

85884_Auto_Edited.docx

Name of Journal: *World Journal of Neurology*

Manuscript NO: 85884

Manuscript Type: ORIGINAL ARTICLE

Retrospective Study

Role of lumbar puncture in clinical outcome of suspected acute bacterial meningitis

Arunava Saha, Shihla Shireen Kanamgode, Sarat Chandra Malempati, Sirshendu Chaudhuri, Jeffrey Scott

Abstract

BACKGROUND

Meningitis remains a significant source of mortality and morbidity, with an incidence of 1 per 100,000 persons in the USA. Guidelines recommend obtaining blood cultures and CSF studies in patients presenting with acute meningitis syndrome, and beginning treatment with broad spectrum antibiotics based on the age and certain predisposing conditions. In some patients however, the diagnostic lumbar puncture (LP) is not performed due to a multitude of reasons, ranging from increased intracranial pressure to failed attempt. In such situations, appropriate therapy is initiated empirically and often continued without establishment of a definitive diagnosis.

AIM

To determine whether a diagnostic LP in acute meningitis syndrome was associated with a better outcome and less duration of antibiotic therapy, along with potential causes for deferral of procedure.

METHODS

A retrospective study was conducted amongst the patients presenting to a 360 bedded community hospital in central Massachusetts with a diagnosis of acute meningitis

syndrome between January 2010 – September 2022. The electronic health records were accessed to collect necessary demographic and clinical data, including etiology of meningitis, lumbar puncture results, reason for procedure deferral, duration of antibiotic therapy and clinical outcome. The patients were subsequently divided into two groups based on whether they received a LP or not, and data was analyzed.

RESULTS

A total of 169 patients admitted with acute meningitis syndrome between September 2010-2022 were included in the study. The mean age of the participants was 54.3 years (SD +/-19.2 years). LP was performed for 130 (76.9%) participants, out of which, 28 (21.5%) showed some growth in CSF culture. The most commonly identified organism was *streptococcus pneumoniae*. Amongst the 39 patients in whom LP was deferred, the major reasons recorded were: body habitus ($n = 6$, 15.4%), and unsuccessful attempt ($n = 4$, 10.3%). While 93 (71.5%) patients with LP received antibiotic therapy, only 19 (48.7%) patients without LP received the antibiotics, with the principal reason being spontaneous improvement in sensorium without any diagnosed source of infection. The mean duration of antibiotic use was 12.3 days (SD +/- 5.6) in the LP group and 11.5 days (SD +/- 7.0) in the non-LP group ($P = 0.56$; statistically not significant). We observed higher long term sequelae in the non-LP group ($n = 6$, 15.4%) compared to the LP group ($n = 9$, 6.9%). Similarly, the death rate was higher in the non-LP group ($n = 7$, 18.0%) compared to the LP group ($n = 9$, 6.9%).

CONCLUSION

LP remains the cornerstone for diagnosing meningitis, but often CSF results are unavailable, leading to empiric treatment. Our study identified that body habitus and unsuccessful attempts were the most common reasons for LP not being performed, leading to empiric antibiotic coverage. There was no difference between the duration of antibiotics received by the two groups, but a lower proportion of patients without LP received antibiotics, attributed to a spontaneous improvement in sensorium. However,

the residual neurological sequelae and death rates were higher in patients without LP, signifying a potential under-treatment.

A LP remains crucial to diagnose meningitis, and a lack of CSF analysis predisposes to under-treatment, leading to higher neurological sequelae and increased chances of death.

INTRODUCTION

Acute bacterial meningitis (ABM) continues to be a significant cause of mortality and morbidity, with an incidence of 1 per 100,000 in the USA [1]. However, the incidence is considerably higher in lower-income countries, such as the meningitis belt of Africa, where it is around 80 per 100,000 individuals. The mortality rate is also significantly high, ranging from 10-50% [2]. Many patients who receive inadequate treatment or survive the acute infection develop chronic neurological sequelae, significantly impairing their quality of life. The most commonly responsible organisms include *Streptococcus pneumoniae*, *Neisseria meningitidis*, and *Haemophilus influenzae* type B, with *Listeria monocytogenes* affecting certain age groups [3].

