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Research Paper

Epidemiological and bacteriological profile of postoperative meningitis at Hassan II University Hospital in Fes.

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ABSTRACT: *The study focuses on postoperative meningitis in patients who underwent craniotomy or spinal surgery at the University Hospital of Fez.. The results show that meningitis is more common in men than in women and that adults are at higher risk than children. The most common causes of meningitis are head trauma and brain tumors. Tests on cerebrospinal fluid (CSF) from patients with postoperative meningitis show that levels of proteins, white blood cells, red blood cells, and glucose vary depending on the underlying pathology and bacterial culture results. Patients with abnormal CSF with high levels of neutrophils have a higher risk of complications and mortality. The identified bacteria include Proteus mirabilis, Acinetobacter baumannii, Pseudomonas aeruginosa, Klebsiella pneumoniae, Klebsiella oxytoca, Enterococcus faecalis, Staphylococcus coagulase-negative, and Staphylococcus aureus. The study also highlights the predominance of Klebsiella pneumoniae, a bacterium often associated with nosocomial infections and antibiotic resistance, as well as variability in bacterial antibiotic susceptibility profiles.*

KEYWORDS: *Postoperative meningitis- Epidemiological profile- Biochemistry-Bacteriology*

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I. INTRODUCTION

Postoperative meningitis is a rare complication of intracranial surgery[1][2]. Its diagnosis is challenging due to the subtle and nonspecific symptoms observed in the postoperative period[3]. The cerebrospinal fluid (CSF) is also altered by the surgical procedure, making its interpretation difficult[4]. Furthermore, direct bacteriological examination is often negative[3]. However, prompt diagnosis and appropriate antibiotic therapy are crucial because postoperative bacterial meningitis has a grave prognosis, with a mortality rate that can exceed 20% [3] [5]. Within this group of meningitis cases, there is a subgroup referred to as aseptic or chemical meningitis, which has a different mechanism and a consistently favorable outcome. Identifying this subgroup is important to provide specific management [6] [7]. The neurological functional prognosis can be rapidly compromised. The literature provides substantial evidence on the importance of early initiation of antibiotic therapy in sepsis and septic shock scenarios [7] for reducing patient morbidity and mortality.

The aim of this study is to describe the different epidemiological and bacteriological profiles, as well as the biological progression, of postoperative meningitis encountered in patients undergoing surgery at the Hassan II University Hospital in Fes.

II. MATERIALS AND METHODS

This is a retrospective descriptive study of the different epidemiological profiles of bacterial meningitis encountered in 117 postoperative patients hospitalized in various departments of the Hassan II University Hospital over a period of 3 years (2019-2020-2021).

During the study period, we included all patients who underwent a cytobacteriological study of cerebrospinal fluid (CSF) at the microbiology laboratory, which indicated postoperative meningitis in the intensive care and surgical departments of the hospital.

Excluded from the study were postoperative samples with negative cytobacteriological study results and patients with undocumented meningitis (possibly aseptic) who were treated with antibiotics.

CSF samples were obtained either by lumbar puncture or from the proximal latex end of the drainage tap after careful disinfection and handling in cases of external ventricular drainage placement.

CSF samples were collected in sterile tubes without anticoagulants, preferably before initiating any antibiotic treatment. The total volume of CSF collected depended on the indication and requested examinations, with a minimum of 3 tubes required for biochemical, cytological, and bacteriological analyses. Approximately 10 drops of CSF (~500 µL) were placed in each tube. The tubes were numbered according to the order of collection. The volumes required for commonly performed examinations were as follows: -Biochemistry (Proteins, glucose): 1 tube (500 µL) -Cytology: 1 tube (500 µL) -Bacteriology (culture): 1 tube (500 µL).

The cytobacteriological study involved macroscopic evaluation of the CSF appearance, followed by microscopic analysis for cell counting. After homogenization of the CSF, the number of leukocytes and erythrocytes was determined using a Malassez cell.

