

ETIOLOGIC SPECTRUM OF POST-OPERATIVE MENINGITIS IN NEUROSURGERY

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ETIOLOGIC SPECTRUM OF POST-OPERATIVE MENINGITIS IN NEUROSURGERY (Abstract): Postoperative meningitis is a rare neurosurgical complication with an incidence of 0.3%-1.5%. The most common pathogen in postoperative meningitis in many studies was *Staphylococci*, especially *Staphylococcus aureus*, however recent data reports increasing rates of gram-negative organisms. **Material and methods:** We performed a retrospective study including 32 patients, diagnosed with post-craniotomy meningitis, who underwent neurosurgery, hospitalized between 2016 and 2019 in “Sf. Parascheva” Clinical Hospital of Infectious Diseases from Iasi, in order to evaluate the presence of pathogens in cerebrospinal fluid samples. **Results:** The most common pathogens were *Staphylococcus aureus*, *Streptococcus pneumoniae*, followed by *Acinetobacter speciae*, *Pseudomonas aeruginosa*, *Enterococcus faecalis* and *Escherichia coli*. Antibiotherapy was properly administrated according to the antibiogram. **Conclusions:** Early diagnosis, appropriate antibiotic treatment and an interdisciplinary approach can lead to a favorable outcome. **Keywords:** POST-OPERATIVE MENINGITIS, ETIOLOGIC AGENT. NEUROSURGICAL COMPLICATION.

Postoperative meningitis is a rare neurosurgical complication, related to intraoperative incidental durotomy, with a high mortality and morbidity rate, associated with severe neurological symptoms, prolonged hospitalization and expensive treatment (1). The incidence of meningitis after neurosurgery ranges between 0.3% and 1.5% but increases up to 22% if the patient requires shunts or devices to drain cerebrospinal fluid (CSF) or to monitor intracranial pressure (external ventricular

drains or external spinal drains) (2). There is fewer data regarding the clinical course of postoperative meningitis, however the presence of consciousness disturbance, neck stiffness and fever after neurosurgery can raise suspicions of postoperative meningitis. Any delay in establishing the correct diagnosis and starting proper treatment can lead to high morbidity and mortality (3). The most common pathogen in postoperative meningitis in many studies was *Staphylococci*, especially *Staphylococcus*

aureus, however recent data reports increasing rates of gram-negative organisms (*Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*), *Streptococcus pneumoniae*, *Enterococcus faecalis* and also fungal agents, such as *Candida speciae* (most frequent *Candida albicans*). Bacteria and fungi can be cultured from CSF, but in 54-70% of cases there is no bacterial/fungal growth on CSF cultures (called ‘aseptic meningitis’) (4). Empiric therapy for post-neurosurgical meningitis should be elected taking into consideration the most likely pathogens involved and should be based on the local resistance pattern (5).

MATERIAL AND METHODS

We performed a retrospective study, including 32 patients, diagnosed with post-craniotomy meningitis, from a total of 627 patients, who underwent neurosurgery, hospitalized between 2016 and 2019 in the “Sf. Parascheva” Clinical Hospital of Infectious Diseases, Iasi, in order to evaluate the presence of pathogens in CSF samples.

RESULTS

Our study reported 5,1% incidence of post-craniotomy meningitis. The study group consisted of 20 males (62.5%) and 12 females (37.5%), mostly aged under 60 (75%), living in rural areas (68.75%) (fig. 1). Almost 20% of patients declared a history of meningitis in their medical records.

Over 50% of patients presented underlying medical conditions, such as: cardiovascular diseases (most frequent: arterial hypertension - 50%, myocardial infarction - 31.125%), neoplasia (12.5%), diabetes mellitus (9.375%), pulmonary pathology (9.375%), liver dysfunction (9.375%), renal impairment (6.25%), and obesity (3.125%) (fig. 2).

In 50% of cases, CSF cultures identified a pathogen responsible of post-craniotomy meningitis. The most common pathogen was *Staphylococcus aureus* - 5 cases (25%), followed by *Streptococcus pneumoniae* - 4 cases (20%), *Acinetobacter speciae* - 4 cases (20%), *Pseudomonas aeruginosa* - 3 cases (15%) and *Escherichia coli* - 2 cases (10%), *Enterococcus faecalis* - 2 cases (10%) (fig. 3).