ABM is a medical emergency that requires prompt recognition, evaluation, and initiation of appropriate antimicrobial therapy based on the microbiome, susceptibility profile, and patient risk factors [4]. Early initiation of antibiotics has been significantly linked to better neurological outcomes with a lower risk of clinical deterioration and death [5]. The classic triad of headache, fever, and neck stiffness may not always be present in ABM and has poor sensitivity. Other symptoms include nausea, vomiting, altered sensorium, photophobia, and seizures. Diagnosing ABM requires a high index of clinical suspicion [6]. Immediate lumbar puncture, followed by broad-spectrum antibiotics and corticosteroids, remains the cornerstone of diagnosis and treatment. 3 Vancomycin and ceftriaxone are the empirical antibiotics of choice, especially in areas with ceftriaxone resistance. Ampicillin is added for neonates, older patients, and

immunocompromised individuals. Glucocorticoids such as dexamethasone should also be initiated to decrease inflammation but discontinued if *Listeria monocytogenes* is confirmed [7]. Cerebrospinal fluid (CSF) findings are usually indicative, with an elevated leukocyte count being the most predictive, and gram stain is often used to guide therapy. However, cases of culture-confirmed meningitis without an elevated leukocyte count in the CSF have also been reported [8].

Many patients with meningitis present with an altered level of consciousness, but neuroimaging is not always necessary to rule out raised intracranial pressure before lumbar puncture [9]. The perceived need for baseline neuroimaging may delay lumbar puncture in the USA. Delays in lumbar puncture are associated with significantly lower diagnostic yield from CSF bacterial culture or PCR, and a delay in antibiotic administration is associated with increased mortality [10]. According to recent Swedish guidelines, neuroimaging prior to lumbar puncture is required only for patients who have signs of imminent brain herniation, focal neurological deficits (excluding cranial nerve palsies), or who have had cerebral symptoms for more than 4 days [10]. The use of Swedish guidelines instead of the Infectious Diseases Society of America guidelines has been shown to reduce unnecessary neuroimaging, decrease the time interval to initiation of therapy, and improve outcomes with a 33% reduction in overall mortality and a 24% increase in favorable neurological outcomes [9,10].

Rationale and Knowledge Gap:

However, in certain cases, obtaining CSF may not be possible for various reasons, with the most common being unsuccessful attempts and the need for radiological guidance in the setting of obesity [11,12]. In such cases, empiric antibiotics may be initiated and continued in the absence of an established diagnosis, leading to unnecessary antibiotic use and potentially contributing to antibiotic-related complications and bacterial resistance.

Objective:

We conducted a review of our experience regarding CSF sampling in patients for whom a diagnosis of meningitis was considered. We aimed to determine the percentage of patients who underwent a successful procedure, the reasons why some patients did not, and the impact of a successful procedure on patient treatment in terms of the duration of antibiotic therapy and overall outcomes.

MATERIALS AND METHODS

We conducted a retrospective study among patients admitted to a 360-bed community hospital in central Massachusetts. All patients who presented to the emergency department between January 2010 and September 2022 with a diagnosis of acute meningitis syndrome were identified and included in the study. Acute meningitis syndrome was defined as the presence of fever and headache with or without neck stiffness and clinical concern for meningitis [13]. The patients were divided into two groups based on whether they received a lumbar puncture to confirm the diagnosis of acute bacterial meningitis. Demographic, clinical, radiological, and microbiological data were reviewed. The patient groups were followed, and necessary data, including demographics, clinical course, CSF analysis results, reasons for procedure deferral, duration of antibiotic therapy, and overall outcome, were collected. The data were analyzed with respect to the duration of antibiotic use and overall outcome. A biomedical statistician performed the statistical review of the study.

RESULTS

During the study period, a total of 169 patients admitted with acute meningitis syndrome were included. ⁵ The mean age of the participants was 54.3 years (SD +/-19.2 years) (Table 1). Lumbar puncture (LP) was performed for 130 (76.9%) participants, out of which, 28 (21.5%) showed some growth in CSF culture. The most commonly identified organism was *Streptococcus pneumoniae*. All cases of meningitis were community-acquired, with no post-surgical or post-traumatic etiology identified.

