

ORIGINAL ARTICLE

Analysis and Diagnostic Significance of Cerebrospinal Fluid Laboratory Parameters in Patients with Post-Craniotomy Meningitis

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SUMMARY

Background: Post-craniotomy meningitis (PCM) is a common and serious infectious complication in neurosurgical practice, often associated with considerable morbidity and healthcare burden. Due to the lack of specificity in its clinical manifestations, early diagnosis remains a significant challenge. Although cerebrospinal fluid (CSF) culture is currently regarded as the diagnostic gold standard, its effectiveness is limited by stringent pathogen growth requirements and a relatively low positivity rate, rendering it insufficient to meet clinical needs. Therefore, this study aimed to evaluate the diagnostic value of routine and biochemical CSF parameters in the early identification of PCM.

Methods: A retrospective analysis was conducted on clinical data and CSF test results of 588 PCM patients admitted to our hospital from January 2019 through December 2023. Based on CSF culture results, patients were divided into a culture-positive group (n = 49) and a culture-negative group (n = 539). The distribution of major pathogens was analyzed, and differences in general clinical characteristics as well as routine and biochemical CSF parameters between the two groups were compared. Receiver operating characteristic (ROC) curve analysis was used to assess the diagnostic performance of relevant parameters for predicting CSF culture positivity.

Results: Significant differences were observed between the two groups in terms of gender, history of tumor or traumatic brain injury, ICU admission rate, CSF leakage, and external ventricular drainage ($p < 0.05$), suggesting that these factors may be associated with CSF culture positivity. The most frequently isolated pathogens in the positive group were *Acinetobacter baumannii*, *Staphylococcus aureus*, and *Staphylococcus hominis*. Regarding laboratory findings, the culture-positive group showed significantly higher polymorphonuclear cell counts, mononuclear cell counts, total white blood cell counts, and CSF total protein levels compared to the negative group ($p < 0.05$). ROC analysis revealed good diagnostic performance of these parameters, with AUC values of 0.9398, 0.8516, 0.8687, and 0.7048, respectively. The combined detection of these indicators further improved diagnostic accuracy, with an AUC of 0.9821, significantly outperforming individual parameters.

Conclusions: Routine and biochemical CSF parameters hold significant clinical value for the early identification of PCM. In particular, elevated polymorphonuclear and mononuclear cell counts, total white blood cell counts, and CSF total protein levels are potentially sensitive markers for early screening.

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KEYWORDS

post-craniotomy meningitis, cerebrospinal fluid, laboratory parameters, bacterial culture, diagnostic biomarkers

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INTRODUCTION

Post-craniotomy meningitis (PCM) is a serious and relatively common complication in neurosurgical practice, with an incidence ranging from approximately 0.3% to 8.9% [1]. PCM not only prolongs hospital stay and increases the risk of postoperative infections but may also result in severe neurological impairments and even pose a threat to life [2]. Due to the non-specific clinical manifestations of postoperative infections, early and accurate diagnosis is crucial for timely intervention and improved patient outcomes. However, the current diagnosis of PCM still primarily relies on cerebrospinal fluid (CSF) culture. Although CSF culture is considered the "gold standard" for etiological diagnosis, its positivity rate is influenced by multiple factors such as prior antibiotic administration, specimen collection quality, and culture conditions. Consequently, a considerable number of patients may yield negative CSF culture results despite having meningitis [3,4]. Therefore, PCM diagnosis at present still largely depends on clinical signs and symptoms, underscoring the urgent need for reliable laboratory markers to assist in diagnosis.