A normal CSF sample contains fewer than three white blood cells per mm³. If the CSF contains more than ten white blood cells per mm³, a microscopic examination after staining is performed using two types of stains: methylene blue or May Grunwald-Giemsa stain. This allows the determination of the respective percentages of polymorphonuclear cells, lymphocytes, and monocytes (counting at least 100 elements). The second slide is used for Gram staining to detect the presence of any potential microorganisms.

Culture is performed on enriched media such as chocolate agar and aims to enumerate and isolate the bacteria involved by obtaining well-defined colonies. The calibrated platinum loop method is commonly used for this purpose.

The identification of bacterial strains was based on morphological, cultural, and biochemical characteristics. The precise identification of bacteria (genus and species) was performed using automated methods on the Becton Dickinson Phoenix 100 system.

For each strain, antibiotic susceptibility was determined using automated antimicrobial susceptibility testing (Phoenix 100) in liquid medium and standard disk diffusion antimicrobial susceptibility testing on Mueller-Hinton agar. The interpretation criteria were based on the guidelines of the French Microbiology Society (CASFM/EUCAST 2020).

The detection of extended-spectrum beta-lactamase production is based on the appearance of a "champagne cork" synergy between a CTX, CAZ, or CRO disk and a disk containing clavulanic acid.

The production of carbapenemase by a bacterial strain was suspected when there was reduced susceptibility to Ertapenem (inhibition zone diameter < 25 mm by disk diffusion on agar medium). Any suspected strain was subjected to rapid molecular genotypic screening.

The detection of methicillin-resistant Staphylococcus aureus (MRSA) was performed by testing resistance to cefoxitin (FOX diameter < 22 mm: R; FOX diameter > 22 mm: S).

Data collection was performed by analyzing the bacteriology registry of CSF samples. The following data were collected: patient index, age, sex, results of biochemical and cytobacteriological studies, as well as the antibiogram of isolated bacteria. These data were transcribed into an Excel spreadsheet and presented in the form of percentages, tables, and diagrams.

III. RESULTS

1- Characteristics of the study population :

1.1. Distribution by gender and age groups :

In this study, we identified 117 patients with postoperative meningitis. The distribution by gender showed that 44% of the cases involved female patients, while 56% involved male patients.

We observed that 82% of the meningitis cases were associated with craniotomies, and 18% were associated with spinal surgery. Additional risk factors associated with the initial surgery (craniotomy or spinal surgery) for the development of postoperative meningitis included traumatic context, external ventricular drainage (EVD) placement, and ventriculoperitoneal shunt (VPS) placement. The highest risk factor for the development of postoperative meningitis was the combination of EVD placement and craniotomy, with a risk of 23.1% (Figure 1).

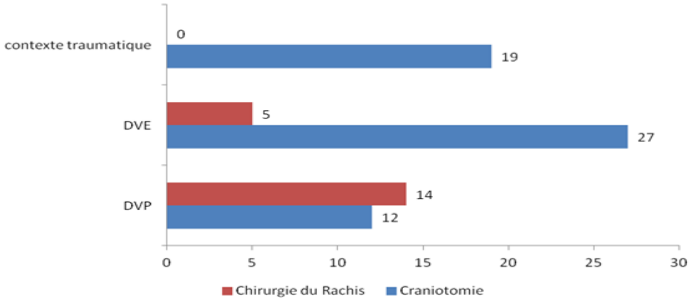

Figure 1: Risk factors for the occurrence of postoperative bacterial meningitis.

The normal values of white blood cells (WBCs) in cerebrospinal fluid (CSF) can vary based on age and the individual's health. The results from CSF samples of patients with postoperative meningitis showed a significant increase in the number of white blood cells, with a maximum value of 64,250 and an average value of 3,056.

The results indicate that patients with brain tumors have the highest levels of white blood cells in their CSF, with a maximum value of 46,000 and an average value of 6,224. In contrast, patients with head trauma have the lowest levels of white blood cells, with a maximum value of 9,000 and an average value of 2,030. The results also demonstrate variation in the neutrophilic response in the CSF among patients. The maximum value of neutrophilic response is 98%, the average value is 80.51%, and the minimum value is 52%.

