were headache in 74.1%, elevated temperature in 70.4%, stiff neck in 63.0% and Brudzinski's upper sign in 55.6%.

Ethical verification from the cerebrospinal fluid was negative in 32 (59.3%) patients, *Klebsiella*, *Pneumococcus* and *Staphylococcus* were found in 4 (7.4%) patients each. It was found that headaches with stiff neck, disturbance of consciousness and elevated temperature represent an absolute indication for lumbar puncture and are in direct correlation with the positive finding in the cerebrospinal fluid. *Acta Medica Medianae* 2017;56(2):32-37.

Key words: CNS infection, meningitis, meningeal syndrome, lumbar puncture

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Introduction

A large number of infectious and other agents can get into the cerebrospinal fluid system by blood, lymphatic or neural route causing the inflammation process on meninges. Regardless of the causative agent, there comes to increased production of cerebrospinal fluid, which results in an increase of intracranial pressure.

Regardless of whether intracranial pressure has been increased due to increased production of cerebrospinal fluid or brain volume, there are always certain characteristic signs known as meningeal syndrome (1).

CNS infections are among the most dramatic of medical conditions, not just because of their clinical presentations, possible ultimate consequences, but also because of the complexity of their diagnosis and treatment (1, 2).

Acute bacterial meningitis belongs to the group of serious infectious diseases, caused by various types of bacteria, during which the pestilent exudate is created in the subarachnoid space and meninges. They are clinically manifested by the appearance of meningeal syndrome with characteristic meningeal signs (3).

Bacterial meningitis, despite the application of most modern antibiotic therapy, represents a huge problem to the healthcare system, since according to Gray's data morbidities in the US range from 2-6 per 100,000 inhabitants with a mortality of 3-33% (4).

Regardless of the applied antibiotic therapy, mortality in the world ranges from 20-30%, while in almost 50% of cases, there are sequelae which appear in the form of hearing damage, neurological outbreaks, learning and behavior disorders, etc (5).

Mortality rate according to Van de Beku is 34%, and up to 50% of patients suffer from the long-term consequences (6).

Aim

Bearing in mind the fact that the clinical picture of meningeal syndrome can be very different and that in some cases, discretely expressed meningeal syndrome can be followed by very rich cerebrospinal fluid findings, we wanted to determine the clinical significance of certain meningeal signs.

Materials and methods

In our prospective analysis, we included 54 patients who were treated at the Clinic for Infectious Diseases, Clinical Centre Niš, with the diagnosis of meningitis bacterialis. Diagnosis is set on the basis of the clinical picture and the LP findings, where cerebrospinal fluid protein content, cerebrospinal fluid glucose content and pleocytosis were determined as parameters for the bacterial or viral etiology of the disease.

For the purpose of ethological verification of the causative agent, the cerebrospinal fluid was sent to the Public Health Institute in Niš, where Gram staining was done, and in cases with posi-

tive findings, the antibiogram was done. Statistical data processing, descriptive and analytical statistics were used. The results are presented in tables and graphs.

Results

Out of 54 respondents, 20 (37%) were women and 34 (63%) were men, with mean age of 52.37 ± 18.10 years, of whom the youngest participant was 19 and the oldest was 85 years old. Table 1

Table 1. Socio-demographic characteristics of the population surveyed

Gender	Male (n)	34(63%)
	Female(n)	20(37%)
Age	$\bar{x} \pm SD$ (min-max)	52.37 ± 18.10 (19-85)

Men were statistically significantly older than women (56.58 ± 19 , 35 vs 45.20 ± 13.34 , $t = 2.323$, $p = 0.024$) (Chart 1).