Although certain hematologic parameters, such as C-reactive protein (CRP) and interleukin-6 (IL-6), are widely used in the preliminary screening of meningitis, these indicators are easily influenced by systemic inflammatory states and lack sufficient specificity to accurately reflect the presence or severity of central nervous system (CNS) infection [5]. As a direct reflection of the CNS and ventricular environment, CSF routine and biochemical parameters, including white blood cell count, protein, glucose, and chloride levels, are of considerable diagnostic value in infectious diseases. This is especially relevant in culture-negative PCM cases, where CSF routine and biochemical tests can provide critical diagnostic clues and assist in assessing infection severity [6, 7]. Nevertheless, due to the invasive nature and technical difficulty of CSF sampling, its use in clinical practice is relatively limited, contributing to the current paucity of CSF-based studies. Against the backdrop of lim-

ited availability of cerebrospinal fluid samples and low culture positivity rates, clinical research on PCM remains particularly scarce.

Therefore, this study aimed to retrospectively analyze CSF culture results in PCM patients, identify the spectrum of major pathogens in culture-positive cases, and compare the differences in CSF routine and biochemical parameters between culture-positive and culture-negative patients. By identifying key laboratory markers with diagnostic value, we hope to provide more reliable reference indicators for the early recognition and etiological assessment of PCM, thereby facilitating its clinical diagnosis and treatment.

MATERIALS AND METHODS**Study population**

A retrospective cohort study was conducted involving patients diagnosed with PCM following neurosurgical procedures at our hospital between January 2019 and December 2023. The study was carried out in a tertiary care neurology-specialized hospital equipped with comprehensive neurology and neurosurgery departments. A total of 588 PCM cases were included, consisting of 539 patients with negative CSF cultures and 49 with positive CSF cultures.

Inclusion criteria

The inclusion criteria were the following: Patients who underwent their first craniotomy at our center; no documented history of pulmonary, urinary tract, or other systemic infections prior to surgery; axillary body temperature $\geq 38^{\circ}\text{C}$ on at least three occasions within three days postoperatively; complete and accessible clinical data.

Exclusion criteria

The exclusion criteria were the following: Patients with confirmed intracranial infections prior to surgery; patients with severe hepatic, renal, or cardiac dysfunction; postoperative concurrent infections in other organ systems; death from any cause within 24 hours after surgery.

Cerebrospinal fluid analysis

CSF was obtained by lumbar puncture, and 5 - 10 mL of CSF were collected and distributed into three sterile tubes. The first tube was used for biochemical analysis (chloride, total protein, and glucose), the second for microbiological culture, and the third for routine cytological analysis (polymorphonuclear cells, mononuclear cells, red blood cells, and white blood cells). All specimens were delivered to the laboratory at room temperature immediately after collection, and cerebrospinal fluid inoculation along with all routine and biochemical tests were completed within one hour. Routine CSF tests were performed using the Sysmex UF-4000i fully automated body fluid analyzer and matched reagents. After centrifugation, the supernatant was used for bio-

chemical testing using the Hitachi 7600 automated biochemistry analyzer and reagents manufactured by Ningbo Meikang. All procedures strictly followed standard operating protocols. For microbiological cultures, CSF samples were centrifuged, the supernatant was discarded, and 1 mL of the precipitate was inoculated onto blood agar plates. Cultures were incubated at 35°C under 5% - 10% CO₂ for 18 - 24 hours. After visible colony formation, bacterial identification was performed using the Smart MS 5020 system based on matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS).

Statistical analysis

All data were analyzed using SPSS version 22.0. Continuous variables were expressed as mean \pm standard deviation ($\bar{x} \pm SD$) and compared between groups using one-way analysis of variance (ANOVA). Pairwise comparisons were conducted using the least significant difference (LSD) *t*-test. Categorical variables were expressed as frequencies and percentages, and intergroup comparisons were made using the chi-squared test or Fisher's exact test, as appropriate. Correlation analysis was employed to examine the associations between various parameters and CSF culture results. To evaluate the diagnostic performance of CSF laboratory parameters in predicting culture positivity, receiver operating characteristic (ROC) curve analysis was performed. The area under the curve (AUC), sensitivity, and specificity were calculated as primary performance indicators. All statistical tests were two-sided, and a *p*-value of < 0.05 was considered statistically significant.