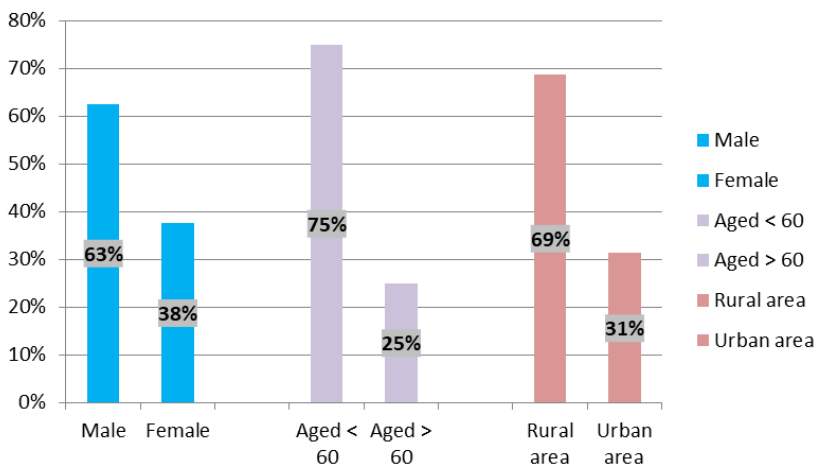


Fig. 1. Characteristics of the patients included in the study

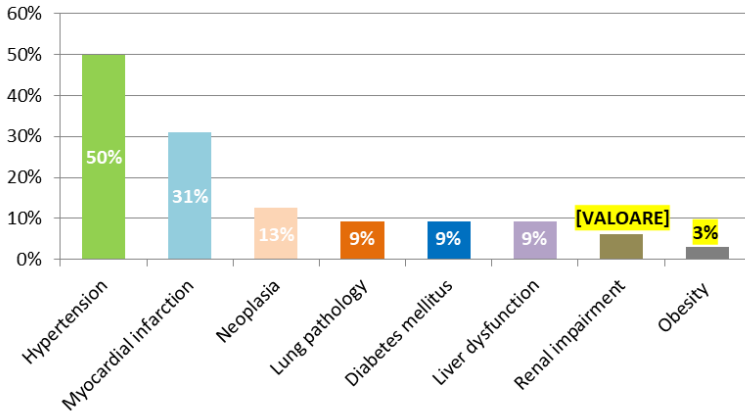


Fig. 2. Associated medical conditions in patients with post-craniotomy meningitis

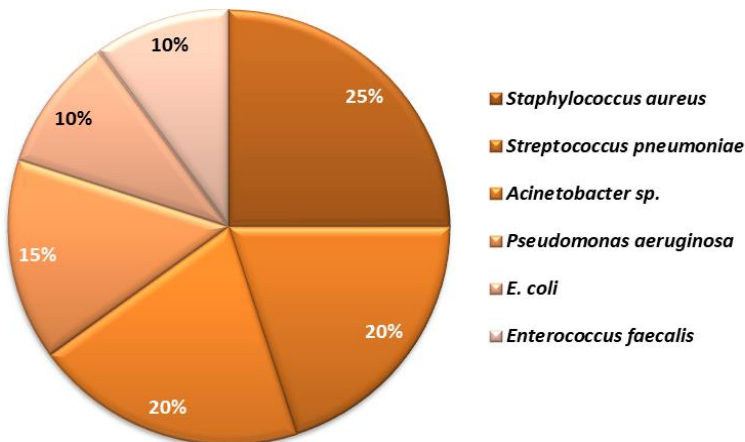


Fig. 3. Most common pathogens identified in CSF cultures

Antimicrobial susceptibility of isolates was determined using the disk diffusion method and every antibiotherapy was administered according to antibiogram. Most commonly, *Staphylococcus aureus* strains were methicillin resistant, with antimicrobial susceptible to glycopeptides (Vancomycin). All *Streptococcus pneumoniae* strains were sensitive to vancomycin, linezolid, levofloxacin, rifampicin and chloramphenicol (not used due to hematologic side effects) and resistant to penicillin. The high rate of *Acinetobacter baumannii* car-

bapenam-resistant has led to polymyxin B administration (intrathecal use of colistin). The treatment of *Pseudomonas aeruginosa* initially included cephalosporins (Ceftazidime), but afterwards it was switched to carbapenems (Meropenem). A switch from cephalosporins (Cefotaxime, Ceftriaxone) to carbapenems (Meropenem) was also performed in *Escherichia coli* strains. *Enterococcus faecalis* isolates were mostly treated with beta-lactam antibiotics and carbapenems, due to high incidence of vancomycin-resistance (tab. I).

