



Brief Report

Cerebrospinal fluid/blood glucose ratio as an indicator for bacterial meningitis[☆]

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ABSTRACT

Background: Bacterial meningitis is an emergent disease requiring prompt diagnosis and treatment with appropriate antimicrobials. Although the lumbar puncture is widely used as a diagnostic tool for bacterial meningitis, it remains unclear which value in cerebrospinal fluid (CSF) analysis in emergency laboratory tests precisely predicts the presence of bacterial meningitis.

Methods: This is a single-center, retrospective review of medical records to determine which emergency laboratory CSF test results are useful for predicting bacterial meningitis. The diagnosis of meningitis is made when the white blood cell count in CSF exceeds 5 cells/ μL , while the diagnosis of bacterial meningitis additionally requires the growth of a pathogen from a CSF culture or the identification of a pathogen in Gram staining of CSF specimen.

Results: We identified 15 patients with bacterial meningitis and 129 patients with aseptic meningitis. While neutrophil-predominant pleocytosis and a decreased glucose level in CSF can predict the presence of bacterial meningitis, the CSF/blood glucose ratio is more precise (optimal cut-off = 0.36, sensitivity = 92.9%, specificity = 92.9%, area under the curve = .97) even after administration of antimicrobials prior to examination in the emergency department.

Conclusion: This study suggests that the CSF/blood glucose ratio may be a better single indicator for bacterial meningitis. Since the CSF glucose and blood glucose values are promptly and easily obtained from a lumbar puncture, the CSF/blood glucose ratio should be considered as a timely diagnostic indicator of bacterial meningitis. It may also help exclude the diagnosis of bacterial meningitis especially in cases in which no microorganisms can be cultured.

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1. Introduction

Bacterial meningitis is an emergent, life-threatening, infectious disease which requires prompt diagnosis and appropriate antimicrobial therapy. Keeping meningitis in mind as a differential diagnosis, the physician should perform a lumbar puncture if none of the clinical findings can adequately rule out this disease [1]. The presence of pleocytosis confirms the diagnosis of meningitis, but it may not always predict the presence of bacterial meningitis, which requires treatment with antimicrobials. The use of empiric antimicrobials is justified if the physician suspects bacterial meningitis; however, whenever possible, the physician should

refrain from administering antimicrobials without adequate medical grounds for their use.

The association between emergency laboratory examinations of cerebrospinal fluid (CSF) and the diagnosis of bacterial meningitis has rarely been reassessed since the 1980s [2–4]. A recent study reported that CSF lactate concentration is a better, single indicator for predicting bacterial meningitis than conventional markers such as CSF glucose, CSF/blood glucose ratio, CSF protein and CSF total number of leukocytes [5,6]. However, the CSF lactate level is likely to be affected by the administration of antimicrobials [6], and measuring CSF lactate is not routinely performed. Several management guidelines for bacterial meningitis have noted that the measurement of conventional markers in CSF should be considered when assessing the possibility of bacterial meningitis. Given the lack of recent studies examining the utility of emergency laboratory examinations of CSF for predicting the presence of bacterial meningitis, we investigated the diagnostic value of this method for predicting bacterial meningitis at a Japanese tertiary care center.

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2. Methods

2.1. Study setting

This study was conducted at the Tokyo Metropolitan Tama Medical Center, a 789-bed tertiary care teaching hospital in Tokyo, Japan. The emergency department (ED) at this institution takes in an average of approximately 38,000 patients, including 7,200 ambulances, annually. The study was approved by the institutional review board of Tokyo Metropolitan Tama Medical Center with a waiver of informed consent to review the patient records.

2.2. Study design and participants

The current retrospective study consists of a review of medical records to assess the predictive value of emergency laboratory examinations of CSF for bacterial meningitis. We initially included all ED patients who underwent a lumbar puncture between January 1, 2007 and November 31, 2012, as potential candidates for the study. In addition, patients with confirmed bacterial meningitis who were seen at the hospital between January 1, 2005, and December 31, 2006, were included for analysis of the sensitivity and specificity of emergency laboratory examinations in order to offset the small number of cases for this period. Patients who had received a lumbar puncture for the purpose of primary diagnosis other than meningitis, or those with insufficient data in their medical records, were excluded from the analysis. Since the study focused on bacterial meningitis, patients with confirmed tuberculous, carcinomatous, or fungal meningitis were also excluded. In this study, all patients were older than 15 years of age. There were no pediatric patients due to the proximity of a children's hospital, which receives most of the pediatric patients in the area.

2.3. Criteria

Patients with clinical evidence suggesting meningitis and a total cell count in the CSF of more than 5 cells/ μL were, in accordance with previous reports, considered to have meningitis [2,7,8]. Bacterial meningitis was defined as the growth of a pathogen from CSF culture or the identification of a pathogen in a CSF specimen by Gram staining. A patient was considered to have aseptic meningitis if the pleocytosis exceeded 5 cells/ μL , and no pathogens could either be grown in the CSF culture, or identified in the CSF by Gram staining.

