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Features of Nosocomial Meningitis in Patients of a Neurosurgical Critical Care Unit

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We report the results of a prospective study on the development of bacterial meningitis in postoperative complicated patients of a neurosurgical critical care unit for the period of 2010—2014. **The aim of this study** is to determine the incidence rate and risk factors of nosocomial meningitis in postoperative complicated patients. **Material and methods.** Disease complications requiring stay in the neurosurgical critical care unit for more than 48 h were observed in 1,153 (14.3%) patients. The data of these patients were systematized and added to the database. **Results.** Nosocomial meningitis (NM) developed in 146 patients, which accounted for 12.6±1.0% (CI, 10.74—14.66). The meningitis patients were characterized by a longer stay in the critical care unit (CCU), prolonged mechanical ventilation, the need for central venous access, and invasive monitoring of systemic hemodynamics as well as longer antibacterial therapy. The frequency of invasive monitoring of intracranial pressure had a similar effect in groups of patients with and without NM. The NM patients were more often detected with bloodstream infections (14.8% vs. 4.9%; $p<0.000$), respiratory tract infections (55% vs. 35.6%; $p<0.000$), and urinary tract infections (56.4% vs. 30.9%; $p<0.000$). The following significant differences were observed between the group of NM patients and the control group: more frequent use of external ventricular drainage (72.5% vs. 26.1%, respectively; $p<0.000$), a higher number of reoperations (64.7% vs. 36.3%, respectively; $p<0.000$), and a longer total operating room stay (417.3 min vs. 337.5 min, respectively; $p<0.000$). The etiology was identified in 61.0±4.0% of NM cases. CoNS (33.0%) and *Acinetobacter baumannii* (21.3%) were the main pathogens isolated from the cerebrospinal fluid. The mortality in the patients with meningitis was 31.5±3.8%. Conclusion. External ventricular drainage, repeated surgery, long-term stay in the operating room as well as infections of a different localization may be considered as the risk factors for developing nosocomial meningitis in neurosurgical patients in a CCU.

Keywords: *nosocomial meningitis, risk factors, CCU, prospective observation.*

Health-care-associated nosocomial infections (NIs) are a major concern for the current health service since they result in ancillary diseases, increased mortality, longer treatment, and higher cost of therapy [1—3].

Because of objective reasons, the NI incidence rate in patients in critical care units (CCUs) accounts for 20—25%, which is significantly higher compared to that in other hospital departments [4]. The main risk factors include more frequent use of invasive devices and procedures, immediate severity of the condition of patients in a CCU and the extent of organ injury, immune status impairment in patients in critical conditions, and the need for extensive use of antibiotic therapy facilitating selection of multidrug-resistant pathogens — causative NI agents [2, 5, 6].

The features of health care to patients with neurosurgical pathology include the abolishment of the brain protective barriers during surgical interventions, longer surgery duration as well as use of invasive neuromonitoring techniques. The rate of infectious complications of the central nervous system (CNS) in CCU patients is expectedly different from that in patients at general surgical hospitals.

An epidemiological survey conducted at the Critical Care Department of the Burdenko Neurosurgical Institute in 2009 revealed that meningitis ranks third after lower respiratory tract infections (LRTIs) and urinary tract infections (UTIs) in the structure of NIs.

According to the literature data [7—11], the major risk factors of nosocomial meningitis include intraventricular hemorrhage, craniotomy, wound liquorrhea, and duration of neurosurgery and external ventricular drainage, with a significantly increased risk of infection after five days of drain use. Ventriculoperitoneal shunting, use of an intracranial pressure (ICP) sensor, and repeated surgery also play an important role [11].

The aim of this study is to determine the incidence rate of NMs and their clinical and epidemiological features in patients of a neurosurgical critical care unit.

Material and Methods

The study was conducted at the Neurosurgical Critical Care Department (NCCD) of the Burdenko Neurosurgical Institute from October 2010 to January 2014. The prospective study included all patients with stay in the CCU of more than 48 h. The features of somatic and neurological status of patients, signs of infection (systemic inflammatory response), and risk factors (external ventricular drain, ICP sensor, mechanical ventilation, central venous catheter, etc.) were recorded each day [3].

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The results were added to a specifically developed database integrated into an electronic medical record of a patient. CNS infections (CNSIs) were diagnosed based on conventional Definitions of Nosocomial Infections developed by the United States Centers for Disease Control [12].