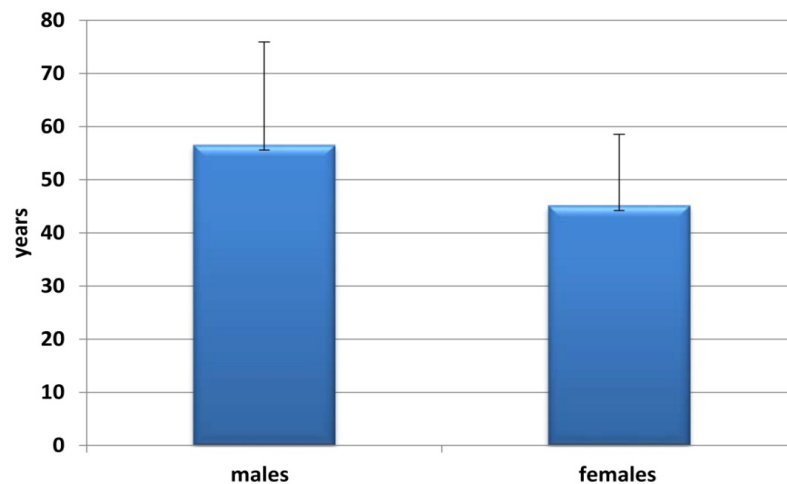


Chart 1. Age of respondents by gender

Table 2. Diagnosis on admission

	n(%)
Meningitis of unknown origin	48(88.9)
Febrile state	2(3.7)
Bacterial meningitis	2(3.7)
Coma	2(3.7)

Table 3. Diagnosis on discharge

	n(%)
Bacterial meningitis	48(88.9)
TBC meningitis	2(3.7)
Meningitis Bact. Otogenes	2(3.7)
Meningitis of unknown origin	2(3.7)

The most common diagnosis on admission was meningitis of unknown, origin set up in 48

(88.9%) patients, while the diagnoses of febrile state, bacterial meningitis, and coma were found in two (3.7%) patients each. (Table 2, 3)

Almost half of the subjects, 24 (44.4%), were without comorbidity. Diabetes mellitus was diagnosed in 6 (11.1%) patients, cardiac insufficiency and brain tumor were found in four patients each (7.4%); two (3.7%) were alcoholics, had ear infections, glaucoma, hypertension, lupus nephritis, heart valve operation, head injury, and prostate tumor. (Table 4, 5)

On average, patients were awaiting 4.70 ± 4.62 days until hospitalization. On admission, 38 (70.4%) patients were febrile, 14 (25.9%) afebrile, while 2 (3.7%) subjects were in hypothermia. The average temperature of the entire population was 37.77 ± 1.14 OC. (Table 6)

Table 4. Comorbidities

	n(%)
No comorbidity	24(44.4)
Diabetes mellitus	6(11.1)
Ethylusmus	2(3.7)
Ear infections	2(3.7)
Glaucoma	2(3.7)
Hypertension	2(3.7)
Lupus nephritis	2(3.7)
Heart valve injury	2(3.7)
Head injury	2(3.7)
Cardiac insufficiency	4(7.4)
Brain tumor	4(7.4)
Prostate tumor	2(3.7)

Table 5. Characteristics of patients on admission

		$\bar{x} \pm SD, n(\%)$
Days of hospitalization		4.70 \pm 4.62
Febrillity	Afebrile	14(25.9)
	Febrile	38(70.4)
	Hypothermia	2(3.7)
Temperature ($^{\circ}C$)		37.77 \pm 1.14

Table 6. Meningeal signs

		n(%)
Stiff neck	negative	20(37)
	positive	34(63)
Kerning's sign	negative	46(85.2)
	positive	8(14.8)
Brudzinski's upper sign	negative	24(44.4)
	positive	30(55.6)
Brudzinski's lower sign	negative	28(51.9)
	positive	26(48.1)
Lazarević's sign	negative	42(77.8)
	positive	12(22.2)
Vujić's sign	negative	44(81.5)
	positive	10(18.5)
Meningeal position	negative	46(85.2)
	positive	8(14.8)
Bradycardia	absent	44(81.5)
	present	10(18.5)
Headache	absent	14(25.9)
	present	40(74.1)
Vomiting	absent	32(59.3)
	present	22(40.7)
Aphasia	absent	28(51.9)
	present	26(48.1)
Hyperacusis	absent	50(92.6)
	present	4(7.4)
Photophobia	absent	48(88.9)
	present	6(11.1)