Bacterial culture results in the CSF of patients with postoperative meningitis showed that 68% of the culture results were negative, while 32% showed positive culture results. This indicates that the majority of patients (68%) did not have bacterial growth in the CSF.

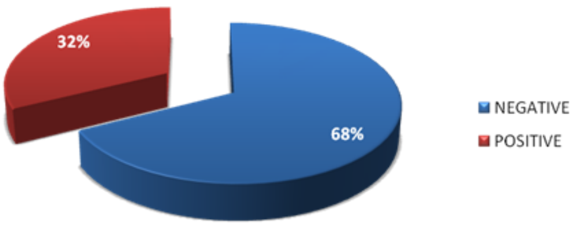

Figure 2: Distribution based on cerebrospinal fluid (CSF) culture results

The results of this study show that the most frequently identified bacteria in the cerebrospinal fluid (CSF) of our patients is Klebsiella pneumoniae, with a rate of 33%. Other bacteria identified in the CSF include Acinetobacter baumannii (23%), Pseudomonas aeruginosa (13%), Staphylococcus aureus (3%), E. coli, Enterococcus faecalis, and coagulase-negative Staphylococcus (8% each), as well as Klebsiella oxytoca and Proteus mirabilis (2% each).

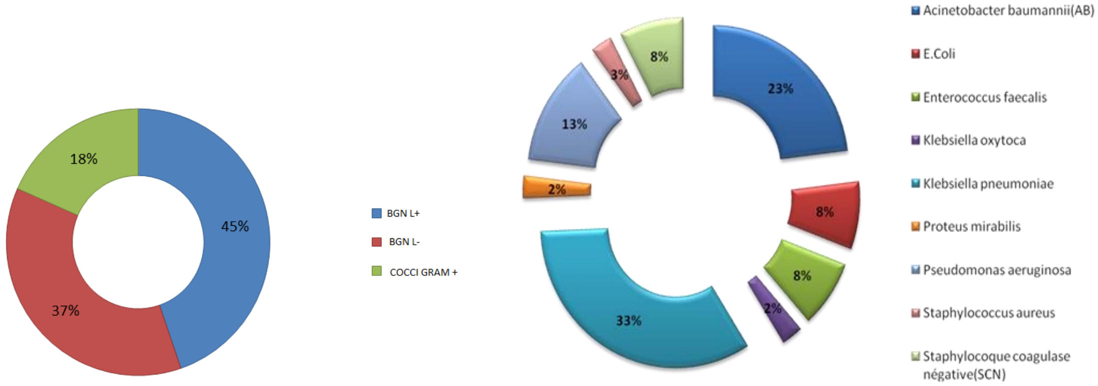

Figure 3 : Distribution of results based on identified bacterial species.

Table 1: Sensitivity profile of Gram-negative bacilli (GNB+).

BGNL + N 17	E.Coli			Klebsiella pneumoniae			Klebsiella oxytoca		
	N3			N13 BLSE N5 Carbapenemase N2			N1		
	S	R	NT	S	R	NT	S	R	NT
AP	1	2	0	0	13	0	0	1	0
AL	1	2	0	0	13	0	0	1	0
AMC	2	1	0	2	11	0	0	1	0
KF	2	1	0	3	10	0	0	1	0
CTX	3	0	0	6	7	0	1	0	0
CRO	3	0	0	6	7	0	1	0	0
CFM	3	0	0	6	7	0	1	0	0
IMP	3	0	0	12	1	0	1	0	0
ETP	3	0	0	12	1	0	1	0	0
NOR	3	0	0	9	4	0	1	0	0
CIP	3	0	0	9	4	0	1	0	0
NA	3	0	0	9	4	0	1	0	0
AK	3	0	0	12	1	0	1	0	0
GN	3	0	0	12	1	1	1	0	0
SXT	2	1	0	4	9	0	0	0	0
CT	3	0	0	13	0	1	0	0	0

The results of this study show that all isolates of E. coli in the cerebrospinal fluid (CSF) samples were sensitive to most tested antibiotics, including third-generation cephalosporins (CTX and CRO), fluoroquinolones (CIP and NOR), carbapenems (IMP and ETP), and aminoglycosides (AK and GN), with a sensitivity percentage of 100%. All isolates were also sensitive to colistin (Table 1).