A total of 8,062 patients were hospitalized to the NCCD over the studied period. A complicated course of disease requiring stay in the CCU for longer than 48 h was observed in 1,153 (14.3%) patients. The information on these patients was systematized and included in the database. The clinical diagnosis of meningitis was made in 146 patients, which accounted for 12.6±1.0% (CI, 10.74—14.66). The diagnostic criteria included neutrophilic cytosis (number of cells in a counting chamber) of more than 150/3, the cerebrospinal fluid (CSF) glucose level of more than 50% of blood glucose, the presence of a CSF pathogen, signs of the systemic inflammatory response syndrome (SIRS), meningeal symptoms, and negative dynamics in the neurological status [12].

The age of meningitis patients ranged from 4 months to 88 years (the mean age was 37.6 years). The proportion of pediatric patients (under 18 years) was similar both in the NM group and in the control group.

Most of the meningitis patients were characterized by the supratentorial localization of the pathological process (72.8±3.7%). The posterior cranial fossa was affected in 20.4% of the examined patients. Spread of the pathological process to the supratentorial and subtentorial regions was observed in 5.4% of the patients, and the spinal level (thoracic spine) was affected only in 1.4% of the meningitis patients **(Fig. 1)**.

The structure of neurosurgical pathologies in the meningitis patients included tumors of a various localization — 67.3%, traumatic brain injuries (TBIs) — 13.6%, and arterial aneurysms and cerebral arteriovenous malformations (AVMs) — 11.6% **(Fig. 2)**. The proportion of patients with acute TBI in both groups was comparable.

According to the severity of the general condition at the time of admission to the Burdenko Neurosurgical Institute, the distribution of patients was as follows: 34 (23.1%) patients had the maximum grade of disability (score of 40 and lower by the Karnofsky scale) and 92 patients (62.6%) were in the compensated condition. The Charlson comorbidity index [13] reflecting comorbid somatic conditions and age was used to estimate the long-term prognosis in patients. In the NM patients, the index ranged from 0 to 10, with the mean of 3.

139 patients underwent surgery (94.6±1.9%). Brain tumors of different localizations were resected in 90 (64.7%) patients, with 1 patient having a combination of a tumor process and a vascular disease (multiple arterial aneurysms). Resection of AVM and clipping of intracranial aneurysms were carried out in 12 (8.6%) patients. Decompressive craniotomy as the primary surgical intervention (mainly in the case of TBI) was made in 6.5% of cases. Endoscopic, endovascular, and shunt surgeries were less common in the meningitis patients **(Fig. 3)**.

The structure of complications at the NCCD was dominated by wound liquorrhea (34±3.9%), wound edge diastasis (17.7±3.1), and hematomas in the surgical field; the last required surgical wound revision in 18 patients (12.2±2.7%).

The duration of stay of the meningitis patients in the CCU varied from 1 to 167 days (mean of 40 bed-days), with 57 patients (38.8±4.0%) being re-admitted to the CCU.

The data were processed by means of parametric and nonparametric statistics, analysis of variance, and contingency tables usually using Statistica v.6 software and a set of programmes based on a book by S. Glants Medicobiological Statistical Data [14].

Results and Discussion

Over 3 years, the rate of meningitis in the group of complicated neurosurgical patients was 12.6±1.0% (CI, 10.74—14.66), and the mortality in the meningitis patients was 31.5±3.8%.

The etiology of meningitis was identified in 89 (61.0±4.0%) of 146 cases. The absolute number of isolated pathogens (gram-positive, gram-negative, and fungi of the genus *Candida*) in patients with meningitis of the identified etiology was 103 **(Table).** The prevailing pathogens in the study were gram-positive cocci, including coagulase-negative staphylococci (CoNS) (33.0±4.6% of the total pathogen number), as well as

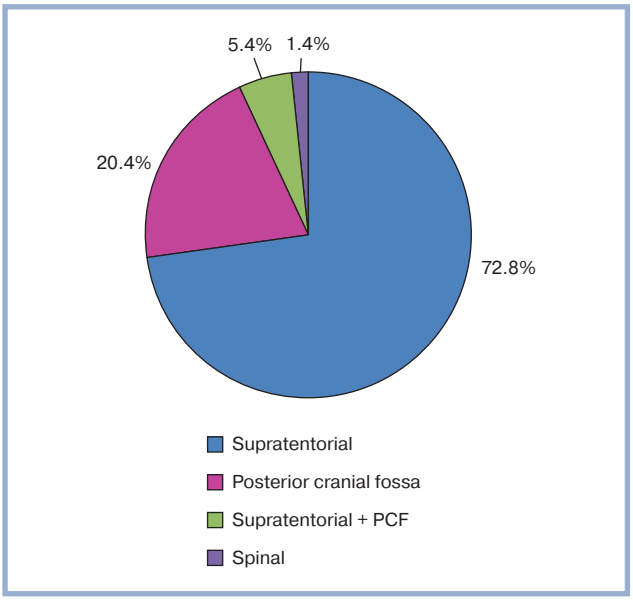

Fig. 1. **The distribution of cases by the localization of neurosurgical pathology in patients with meningitis, %.**

Footnote. PCF — posterior cranial fossa.