Table 6 shows the meningeal signs. Positive signs were registered in the following distribution: stiff neck 34 (63.0%), Kerning's 8 (14.8%), Brudzinski's upper 30 (55.6%), Brudzinski's lower 26 (48.1%), Lazarević's 12 (22.2%), Vujić's 10 (18.5%), meningeal position 8 (14.8%), brady-

cardia 10 (18.5%), headache 40 (74.1%), vomiting 22 (40.7%), aphasia 26 (48.1%), hyperacusis 4 (7.4%) and photophobia 6 (11.1%). (Table 7) On admission, 42 (77.8%) patients had a disorder of consciousness (Table 7). Sixteen (26.9%) patients were disorientated, 26 (48.1%) somnolent, 14 (25.9%) were in coma, while 12 (22.2%) patients were upset. (Table 8)

Table 7. Awareness state

		n(%)
Consciousness	disorder	42(77.8)
	neat	12(22.2)
Disorientation	no	38(70.4)
	yes	16(26.9)
Somnolence	no	28(51.9)
	yes	26(48.1)
Sopor	no	40(74.1)
	yes	14(25.9)
Coma	no	48(88.9)
	yes	6(11.1)
Anxiety	no	42(77.8)
	yes	12(22.2)

Table 8. Values of the parameters from the cerebrospinal fluid on admission

	n(%), $\bar{x} \pm SD$
Color	
Clear	38(70.4)
Blurred	16(29.6)
Segmented Leukocytes	282.74 \pm 372.75
Lymphocytes	26.89 \pm 30.77
Cerebrospinal fluid Protein content	2.35 \pm 2.44
Cerebrospinal fluid Glucose content	3.20 \pm 2.20
SHR	7.56 \pm 2.99

Table 9. Bacteriological findings on admission

	n(%)
Without isolates	32(59.3)
Pneumococcus	4(7.4)
Klebsiella	6(11.1)
Gram+	2(3.7)
Staphilococcus	4(7.4)
Pseudomonas	2(3.7)
Listeria monocytogenes	2(3.7)
Meningococcus	2(3.7)

Table 10. Laboratory parameters from the blood taken on admission

	n(%)
Sedimentation	42.0 \pm 40.05
Leukocytes	13.29 \pm 6.89
Segmented leucocytes	80.17 \pm 17.87
CRP	145.64 \pm 135.96
PCT	0.79 \pm 2.85

The values and parameters from the cerebrospinal fluid measured in patients on admission are shown in (Table 8).

Table 9 shows the distribution of bacteria isolated from the cerebrospinal fluid in patients on admission. In 32 (59.3%) patients, the finding was negative, 6 (11.1%) had *Klebsiella*, *Pneumococcus* and *Staphylococcus* were found in 4 (7.4%) patients each, while Gram-positive bacteria, *Pseudomonas*, *Listeria monocytogenes* and *Meningococcus* were found in 2 patients each. (Table 9, 10)

After hospitalization, the course of the disease was as follows: 10 (18.5%) patients died, 32 (59.3%) recovered, and 12 (22.2%) were transferred to another department (Chart 2). The average time to final outcome was 18.79 ± 14.08 days. (Chart 2)

Thirty-six (66.7%) patients received the therapy following the guide, 4 (7.4%) according to antibiogram, while 6 patients (11.1%) did not have any response to therapy (Chart 3).