RESULTS

Comparison of general characteristics between CSF culture-positive and culture-negative groups

Among the 588 patients included in this study, 49 cases were positive for cerebrospinal fluid (CSF) culture, while 539 were culture-negative. A comparative analysis of baseline characteristics between the culture-positive and culture-negative groups revealed several key findings. First, regarding gender and age, the proportion of male patients differed significantly between the two groups ($p < 0.05$), whereas age did not show a statistically significant difference ($p > 0.05$), suggesting that gender may be a contributing factor to CSF culture outcomes. Second, in terms of medical history, a significantly higher proportion of patients in the culture-positive group had comorbid conditions such as tumors and traumatic brain injury ($p < 0.05$), which may be associated with the development of meningitis and a higher likelihood of positive culture results. In addition, a higher proportion of patients in the culture-positive group were admitted to the ICU, experienced cerebrospinal fluid leakage, or underwent external ventricular drainage ($p < 0.05$), possibly reflecting more severe clinical conditions and an increased risk of CSF culture

positivity (Table 1).

Pathogen distribution in CSF culture-positive cases

An analysis of the pathogens isolated from CSF cultures of 49 meningitis patients revealed that *Acinetobacter baumannii*, *Staphylococcus aureus*, and *Staphylococcus hominis* were the most frequently detected organisms, with 8, 5, and 5 cases, respectively. These findings suggest that these pathogens may play critical roles in the pathogenesis of meningitis. Other commonly isolated organisms included *Klebsiella pneumoniae*, *Streptococcus haemolyticus*, and *Pseudomonas aeruginosa*, each found in 4 cases. *Staphylococcus epidermidis* and *Kocuria kristinae* were less common, with 3 isolates each. Less frequently detected organisms included *Acinetobacter calcoaceticus*, *coagulase-negative Staphylococcus*, *Streptococcus sanguinis*, and others. Although these rare pathogens were detected in smaller numbers, they should not be overlooked, as they may also contribute to disease progression and complications. Timely identification and targeted treatment based on culture results are essential to improve clinical outcomes (Table 2).

Comparison of CSF routine and biochemical parameters between groups

A comparison of CSF routine and biochemical indices between the two groups demonstrated significant differences in several parameters. Notably, polymorphonuclear and mononuclear cell counts, white blood cell (WBC) counts, and total protein levels were all significantly elevated in the culture-positive group. These findings provide insight into the biomarker profiles associated with meningitis and offer valuable guidance for clinical diagnosis and therapeutic decision-making (Table 3).

Diagnostic value of CSF routine and biochemical parameters for predicting CSF culture positivity

Receiver operating characteristic (ROC) curve analysis demonstrated that polymorphonuclear cell count, mononuclear cell count, WBC count, and total protein level had good diagnostic value for predicting CSF culture positivity, with area under the curve (AUC) values of 0.9398, 0.8516, 0.8687, and 0.7048, respectively. When these parameters were combined, the AUC increased to 0.9821, indicating further improvement in diagnostic performance (Table 4, Figure 1).

DISCUSSION

This study retrospectively analyzed cerebrospinal fluid (CSF) laboratory parameters in patients with post-craniotomy meningitis (PCM), aiming to explore their potential diagnostic value. This study categorized meningitis cases based on the gold standard of infection and clinical symptoms, effectively excluding non-bacterial meningitis and providing high clinical value data derived

Table 1. Comparison of baseline characteristics between CSF culture-positive and culture-negative groups.

Characteristic	Culture-positive group (n = 49)	%	Culture-negative group (n = 539)	%	p-value
Male (%)	35	71.43	301	55.84	0.035
Age (years)	53.9 ± 15.6	-	53.9 ± 18.2	-	0.252
Tumors	5	10.20	196	36.36	< 0.001
Traumatic brain injury	11	22.45	64	11.87	0.034
Diabetes mellitus	5	10.20	66	12.24	0.675
Hypertension	21	42.86	250	46.38	0.636
Repeat surgery	7	14.29	71	13.17	0.826
ICU admission	22	44.90	396	73.47	< 0.001
CSF leakage	2	4.08	151	28.01	< 0.001
External ventricular drainage	16	32.65	381	70.69	< 0.001
Lumbar drainage	42	85.71	466	86.46	0.885
Mechanical ventilation	18	36.73	226	41.93	0.480

Table 2. Distribution of pathogens isolated from CSF cultures.