TABLE I.
Etiologic agents in post-operative meningitis

Identified etiologic agent	Antimicrobial susceptibility	Number of cases	Percentage
<i>Staphylococcus aureus</i>	Glycopeptides (Vancomycin)	5	25%
<i>Streptococcus pneumoniae</i>	Glycopeptides (Vancomycin), Fluoroquinolones, Linezolid, Rifampicin	4	20%
<i>Acinetobacter baumannii</i>	Carbapenems (Meropenem) or Polymyxin (Colistin)	4	20%
<i>Pseudomonas aeruginosa</i>	Cephalosporins (Ceftazidime), Carbapenems (Meropenem)	3	15%
<i>Escherichia coli</i>	Cephalosporins (Cefotaxime, Ceftriaxone), Carbapenems (Meropenem)	2	10%
<i>Enterococcus faecalis</i>	Beta-lactam antibiotics, Carbapenems (Meropenem)	2	10%

The median period of treatment was 18 days, with favorable course in 23 cases (71.87%) and fatal evolution in 4 cases (12.5%).

DISCUSSION

Our study aimed to evaluate the presence of pathogens in CSF samples submitted to conventional culture, from patients who underwent craniotomy and had presented acute clinical manifestations compatible with meningitis, confirmed by neurologists, neurosurgeons or infectious diseases specialists. Diagnosis of meningitis was defined as a positive CSF culture, associated with meningitis signs and/or symptoms (fever, headache, neck stiffness, photophobia, neurologic symptoms) (6, 7).

It is unlikely that our results were obtained through contamination of the samples, since other postoperative patients without symptoms of meningitis were tested under the same conditions and none produced a positive CSF culture. Therefore, the etiologic agent was not identified in all 32 cases, due to the fact that patients were ad-

ministered pre-operative antibiotherapy.

Blood and CSF samples were periodically tested in order to evaluate improvement or normalization of the biological parameters.

Also, daily clinical evaluations were performed on every patient by an interdisciplinary team (neurologist/neurosurgeon, infectious diseases and intensive care specialists).

CONCLUSIONS

This study confirmed that postoperative meningitis is a rare post-neurosurgical complication. A lumbar puncture should be performed for every patient with suspected meningitis, after undergoing neurosurgery, if there are no contraindications.

Early diagnosis, appropriate antibiotic/antifungal treatment and an interdisciplinary approach can lead to a favorable outcome.

CONFLICT OF INTEREST AND FUNDING

The authors declare that there is no conflict of interest, and they received no specific funding regarding this scientific research.

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NEWS

NEW INTRANASAL AND INJECTABLE GENE THERAPY FOR HEALTHY LIFE EXTENSION

As the global elderly population grows, it is socioeconomically and medically critical to provide diverse and effective means of mitigating the impact of aging on human health. Previous studies showed that the adeno-associated virus (AAV) vector induced overexpression of certain proteins, which can suppress or reverse the effects of aging in animal models. In our study, we sought to determine whether the high-capacity cytomegalovirus vector (CMV) can be an effective and safe gene delivery method for two such protective factors: telomerase reverse transcriptase (TERT) and follistatin (FST). We found that the mouse cytomegalovirus (MCMV) carrying exogenous TERT or FST (MCMVTERT or MCMVFST) extended median lifespan by 41.4% and 32.5%, respectively. We report CMV being used successfully as both an intranasal and injectable gene therapy system to extend longevity. Specifically, this treatment significantly improved glucose tolerance, physical performance, as well as preventing body mass loss and alopecia. Further, telomere shortening associated with aging was ameliorated by TERT and mitochondrial structure deterioration was halted in both treatments. Intranasal and injectable preparations performed equally well in safely and efficiently delivering gene therapy to multiple organs, with long-lasting benefits and without carcinogenicity or unwanted side effects. Translating this research to humans could have significant benefits associated with quality of life and an increased health span (Jaijyan DK, Selariu A, Cruz-Cosme R, *et al.* New intranasal and injectable gene therapy for healthy life extension. *Proc Natl Acad Sci USA* 2022; 119(20): e2121499119).