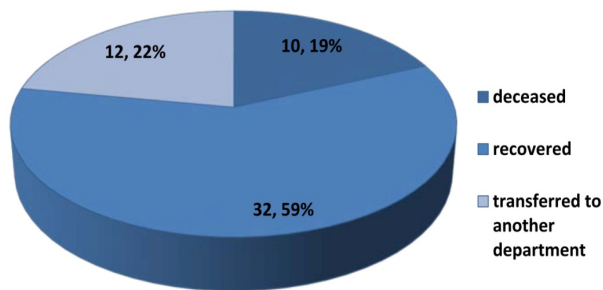


Chart 2. Outcome of the disease

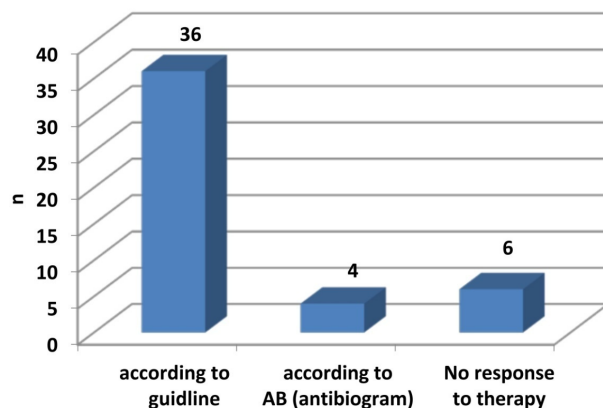


Chart 3. Therapy

Discussion

Bacterial meningitis is the most significant and most severe manifestation of central nervous

system infections. They can have very rapid and unfavorable clinical evolution, and despite the use of antibiotics and the most modern methods of treatment, a relatively high mortality rate is still present. Their frequency ranges from 0.2 to 6 cases per 100,000 inhabitants in the United States according to Gray and mortality of 3-33% for untreated and inadequately treated cases of bacterial meningitis (4). Vikse states that 1.2 million people in the world get ill annually, with 135,000 deaths (7). Petra observes that the world's mortality rate is 20-30%, regardless of the treatment applied (5), Miyazaki found 10-40% (8) and Bamberger 21% in developed countries (9), De Jong 5% (10), Thigpen 14,3% (11).

Out of 54 respondents in our study, 63% were male and 37% female. Egidia Miftode, on a sample of 127 adults and 77 children with TB meningitis, found that in the child group, 61% were male and 39% female. In adults, this ratio was 58% versus 42% in favor of the male sex (12).

The timely diagnosis is in direct correlation with the outcome of the disease and is based on the clinical picture, LP and the etiological verification of the causative agent. Early recognition of meningeal signs is decisive for raising the suspicion of the presence of meningeal syndrome.

In our respondents, positive meningitis signs were registered in the following distribution: headache in 74.1%, temperature in 70.4%, stiff neck in 63.0%, Brudzinski's upper sign in 55.6%, Brudzinski's lower sign in 48.1%, aphasia in 48.1%, vomiting in 40.7%.

Bamberger states the following representation of meningeal signs (9).

In 95% of cases, two of the following were present: temperature, stiff neck, headache, mental state disorder. The most common symptom was headache: 87%, neck stiffness 83%, temperature above 38°C, and loss of consciousness 69%.

We found difficult mobility of the neck in 20% less cases, which may be due to different assessment criteria. Also, our respondents had a 13% less headache, which can be a result of the state of consciousness of patients on admission, since a patient with a consciousness disorder cannot give information about the existence of a headache. The diagnosis of meningitis can only be made by lumbar puncture, and it is very interesting that 70.4% of cerebrospinal fluid samples were clear and only 29.6% were blurred. All authors state that in the first lumbar puncture the appearance of the cerebrospinal fluid can range from slightly turbid resembling "cigarette smoke" to the purulent content that cannot pass through a needle for lumbar puncture (14, 15).