Pathogen	Number of isolates
<i>Acinetobacter baumannii</i>	8
<i>Staphylococcus aureus</i>	5
<i>Staphylococcus hominis</i>	5
<i>Klebsiella pneumoniae</i>	4
<i>Streptococcus haemolyticus</i>	4
<i>Pseudomonas aeruginosa</i>	4
<i>Staphylococcus epidermidis</i>	3
<i>Kocuria kristinae</i>	3
<i>Acinetobacter calcoaceticus</i>	2
<i>Coagulase-negative Staphylococcus</i>	2
<i>Streptococcus sanguinis</i>	2
<i>Moraxella osloensis</i>	1
<i>Escherichia coli</i>	1
<i>Enterococcus faecium</i>	1
<i>Staphylococcus saprophyticus</i>	1
<i>Streptococcus constellatus</i>	1
<i>Enterobacter cloacae</i>	1

from real-world settings. The results revealed significant differences between the CSF culture-positive and culture-negative groups in terms of general clinical characteristics as well as routine and biochemical CSF indices, suggesting that certain laboratory parameters may play a crucial role in the early diagnosis of PCM. Additionally, the pathogenic spectrum in culture-positive patients was analyzed, providing evidence to sup-

port optimization of antimicrobial therapy. Notably, the proportion of males in the CSF culture-positive group was significantly higher than that in the negative group ($p < 0.05$), suggesting that gender may be an important factor influencing infection susceptibility. This finding aligns with previous studies and may be attributable to differences in gender hormone levels, immune responses, and behavioral habits. Furthermore,

Table 3. Comparison of CSF routine and biochemical indices.

Indicator	Culture-positive group	Culture-negative group	F-value	p-value
CSF routine parameters				
Polymorphonuclear cells (10 ⁶ /L)	1,325.55 ± 271.14	724.2 ± 137.25	43.241	0.000
Mononuclear cells (10 ⁶ /L)	184.71 ± 68.02	147.11 ± 59.96	23.394	0.000
Red blood cells (10 ⁹ /L)	15.69 ± 5.35	14.78 ± 6.95	0.142	0.706
White blood cells (10 ⁶ /L)	1,510.14 ± 463.06	871.46 ± 257.97	44.115	0.000
CSF biochemical parameters				
Chloride (mmol/L)	120.92 ± 6.94	116.92 ± 7.91	2.670	0.103
Total protein (mg/dL)	165.55 ± 21.97	139.05 ± 19.39	94.279	0.000
Glucose (mmol/L)	2.45 ± 1.34	3.35 ± 1.41	0.827	0.363

Table 4. Diagnostic value of CSF parameters for predicting culture positivity.

Indicator	AUC	95% confidence interval	p-value
Polymorphonuclear cells	0.9398	0.9195 - 0.9601	< 0.0001
Mononuclear cells	0.8516	0.8053 - 0.8979	< 0.0001
White blood cells	0.8687	0.8288 - 0.9086	< 0.0001
Total protein	0.7048	0.6228 - 0.7868	< 0.0001
Combined model	0.9821	0.9713 - 0.9929	< 0.0001

