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Diagnosing Meningitis at the Emergency Department – How Accurate are we?

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Abstract

Objectives: Meningitis is associated with a high mortality rate and neurologic sequelae are common among survivors. However, it is a diagnostic challenge and can be under-recognized at the Emergency Department (ED). We aimed to determine the accuracy of the diagnosis of meningitis made in the ED and identify features associated with diagnostic accuracy.

Methods: A retrospective review of case records was carried out. Cases presenting to the ED an urban tertiary center from 2013 to 2017 with a diagnosis of meningitis in its records were selected. Information about patient demographics, clinical features and course were collected for analysis. Accuracy was determined by comparing the ED diagnosis with discharge diagnosis on inpatient record.

Results: There were 83 cases of meningitis diagnosed in the ED during the study period. The median age was 36 (range 15 to 96) years old and 54 (65.1%) of the patients were male. Fever (n=76, 91.6%), headache (n=50, 60.2%) and altered mental status (n=24, 28.9%) were the most common symptoms and neck stiffness (n=28. 33.7%), Glasgow Coma Score less than 15 (n=16, 19.3%) and Kernig's sign (n=11, 13.3%) were the most common signs. The accuracy of ED diagnosis of meningitis was 28.9%. Among the cases which were not meningitis, the most common diagnoses were other infections followed by conditions involving the musculoskeletal and central venous systems. Vomiting (OR 3.33, 1.24-9.09, p=0.021) was the only feature associated with diagnostic accuracy.

Conclusion: Meningitis is a great mimicker and can be difficult to diagnose in the ED. Given the lack of clinical features which can be used to differentiate meningitis from other conditions, a high index of suspicion is required so that interventions can be promptly initiated to reduce mortality and morbidity.

Keywords: Diagnosis, Emergency Department, Meningitis

Introduction

Meningitis is defined as the inflammation of the meninges which consist of the pia, arachnoid and dura mater. It is typically characterised by an elevated number of white blood cells in the cerebrospinal fluid. Causes include infection due to bacteria, viruses, fungi and parasites, as well as medications such as non-steroidal anti-inflammatory drugs. Streptococcus pneumoniae and Neisseria meningitidis are the main causative organisms responsible for community-acquired bacterial meningitis in adults.

There are approximately 1.2 million cases of meningitis per annum worldwide[1]. Meningitis is associated with high mortality rates in the world and is among the 10 most common infectious disease contributors. It is responsible for approximately 135,000 deaths throughout the world each year[2]. Mortality is higher in the elderly and healthcare associated bacterial meningitis[3]. Neurologic sequelae are common among survivors.

The diagnosis of meningitis is crucial but may prove to be challenging at the Emergency Department (ED) as patients may present with non-specific signs and symptoms. A study of 650 patients showed mimics were common and included right-sided pneumonia, gastroenteritis, otitis, tonsillitis, exanthema subitum, and urinary tract infections[4]. Therefore, the aims of this observational study are to determine the diagnostic accuracy of meningitis in the ED and to identify features associated with diagnostic accuracy. We hypothesize that the accuracy was low as diagnosis of meningitis can be difficult in the ED.

Materials and Methods

Setting

This study was conducted in the ED of an urban tertiary hospital which had an annual attendance of about 150,000 patients.

Design

This was a retrospective study based on the review of case records. All cases that presented to the ED from 1 January 2013 to 31 December 2017 with the ICD-10 diagnosis codes containing meningitis were included. The patients' medical

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records were accessed for data collection and tabulated in a standardized form. Information including demographics, clinical features, investigations performed, clinical progress in the ED and hospital, length of the patient's stay in the hospital, as well as the diagnosis in ED and at discharge were collected for analysis. Any information which was not documented was analysed as not present. The discharge diagnosis on inpatient record was used as the standard to determine the accuracy of the diagnosis at the ED.

This study was approved by Institutional Review Board (CIRB 2018/2241). Waiver of patient consent was granted.

Statistical Methods

Statistical analysis was performed using SPSS version 22 (SPSS, Chicago, L). Categorical and continuous data were presented as frequency with percentage and median with range respectively. Association between categorical variable was assessed using chi-square test.

RESULTS

Patient Characteristics

There were 83 cases of meningitis diagnosed in the ED during the study period, average to about 17 cases per year. (Table 1).

Clinical Features

At presentation to the ED, fever, headache and altered mental status were the most common symptoms, whereas neck stiffness, Glasgow Coma Score less than 15 and Kernig's sign were the most common signs (Table 2). The classic triad of fever, headache and neck stiffness was only present in 16 (19.3%) patients.