By a cytologic examination, pleocytosis with the prevalence of polymorphonuclears was found, which is in line with other authors. Garlicki (15) states that pleocytosis is over 1,000 cells in mm^3 , with over 80% predominance of polymorphonuclears. Machado (14) states that polymorphonuclears are the evidence of the presence of bac-

terial antigens and that they exceed 90% of cell elements. In our respondents, expressed cerebrospinal fluid protein content and reduced cerebrospinal fluid glucose content were observed. Garlicki (15) also finds that protein values are elevated from 1-5gr/l and glucose levels are reduced to even undetectable values.

Thirty-six (66.7%) patients received treatment following the guideline, 4 (7.4%) received antibiotics after obtaining isolates from the cerebrospinal fluid (in which *Klebsiella* was identified), while 6 patients (11.1%) had no response to therapy that had to be changed *ex juvantibus* by including more potent carbapenem antibiotics and colistin.

Duszynska states that developed countries recommend cefotaxime or ceftriaxone as empirical treatment, often with vancomycin, to microbiological confirmation and antibiograms (16).

Conclusion

Clinical picture with the presence of meningeal syndrome and characteristic meningeal signs, headache, elevated temperature, stiffness of the neck were the most significant in raising suspicion of CNS infection. The diagnosis is made exclusively by the LP and there is no wrongly done LP, because sometimes clinical symptomatology can be very discrete, especially in elderly people.

All our respondents had pleocytosis with polynucleosis, which, with chemical findings of the cerebrospinal fluid, high cerebrospinal fluid protein content and low cerebrospinal fluid glucose content, indicated the bacterial etiology of the disease and prompted the clinician to start antibiotic therapy in time. A high percentage of 59.3% of the cerebrospinal fluid samples, from which there were no isolates, were the result of the previous use of antibiotics and irregular transport of cerebrospinal fluid.

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doi:10.5633/amm.2017.0205**MENINGEALNI SINDROM U PRAKSI INFЕКТОLOGA***Aleksandar Ranković¹, Miodrag Vrbić^{1,2}, Maja Jovanović^{1,2},
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Infekcije CNS-a spadaju u najdramatičnija stanja u medicini, ne samo zbog svoje kliničke prezentacije, mogućih krajnjih posledica, već i zbog složenosti njihovog dijagnostikovanja i tretmana, a klinički se manifestuju meningealnim sindromom bez obzira na vrstu prouzrokovaca. Cilj rada bio je utvrđivanje korelacije pojedinih kliničkih znakova meningealnog sindroma i rezultata lumbalne punkcije, kojom se jedino postavlja dijagnoza infekcije centralnog nervnog sistema. Ispitivanjem je obuhvaćena grupa od 54 bolesnika sa kliničkom slikom bakterijskog meningitisa, koji su lečeni u Klinici za infektivne bolesti Kliničkog centra u Nišu. Dijagnoza bolesti je postavljana na osnovu kliničke slike, nalaza lumbalne punkcije i izolacije prouzrokovaca iz likvora. Kod svih bolesnika je u likvoru postojala pleocitoza sa predominacijom polimorfonukleara. Osoba ženskog pola bilo je 20 (37%) i 34 (63%) muškog, prosečne starosti 52,37±18,10 godina. Najdominantniji klinički simptomi bili su glavobolja, 74,1%, povišena temperatura, 70,4%, ukočen vrat, 63% i gornji znak Brudžinskog u 55,6% ispitanika. Etiološka verifikacija iz likvora je kod 32 (59,3%) bolesnika bila negativna, 6 (11,1%) je imalo Klebsielu, po četiri (7,4%) *Pneumococcus* i *Staphylococcus*. Utvrđeno je da glavobolja uz ukočeni vrat, poremećaj stanja svesti i povišena temperatura predstavljaju apsolutnu indikaciju za lumbalnu punkciju i u direktnoj je korelaciji sa pozitivnim nalazom u likvoru. *Acta Medica Medianae* 2017;56(2):32-37.

Ključne reči: infekcija CNS, meningitis, meningealni sindrom, lumbalna punkcija

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