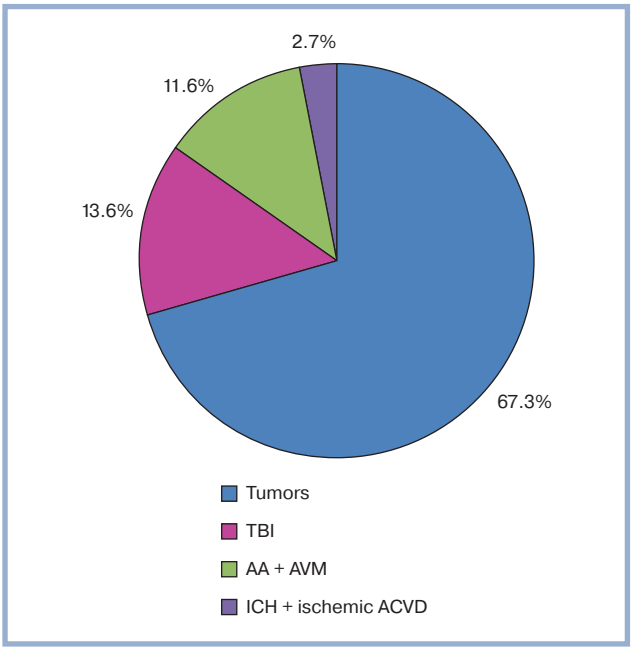

Fig. 2. **The distribution of patients by the major disease, %.**

Footnote. Here and in Fig. 3: AA — cerebral arterial aneurysms; AVM — cerebral arteriovenous malformation; ICH — intracerebral hematoma; ACVD — acute cerebrovascular disorder.

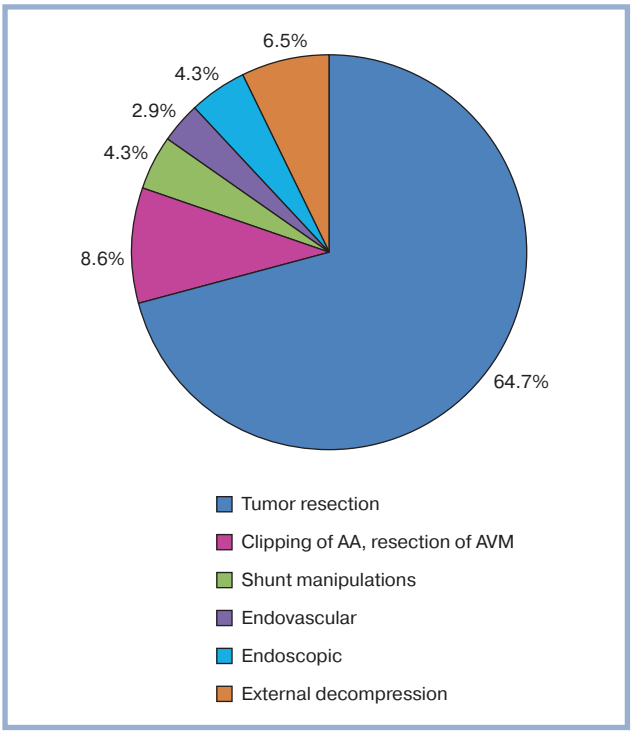

Fig. 3. **The distribution of patients by the type of operative intervention, %.**

gram-negative bacteria (32.0±4.6%). In this case, the proportion of *Acinetobacter baumannii* as an etiologic NM agent was 21.3±4.0%.