Table 1. Patient Characteristics

Median age, in years (range)	36 (15 to 96)
Gender	n (%)
Male	54 (65.1)
Female	29 (34.9)
Race	n (%)
Chinese	37 (44.6)
Malay	25 (30.1)
Indian	13 (15.7)
Others	8 (9.6)

Investigations Performed

Computed Tomography of the head (CT head) was performed at the ED for 79 (95.2%) patients. Only 2 scans showed features suggestive of meningitis – one was reported as mild diffuse brain parenchymal edema as evidenced by crowding of sulci and relative narrowing of the basal cisterns, the other was reported as suggestion of diffuse leptomeningeal enhancement, which may be due to meningitis in the context of sepsis.

Blood culture was taken for 77 (92.7%) patients, with Streptococcus agalactiae (n=3, 3.6%) being the most common organism detected. Lumbar puncture was performed in 29 (34.9%) patients. Among these, cerebrospinal fluid culture grew Streptococcus agalactiae, Streptococcus intermedius and Eikenella corrodens. (Table 3)

Clinical Management at the ED

All patients were admitted to the hospital for further care. Empirical antibiotic coverage was initiated at the ED according to institutional guidelines in 73 (88.0%) patients. Acyclovir was given in 28 (33.7%) patients and dexamethasone in 3 (3.6%) patients. One (1.2%) patient required emergent right frontal extra ventricular drain insertion for relief and monitoring of raised intracranial pressure.

Clinical Outcome

The mortality in this case series was 3.6%. Two (2.4%) patients had residual neurological deficits at discharge from

Table 2. Clinical features

Clinical symptoms	n (%)
Fever	76 (91.6)
Headache	50 (60.2)
Altered Mental Status	24 (28.9)
Vomit	22 (26.5)
Neckache	18 (21.7)
Lethargy	9 (10.8)
Photophobia	8 (9.6)
Seizure	7 (8.4)
Giddy	5 (6.0)
Clinical signs	n (%)
Neck stiffness	28 (33.7)
Glasgow Coma Score less than 15	16 (19.3)
Kernig's sign	11 (13.3)
Abnormal pupils	3 (3.6)
Neurological deficit	3 (3.6)
Brudzinski's sign	2 (2.4)

Table 3. Patient Characteristics

Blood Culture	n (%)
No bacterial growth	67 (80.7)
Streptococcus agalactiae	3 (3.6)
Klebsiella pneumonia	2 (2.4)
Streptococcus pneumonia	1 (1.2)
Mixed bacterial growth	1 (1.2)
Skin contaminant	3 (3.6)
Cerebrospinal Fluid Culture	n (%)
No bacterial growth	27 (32.5)
Streptococcus agalactiae	1 (1.2)
Mixed bacterial growth	1 (1.2)

Table 4. Diagnosis at Hospital Discharge

Diagnosis	n (%)
Meningitis	24 (28.9
Other infections	33 (39.8)
Upper respiratory tract infection	11
Viral fever	7
Sepsis, source unspecified	4
Pneumonia	4
Sinusitis	2
Cellulitis	2
Urinary tract infection	1
Otomastoiditis	1
Dengue	1
Musculoskeletal conditions	12 (14.5)
Headache	11
Neck pain	1
Neurological conditions	9 (10.8)
Seizure	3
Cerebral abscess	1
Intracranial hypertension	1
Transient ischemic attack	1
Encephalopathy	1
Syncope	1
Central cord stenosis	1
Psychiatric conditions	3 (3.6)
Drug withdrawal	1
Schizophrenia	1
Bipolar disorder	1
Metabolic conditions	2 (2.4)
Diabetes mellitus	1
Gout	1

the hospital. The median length of hospital stay was 4 (range 1 to 42 days), including time spent in the rehabilitation ward.

Accuracy of ED Diagnosis

Among these 83 cases with meningitis diagnosed at the ED, 24 were diagnosed with meningitis based on the discharge diagnosis on inpatient record, giving an accuracy of 28.9%. The most common diagnoses at discharge for those without meningitis included other infections followed by conditions involving the musculoskeletal and central venous systems (Table 4).

Vomiting was the only significant predictor for an accurate ED diagnosis of meningitis among all cases of meningitis suspected in ED, OR 0.30 (95% CI 0.11-0.83, p=0.021).