However, there was resistance to amoxicillin-clavulanate (AMC) and cephalothin (KF), with a resistance percentage of 33.3% for each antibiotic. There was also partial resistance to sulfamethoxazole-trimethoprim (SXT) with a sensitivity percentage of 66.7%.

The results of the five multi-resistant bacteria (MRB) isolated from the CSF of patients with postoperative meningitis show that all patients were infected with the same bacteria, Klebsiella pneumoniae, of which two were carbapenemases.

The sensitivity and resistance profile of Acinetobacter baumannii (AB) in the cerebrospinal fluid (CSF) reveal a high resistance of these strains to most tested antibiotics, with 100% resistance to cefepime, ertapenem, norfloxacin, ciprofloxacin, and netilmicin. However, all AB isolates are sensitive to imipenem and colistin. Additionally, amikacin and trimethoprim/sulfamethoxazole have sensitivity rates of 87.5% and 12.5%, respectively. Antibiotic resistance in AB is concerning, especially for commonly used antibiotics in treating this bacteria.

For the five strains of Pseudomonas aeruginosa, they are sensitive to ceftazidime, imipenem, quinolones, aminoglycosides, and colistin, with a sensitivity of 100% for each tested antibiotic.

For gram-positive bacteria, the three strains of Enterococcus faecalis are sensitive to amoxicillin-clavulanate (AMC), ampicillin (AP), gentamicin (GN), fluoroquinolones, penicillin (P), vancomycin (VA), and teicoplanin (TEIC), with a sensitivity of 100% for each of these antibiotics.

The Staphylococcus aureus isolated in the CSF is sensitive to most tested antibiotics, except for aminopenicillins to which it is resistant. The sensitivity percentage is 100% for AMC, CIP, NA, AK, GN, NOR, LEV, FOX, OX, VA, and TEIC. The resistance percentage is 100% for penicillin (penicillinases), while the three isolates of coagulase-negative Staphylococcus (SCN) are resistant to all tested antibiotics except for vancomycin (VA) and teicoplanin (TEIC), to which they are 100% sensitive. This means that vancomycin and teicoplanin would be the antibiotic choices for treating postoperative meningitis caused by these SCN strains.

Biochemical analysis of cerebrospinal fluid (CSF) provides important information about the health of the central nervous system. The main analyses include protein concentration and glucose levels.

The results of blood glucose in the CSF of 79 patients with postoperative meningitis and negative bacterial cultures show that the maximum value of CSF glucose was 1.43 g/L, the average value was 0.53 g/L, and the minimum value was 0.011 g/L. These results indicate that most patients have normal CSF glucose levels, with an average of 0.53 g/L.

For patients with positive cultures, the results indicate that the glucose level in the CSF significantly differs among different types of bacteria (Table 2).

In the case of infections caused by gram-negative bacilli (GNB-) family bacteria, the average glucose levels were 0.12 g/L. On the other hand, in the case of infections caused by gram-negative bacilli (GNB+) family bacteria, the average CSF glucose levels were 0.23 g/L. For infections caused by gram-positive cocci, the average CSF glucose levels were 0.29 g/L.

Tableau 2 : Table 2: Glucose levels in cerebrospinal fluid (CSF) in postoperative meningitis with positive bacterial culture.

Bacterial Culture Results	Family	Number of Patients	Max Protein Value	Average Value	Min Value
Pseudomonas aeruginosa **Proteus mirabilis** **Acinetobacter baumannii(AB)**	BGN L-	14	0.51	0.12	0.01
Klebsiella pneumoniae **Klebsiella oxytoca** **E.Coli**	BGN L+	17	0.72	0.23	0.01
Enterococcus faecalis **Coagulase-negative Staphylococcus (CNS)** **Staphylococcus aureus**	COCCI GRAM+	7	0.37	0.29	0.27

The results of cerebrospinal fluid (CSF) protein analysis for our patients indicate a significant increase in the average protein quantity in the CSF. The average value is 2.89, with a maximum value of 10.96 and a minimum value of 0.33.