Analysis of the NM group and the control group revealed that the mean age (37.6 years) of patients with CNS infection was significantly lower than that of patients without CNS infection (42.4 years). In the group of patients without meningitis, the distribution by gender was about the same in contrast to the patients with meningitis among whom males reliably predominated. The Charlson index was lower in the NM group compared to the control group (score of 3 vs. 3.4, respectively). The meningitis patients were characterized by a longer stay at the NCCD (by 22.9 days), prolonged mechanical ventilation (by 21.4 days), the need for central venous access (by 24.5 days), urinary catheterization, feeding through a nasogastric tube as well as a longer course of antibacterial therapy (by 20.1 days). In the group of NM patients, noninvasive monitoring of systemic hemodynamics was used more frequently (42.2%) compared to the group without NM (29.7%; $p<0.003$). The frequency of ICP monitoring was similar in the two groups of patients. The meningitis patients in comparison with patients without meningitis were more often detected with bloodstream infections (14.8% vs. 4.9%, respectively; $p<0.000$), respiratory tract infections (55% vs. 35.6%, respectively; $p<0.000$), and urinary system infections (56.4% vs. 30.9%, respectively; $p<0.000$). There were statistically significant differences between the NM group and the control group: more frequent use of external ventricular drainage (72.5 and 26.1%, respectively; $p<0.000$); the number of repeated surgeries (64.7 and 36.3%, respectively; $p<0.000$); total operating room stay (417.3 and 337.5 min, respectively; $p<0.000$).

Thus, the risk factors of NM may be tentatively classified into internal and external factors. The internal factors include: age, gender, severity of the patient's condition at the time of neurosurgical disease manifestation, and the nature of the disease. The main external risk factors, according to the literature data [7—11, 15], include external ventricular drainage, shunt surgery, liquorrhea, use of a ICP sensor, and repeated surgery.

In this study, the meningitis patients were characterized by a younger age (despite that the proportion of children in the two groups was not statistically different) and a low Charlson comorbidity index, which may indirectly indicate less comorbid pathology in these patients. These data are consistent with the data of foreign studies on NM [16]. Furthermore, the meningitis patients stayed longer at the NCCD, required the use of appropriate invasive devices (including prolonged mechanical ventilation), and significantly more often underwent neurosurgical interventions (external drainage and repeated surgery). It is remarkable that we did not observe a convincing impact of invasive ICP monitoring on the rate of meningitis.

Thus, the external risk factors were proved to prevail in the etiology of NM in patients of the NCCD, which may indicate the exogenous nature of infection. The

Structure of pathogens isolated from patients with purulentl meningitis

Causative agent	Absolute number of pathogens, *n*=103	%±m
Gr(+)	**41**	39.8±4.8
CoNS	34	33.0±4.6
including		
S. epidermidis	23	22.3±4.1
Streptococcus spp.	3	2.9±1.7
Enterococcus spp.	4	3.9±1.9
Gr (–)	**60**	58.2±4.9
Enterobacteriaceae	**33**	32.0±4.6
including		
K. pneumoniae	16	15.5±3.6
Enterobacter spp.	7	6.8±2.5
S. marcescens	4	3.9±1.9
M. morganii	3	2.9±1.7
E. coli	2	1.9±1.4
P. mirabilis	1	1.0±0.9
Nonfermenting gram-negative bacteria	**27**	26.2±4.3
including		
A. baumannii	22	21.3±4.0
P. aeruginosa	5	4.8±2.1
Candida albicans	**2**	1.9±1.4

presence of infections of a different localization may be considered as an additional factor contributing to the severity of condition of patients with meningitis.

Conclusion

Meningitides in neurosurgery are a serious problem leading to longer treatment, an increased need in antibacterial drugs, and an unfavorable disease prognosis. The risk factors of NM in patients in the CCU may include external ventricular drainage, repeated surgery, long-term stay in the operating room as well as infections of a different localization.

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Commentary

The article analyzes the effect of internal (age, gender, and initial severity of the patient's state) and external (external ventricular drainage, shunting surgery, craniotomy, liquorrhea, and repeated neurosurgical intervention) risk factors on the rate of nosocomial meningitis in patients of the neurosurgical critical care department. The external risk factors were found to dominate, which indicates predominantly exogenous infection of patients.

The topicality of the article is obvious since meningitis ranks third after lower respiratory tract infections and urinary tract infections in the structure of NIs at neurosurgical departments. The development of NM contributes to a longer stay in the CCU, and significantly lengthens the duration of inpatient treatment.

In this paper, the authors performed prospective observation using a large database including 1,153 patients. It is noteworthy that the diagnostics of nosocomial infectious complications of the central nervous system was based on the up-to-date approaches, and the cases were determined according to the Definitions of Nosocomial Infections.

The work by N.V. Kurdyumova, G.V. Danilov, O.N. Ershova, I.A. Savin, E.Yu. Sokolova, I.A. Aleksandrova, and M.A. Shifrin "Features of Nosocomial Meningitis in Patients of a Neurosurgical Critical Care Unit" was performed at a high scientific level and contains conclusions of practical interest. The references quoted in the article reflect the present-day point of view on the issue under investigation.

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