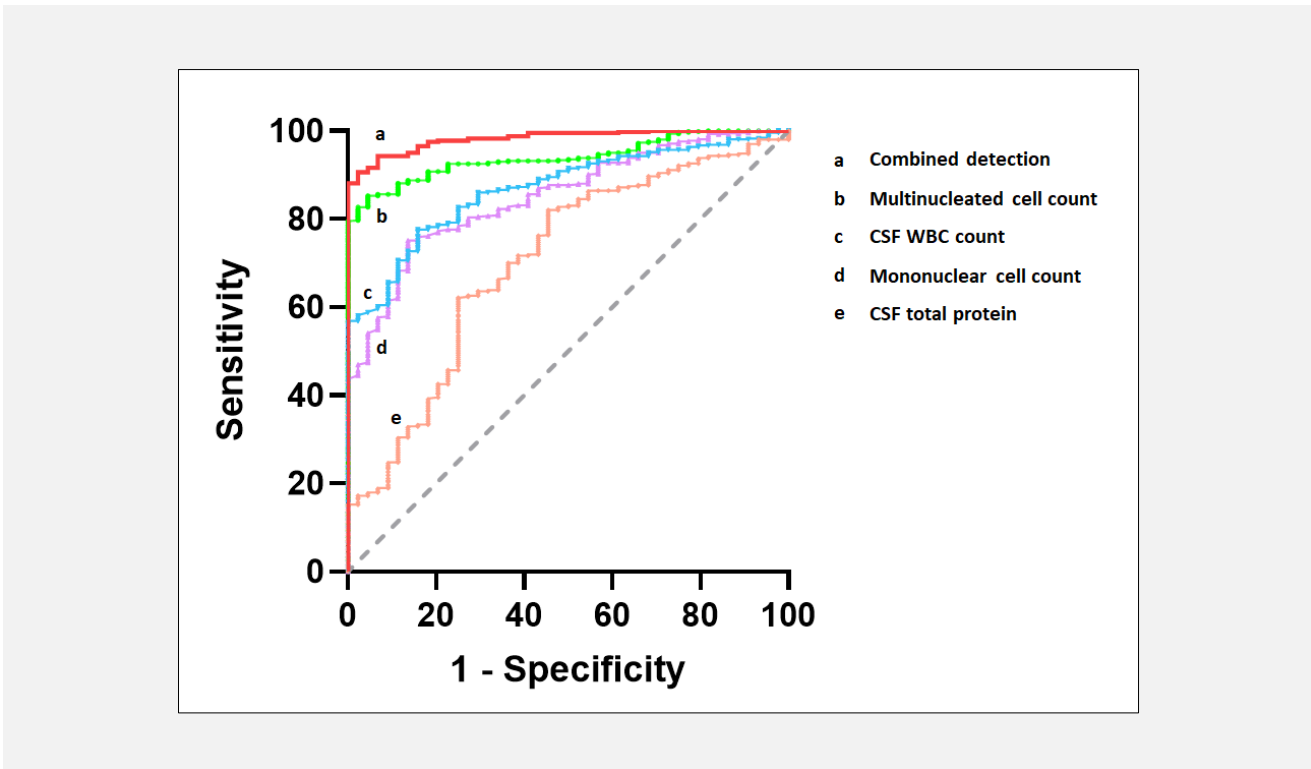


Figure 1. ROC curve analysis demonstrating the diagnostic performance of CSF routine and biochemical parameters for predicting CSF culture positivity.

patients with a history of neoplastic disease or traumatic brain injury were more likely to exhibit positive CSF cultures ($p < 0.05$), potentially due to compromised immune function and prolonged postoperative recovery, both of which elevate the risk of infection. Patients with prolonged ICU stays, postoperative CSF leakage, and external ventricular drainage were also more likely to have positive CSF cultures ($p < 0.05$), highlighting the need for enhanced perioperative management in high-risk individuals. Specifically, minimizing the duration of CSF drainage and ensuring strict adherence to aseptic techniques are essential to reducing the risk of infection [8].

In terms of microbial etiology, *Acinetobacter baumannii* (16.33%), *Staphylococcus aureus* (10.20%), and *Staphylococcus hominis* (10.20%) were identified as the predominant pathogens responsible for PCM. Other detected organisms included *Klebsiella pneumoniae*, *Staphylococcus haemolyticus*, and *Pseudomonas aeruginosa*, which is consistent with previously reported findings [9]. While some Gram-positive cocci, such as *coagulase-negative staphylococci*, are part of normal skin flora, they may play a pathogenic role in postoperative infections. Therefore, antimicrobial regimens should consider both the antimicrobial resistance profiles of the pathogens and the patient's individual infection risk. In addition, less common pathogens such as *Streptococcus sanguinis* and *Moraxella osloensis* were also detected, indicating a diverse spectrum of potential causative agents. This underscores the importance of pathogen-specific diagnostic approaches and individualized antimicrobial therapy based on microbiological findings.