Among the 39 patients in whom LP was deferred, the major reasons recorded were increased body mass index (BMI)/body habitus ($n = 6$, 15.4%) and unsuccessful attempts ($n = 4$, 10.3%). Three patients refused to provide consent for LP, three were hemodynamically unstable on pressors and started empirically on antibiotics, three had spinal deformities with a history of spinal surgery, and two had supratherapeutic INR >8 at presentation, while no reason was documented for 18 of them. All six patients with obese body habitus in whom LP was deferred had a BMI over 35 kg/m². While 93 (71.5%) patients with LP received antibiotic therapy, only 19 (48.7%) patients without LP received antibiotics, with the principal reason being spontaneous improvement in sensorium without any diagnosed source of infection. The mean duration of antibiotic use was 12.3 days (SD \pm 5.6) in the LP group and 11.5 days (SD \pm 7.0) in the non-LP group ($P = 0.56$; not statistically significant). We observed higher long-term sequelae in the non-LP group ($n = 6$, 15.4%) compared to the LP group ($n = 9$, 6.9%), predominantly focal neurological deficits, hearing loss, and cognitive impairment. Similarly, the death rate was higher in the non-LP group ($n = 7$, 18.0%) compared to the LP group ($n = 9$, 6.9%) ($P = 0.04$).

DISCUSSION

Key Findings and Discussion:

Lumbar puncture remains the cornerstone for diagnosing meningitis, and early initiation of antibiotics after obtaining lumbar puncture without waiting for neuroimaging remains the standard of care [14]. In certain situations, although the clinical syndrome is consistent with meningitis, the diagnosis is not established due to an inability to obtain CSF results. This can be attributed to various factors. Morbid obesity, unsuccessful attempts, spinal deformities, or previous spinal surgery were the principal reasons identified in our study [14,15]. All six patients who had body habitus recorded as a reason for deferring LP had a BMI over 35 kg/m². Obesity makes it

difficult to identify important landmarks and often requires longer LP needles to puncture the depth of skin tissue, which is not always readily available [16].

All 28 patients who had a confirmed diagnosis of bacterial meningitis through growth in the CSF culture were attributed to have acquired it from the community. Five of them were immunocompromised, with two being positive for HIV on antiretroviral therapy and three on chemotherapy for malignancy within the last 6 mo of diagnosis. None of them had a history of trauma or brain injury in the past. There were 14 patients in the LP group who had a previous history of brain tumor surgery but did not have any active post-surgical complications or CSF leak, and all of them had sterile CSF cultures.

Delays in lumbar puncture have been associated with increased mortality in a study done using the national inpatient sample database on patients with cryptococcal meningitis [17]. Our study has shown that in a busy community hospital in central Massachusetts, not all patients admitted with a presumed diagnosis of meningitis had a lumbar puncture done, either on admission or during the hospital stay. There was also increased mortality in patients in whom a lumbar puncture was delayed. This could be attributed to potential undertreatment and delay in the initiation of antibiotics while waiting to obtain a radiology-guided lumbar puncture. Although CSF gram stain results can help guide treatment, empirical antibiotics are often warranted to cover potential organisms based on the patient's age, underlying comorbidities, sensitivity profile of the commonly causative organisms, and the microbiome [2,3]. However, it is difficult to differentiate between bacterial meningitis and aseptic meningitis as both the Meningitest and Bacterial Meningitis Score require CSF analysis [18], while blood cultures, white blood cell count, inflammatory markers, and other laboratory investigations may not be very predictive [5]. In such situations, the decision to defer antibiotics to evaluate another potential attributable cause of the presenting symptom complex may prove fatal. The lack of existing guidelines to aid in the management of such patients often leads to significant variability in treatment [19].

LP has traditionally been a procedure conducted by the internal medicine team. However, with an increasing number of patients undergoing spinal surgery and the recent obesity epidemic, ultrasound-guided LP has become the new norm. LP becomes more challenging with an increase in needle size, and landmarks become difficult to palpate ^[11,20]. This also leads to inadvertent delays in achieving a diagnosis, as radiology-guided lumbar puncture slots are not promptly available.

In our study, there was no significant difference in the duration of antibiotics received by the two groups, but a lower proportion of patients without LP received antibiotics. This was mostly attributed to a lack of an established diagnosis of meningitis in these patients. In such situations, the decision to empirically treat lies with the clinician and also depends on other potential confounding factors that can explain the symptom complex. Additionally, many patients experienced spontaneous improvement in sensorium and were deemed not to require antibiotics. However, the residual neurological sequelae and death rates were also found to be higher in these patients, possibly resulting from persistent underlying and untreated infection.