The results presented in Table 3 indicate that the presence of protein in the CSF is high in patients with postoperative meningitis, especially in those whose culture is positive for gram-negative bacteria.

Table 3: Protein levels in cerebrospinal fluid (CSF) based on bacterial culture results.

Bacterial Culture Results	Family	Number of Patients	Max Protein Value	Average Value	Min Value
Pseudomonas aeruginosa **Proteus mirabilis** **Acinetobacter baumannii(AB)**	BGN L-	14	8.62	2.89	0.33
Klebsiella pneumoniae **Klebsiella oxytoca** **E.Coli**	BGN L+	17	10.96	2.95	0.41
Enterococcus faecalis **Coagulase-negative Staphylococcus (CNS)** **Staphylococcus aureus**	COCCI GRAM+	7	3.45	2.89	0.65

IV. DISCUSSIONS

Bacterial meningitis is a significant problem for hospitalized patients. Patients with nosocomial meningitis have been described as a distinct group from community-acquired meningitis with an atypical clinical presentation, unusual bacterial pathogens, and a high rate of unfavorable outcomes [6].

In our study, the external ventricular drain (EVD) associated with craniotomy carries the highest risk of postoperative meningitis. A similar study conducted by Kourbeti et al. in 2015 also identified the placement of a DVST as a significant risk factor, with a risk of 22.4% [7].

Regarding cytology, a study conducted by Huy et al. in 2018 on 115 patients with bacterial meningitis showed that the average white blood cell concentration in the cerebrospinal fluid (CSF) was 634/mm³, with a range from 8 to 4999 cells/mm³. They also linked high levels of white blood cells, including neutrophils, to an increased risk of neurological complications in patients with postoperative meningitis [8].

For culture results, a study conducted in 2018 in Morocco by Ouarssani et al. examined cases of postoperative meningitis in 68 patients and found that culture results were negative in 79.4% of cases [12]. Another study published by Lamsiah et al. in 2020 examined the clinical, microbiological, and evolving characteristics of patients with postoperative meningitis in a hospital center in Rabat. The CSF culture results were positive in 21.4% of cases [13]. This is similar to the results we provided in our study.

Regarding the identified bacterial species, according to a study conducted in Morocco at CHU Ibn Sina in Rabat in 2018 on postoperative meningitis, positive culture results showed that the most frequently identified bacterium in the cerebrospinal fluid (CSF) was Klebsiella pneumoniae, with a rate of 38%. Other bacteria identified in the CSF included Acinetobacter baumannii (26%), Pseudomonas aeruginosa (14%), Staphylococcus aureus (6%), and E. coli (16%) [14], which is very close to our results.

A study conducted in Tunisia showed that patients with postoperative meningitis caused by Gram-negative bacilli (GNB) had significantly higher glucose levels in the cerebrospinal fluid (CSF) than those caused by Gram-negative bacilli with lactose fermentation negative (GNB-). This study is consistent with the results of our study [9]. However, a study conducted in Morocco at the Mohamed V Military Hospital in Rabat showed different results, with higher glucose levels in patients with meningitis caused by GNB- compared to those caused by GNB+ [10].

Rguig et al. in Morocco found that patients with postoperative meningitis had significantly higher levels of protein in the CSF than other groups of patients with bacterial meningitis [11].

V. CONCLUSION

The bacteria responsible for postoperative nosocomial meningitis are numerous, variable, and quite distinct from those found in community-acquired meningitis. They depend on the type of predisposing factor, timing relative to surgery, the type of surgery, and especially the microbiological ecology of the service. However, rapid diagnosis and appropriate antibiotic therapy are essential, as these postoperative bacterial meningitis cases have a formidable prognosis in the absence of early treatment.

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