Regarding laboratory indicators, the CSF culture-positive group exhibited significantly elevated multinucleated cell counts, mononuclear cell counts, total white blood cell (WBC) counts, and CSF total protein levels ($p < 0.001$), which is consistent with the known pathophysiological processes of infectious meningitis. Upon microbial invasion of the CSF, a robust inflammatory response is triggered, resulting in marked increases in leukocyte and protein levels. Elevated counts of multinucleated cells and total WBCs typically reflect enhanced immune activation, particularly in bacterial meningitis, where such changes may correlate with the pathogenic characteristics and intensity of the host immune response [10,11].

These laboratory parameter changes can be explained by the pathogenesis of PCM. After bacteria invade the subarachnoid space, the innate immune response of the central nervous system is rapidly activated. Neutrophils are the first to migrate across the blood-brain barrier into the cerebrospinal fluid (CSF), where they eliminate pathogens and release inflammatory mediators, leading to a significant increase in their count - a hallmark of bacterial meningitis. Subsequently, mononuclear cells contribute to immune regulation and antigen presentation, further enhancing the immune response. Meanwhile, the inflammatory process disrupts the blood-

brain barrier, allowing plasma proteins to leak into the CSF, thereby increasing total protein levels. The overall white blood cell count in CSF also rises, reflecting the extent of immune activation. Although these parameters may be elevated in various infections, their combined pattern, cellular composition, and numerical characteristics in the postoperative setting exhibit relative specificity [12,13].

Receiver operating characteristic (ROC) curve analysis further confirmed the diagnostic value of these parameters in the early identification of PCM. Polymorphonuclear cell count (AUC = 0.9398), mononuclear cell count (AUC = 0.8516), total white blood cell count (AUC = 0.8687), and cerebrospinal fluid total protein level (AUC = 0.7048) all demonstrated good differentiating performance. Notably, the combined analysis of these indicators significantly increased the AUC to 0.9821, indicating excellent overall diagnostic efficacy. These findings suggest that a multi-parameter diagnostic approach offers superior performance compared to individual markers and may help reduce the risk of missed or incorrect diagnoses. Given that all the included indicators are derived from routine testing, this approach is highly accessible and particularly suitable for primary healthcare settings lacking microbiological diagnostic capacity. Furthermore, this result also lays the foundation for constructing a risk prediction model for postoperative meningitis, which is expected to develop into a predictive tool or scoring system to assist clinical decision-making through multi-center and large sample studies.

In conclusion, this study, based on real-world data from 588 patients with post-craniotomy meningitis (PCM), systematically evaluated the clinical utility of routine and biochemical cerebrospinal fluid (CSF) parameters in the diagnosis of intracranial infection. The findings demonstrate that polymorphonuclear cell count, mononuclear cell count, total white blood cell count, and CSF total protein level are key diagnostic markers with high differentiating performance. Notably, the combined use of these parameters significantly enhances diagnostic accuracy. Compared to conventional microbiological culture, these routine CSF indicators offer advantages such as simplicity, low cost, and wide accessibility, making them particularly valuable in resource-limited healthcare settings lacking microbiological diagnostic capabilities. Moreover, the study provides a foundational dataset for the development of risk prediction models for PCM. Future research should incorporate longitudinal and dynamic monitoring to improve the temporal resolution and clinical applicability of these markers. Integration with molecular techniques such as targeted next-generation sequencing (tNGS) may further improve pathogen detection rates and specificity. Large-scale, multi-center prospective studies are warranted to advance the precision and efficiency of postoperative infection management in neurosurgical practice.

Declaration of Interest:

The authors declare that they have no conflicts of interest.

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