2.4. History taking and emergent laboratory examinations

All clinical information, including the background of the patients (such as prolonged steroid and/or immunosuppressant use preceding lumbar puncture and a past history of diabetes mellitus or malignancy), was recorded by an emergency physician. The patients underwent a lumbar puncture at the emergency physician's discretion. The emergency laboratory examinations performed for their predictive value for bacterial meningitis are as follows: initial opening pressure, CSF total cell count, CSF mononuclear cell count, CSF polymorphonuclear cell count, CSF polymorphonuclear/total cell ratio, CSF protein, CSF chloride, CSF glucose, CSF/blood glucose ratio, blood cell count with neutrophil fraction, blood electrolytes, and blood C-reactive protein (CRP).

2.5. Data analysis

Statistical analyses were performed using JMP 10 (SAS Institute Inc, Cary, NC). Each receiver operating characteristic (ROC) curve was drawn based on bacterial meningitis and aseptic meningitis. The point of maximal sensitivity plus specificity on the ROC curve was used as the optimal cut-off value.

3. Results

A total of 573 patients who underwent a lumbar puncture between January 1, 2006, and November 31, 2012, were identified. Fifty-two of these patients were excluded because they met the exclusion criteria (hydrocephalus: 11, subarachnoid hemorrhage: 7, traumatic tap: 5, Guillain-Barré syndrome: 5, multiple sclerosis: 3, neurosarcoidosis: 2, central nervous system metastasis: 2, HIV encephalopathy: 1, and incomplete medical record: 6). We subsequently excluded 10 additional cases of meningitis diagnosed as tuberculous ($n = 5$), carcinomatous ($n = 4$), or fungal meningitis ($n = 1$), even though they met the inclusion criteria for meningitis. Among the 521 eligible patients, 129 were diagnosed with meningitis according to the previously described criterion of a CSF cell count $>5/\mu\text{L}$. Including the 5 bacterial meningitis cases from 2005 and 2006, a final tally of 15 bacterial meningitis cases (2005–2012) and 119 aseptic meningitis cases (2007–2012) were gathered for analysis. Baseline patient characteristics are shown in Table 1 and data from individual cases of bacterial meningitis are shown in Table 2.

The total cell count and polymorphonuclear cell count in CSF were statistically elevated in the bacterial group compared to the aseptic group. The areas under the curve (AUCs) were 0.91 and 0.92, respectively, for the two groups. The AUC of the polymorphonuclear/total cell ratio was 0.85. Importantly, the AUC of the CSF/blood glucose ratio was 0.97 whereas the AUC of CSF glucose alone was 0.90. The sensitivity and specificity figures shown in Table 3 were based on the optimal cut-off.

Other blood tests were also performed but the results were nonspecific. Almost none of the electrolytes and blood chemistries showed any significant difference. The white blood cell count, neutrophil fraction, and CRP showed a significant difference between the bacterial and aseptic groups but their AUCs (0.72, 0.89, and 0.78, respectively) were not as high as in the CSF analysis (Table 3).

We also analyzed whether prior administration of antimicrobials affected the result. Of the total of 134 meningitis cases, 44 cases (6 bacterial and 38 aseptic) had been administered antimicrobials prior to observation at the ED. In the prior administration group, the AUC of the polymorphonuclear cell count, CSF glucose, and the CSF/glucose ratio were 0.96, 0.97, and 0.996, respectively. The other properties in the prior administration group were similar to those for all patients (data not shown).

Table 1
Baseline patient characteristics

Variables	Bacterial N = 15	Aseptic N = 119
Age (median; range)	67; 26–87	37; 16–95
Men	7/15 (46.7%)	62/119 (52.1%)
Current medication		
-Antimicrobial use	6/15 (40%)	38/119 (31.9%)
-Steroid use	2/15 (13.3%)	11/119 (9.2%)
-Immunosuppressant use	0/15 (0%)	1/119 (0.8%)
Diabetes mellitus	3/15 (20.0%)	5/119 (4.2%)
Malignancy	1/15 (6.7%)	8/119 (6.7%)
Signs and symptoms at ED visit		
Glasgow Coma Scale	11.9 (3.2)	14.3 (2.2)
Respiratory rate (breaths/min)	23.7 (7.5)	18.8 (3.7)
Heart rate (in beats/min)	110.2 (17.8)	90.7 (18.1)
Temperature (C)	38.6 (1.4)	37.8 (1.0)
Systolic blood pressure (mmHg)	148.8 (21.9)	123.3 (22.7)
Headache	9/10 (90.0%)	96/101 (95.0%)
Fever ($\geq 38.0^\circ\text{C}$)	10/14 (71.4%)	49/119 (41.2%)
Altered mental status	12/15 (80.0%)	30/119 (25.2%)
Nuchal rigidity	9/10 (90.0%)	44/93 (47.3%)

Values are presented as positive number/number evaluated (percentage) or as mean (SD).

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