Strengths and Limitations:

The strengths of the study include a population presenting to a community hospital over a significant time period, which is representative of the general population and can be extrapolated to day-to-day clinical scenarios. Limitations involved the retrospective nature of the study and the smaller sample size included. Further large-scale studies are needed to develop an optimum guideline for the evaluation of meningitis in the absence of a definitive CSF analysis and to determine the best empirical antibiotic regimen for patients in whom LP is deferred.

CONCLUSION

Lumbar puncture remains the gold standard for diagnosing acute bacterial meningitis, but in certain cases, it may not be feasible to obtain CSF due to various factors. There is a definite association between deferral of lumbar puncture and poor outcomes in patients with suspected acute meningitis syndrome. Lack of CSF analysis may be associated with unnecessary antibiotic therapy in some and poor outcomes related to inadequate treatment in others. Clinicians should be aware of these challenges and make informed decisions based on clinical judgment, patient risk factors, and the need for empiric antibiotic therapy.

ARTICLE HIGHLIGHTS

Research background

The classic triad of headache, fever and neck stiffness is not always present in acute meningitis syndrome; however, diagnosis with lumbar puncture and immediate empirical antibiotic coverage remains cornerstone of therapy. In some cases, CSF analysis is also not available, leading to long term empiric antibiotics use or potential undertreatment.

Research motivation

We aimed to investigate the correlation between lumbar puncture in patients with suspected acute bacterial meningitis and their overall outcome, and determine if empirical therapy was beneficial.

Research objectives

To determine the percent of patients presenting with acute meningitis syndrome who underwent a successful diagnostic procedure, the reasons why some patients did not, and the impact a successful procedure had on patient treatment in terms of duration of antibiotic therapy and overall outcomes.

Research methods

We conducted a retrospective study among patients presenting with acute meningitis syndrome to a 360-bed community hospital in central Massachusetts. The patients were divided into two groups based on whether they received a lumbar puncture to confirm the diagnosis of acute bacterial meningitis. Data was collected and analyzed with respect to duration of antibiotic use and overall outcome.

Research results

A total of 169 patients admitted with acute meningitis syndrome were included. Lumbar puncture (LP) was performed for 130 (76.9%) participants, out of which, 28 (21.5%) showed some growth in CSF culture. Amongst the 39 patients in whom LP was deferred, 21 had no reason documented, 6 had increased BMI ($n = 6$, 15.4%), and 4 had unsuccessful attempts. While 93 (71.5%) patients with LP received antibiotic therapy, only 19 (48.7%) patients without LP received the antibiotics with similar mean duration in both groups. Long term sequelae and death was higher in the non-LP compared to the LP group.

Research conclusions

Deferral of lumbar puncture is associated with poorer outcomes in patients with suspected acute meningitis syndrome. Lack of CSF analysis may be associated with unnecessary antibiotic therapy in some and poor outcomes related to inadequate treatment in others.

Research perspectives

Further prospective studies are needed to determine the exact reasons for deferral of lumbar puncture in patients. This will allow to identify potential caveats and ensure availability of adequate resources to obtain a CSF sample in all patients who need it.

3%

SIMILARITY INDEX

PRIMARY SOURCES

- | | | |
|----------|---|-----------------|
| 1 | onlinelibrary.wiley.com
<small>Internet</small> | 29 words — 1% |
| <hr/> | | |
| 2 | Judith I. van Zwienen-Pot, Ilse Reinders, Lisette C. P. G. M. de Groot, Anne Marie Beck et al. "Effects of Nutritional Interventions in Older Adults with Malnutrition or at Risk of Malnutrition on Muscle Strength and Mortality: Results of Pooled Analyses of Individual Participant Data from Nine RCTs", <i>Nutrients</i> , 2023
<small>Crossref</small> | 26 words — 1% |
| <hr/> | | |
| 3 | Rodrigo Hasbun. "Progress and Challenges in Bacterial Meningitis", <i>JAMA</i> , 2022
<small>Crossref</small> | 16 words — 1% |
| <hr/> | | |
| 4 | www.ncbi.nlm.nih.gov
<small>Internet</small> | 14 words — < 1% |
| <hr/> | | |
| 5 | hdl.handle.net
<small>Internet</small> | 12 words — < 1% |

EXCLUDE QUOTES ON

EXCLUDE BIBLIOGRAPHY ON

EXCLUDE SOURCES

EXCLUDE MATCHES

OFF

< 12 WORDS