Reattendance

Thirteen (15.7%) cases were diagnosed by ED as meningitis at a second attendance. The median number of days between the first and second attendances was 2 (Range 0 to 5). The misdiagnoses at the first attendance included upper respiratory tract infection (n=6, 46.2%), viral fever (n=5, 38.6%), benign paroxysmal position vertigo (n=1, 7.6%) and seizure (n=1, 7.6%). Among these, 6 (46.2%) patients were diagnosed with meningitis based on the discharge diagnosis on inpatient record. The accuracy of ED diagnosis of meningitis was not significantly different for this group of patients (p=0.135).

Discussion

In our study, the accuracy of meningitis diagnosed at the ED was low. Although meningitis was diagnosed in the ED, the inpatient team had decided otherwise following hospital admission. We postulated that the low accuracy could be due to 4 main reasons. Firstly, ED physicians might have erred on the side of caution by assuming the worst and treating the patients as for meningitis. This lower threshold for diagnosis and treatment was likely due to the significant morbidity and mortality associated with this condition. Next, ED physicians could not rely on pertinent features of history or physical examination to make the diagnosis as these patients had non-specific signs and symptoms. For instance, the classic triad of fever, headache and neck stiffness was present in less than 20% of the patients. Similarly, meningeal signs such as neck stiffness was present in about a third of patients while Brudzinski's sign and Kernig's sign were present less commonly. Furthermore, even when present, no isolated feature had been reported to be diagnostic of meningitis[5-7].

Lastly, the length of stay at the ED was shorter than at the inpatient unit. Additional time may be necessary for further clinical evaluation, performing additional investigations and observing the patient's clinical progress in order to improve the diagnostic accuracy of meningitis.

We also found that patients who had experienced vomiting were more likely to have an accurate diagnosis of meningitis at the ED. This could be explained by the following mechanism in meningitis, the intracranial pressure may be elevated as a result of the infectious and/or inflammatory processes, thus stimulating area postrema which is the vomiting centre of the brain, leading to vomiting. However, further research involving different patient populations in the ED setting would be necessary to evaluate this finding before any recommendation can be made for its utility in the ED. For now, we emphasize that ED physicians would need to take into consideration the entire clinical context of the patient and use relevant investigations to confirm or refute the diagnosis.

CT head may be performed when evaluating a patient for meningitis. Potential findings include acute cerebral swelling; moderate widening of basal cisterns, interhemispheric fissure, and subarachnoid convexity space; ventricular widening; subdural collection; focal cortical necrosis; cerebral infarcts; contrast enhancing basal meninges, ependymitis, or generalized cerebral atrophy[8]. CT head could also be used to exclude other intracranial pathology such as a mass lesion which may account for the patient's presentation. In our study, CT head was performed in more than 95% of patients but the incidence of positive finding for meningitis was very low. As with previous reports, CT scan findings may be normal in more than 50% of patients, hence the diagnosis of meningitis could not made on the basis of imaging studies alone[9,10].

Another important diagnostic study to perform in a patient with meningitis would be lumbar puncture. However, caution must be taken in selecting appropriate patients as lumbar puncture was responsible for up to 30% of deaths in the acute stages of meningitis as a result of coning from raised intracranial pressure[11]. Thus, CT head should be done in patients showing signs of raised intracranial pressure before performing lumbar puncture to avoid this fatal complication. In our setting, lumbar puncture was not routinely performed in our ED but was carried out by the inpatient team upon admission. As a result, not all patients had lumbar puncture performed. Lumbar puncture was performed in 29 patients after evaluation by the inpatient team. Of these, 24 patients were eventually diagnosed with meningitis. Cerebrospinal fluid culture was only positive in 2 patients and this was likely due to our institutional practice as antibiotics were administered early at the ED before lumbar puncture was performed at the inpatient unit.

In our study, 88% of patients who were admitted by the ED with presumed meningitis were commenced on guideline-appropriate antibiotics for meningitis. In comparison to this, a study conducted in Netherlands showed that only 33% of patients received appropriate antibiotics in compliance with the Dutch guidelines[12]. The need to administer antibiotics quickly in meningitis must be highlighted as delay between presentation and antibiotic administration was associated with worse patient outcomes[13,14]. Therefore, ED physicians must be aware of institutional guidelines for coverage. An accessible reference guide or use of an electronic prompt are viable options which can serve as a useful reminder as meningitis was uncommonly encountered in the ED. On the other hand, there was no well-designed studies available to assist the ED physician in deciding when to withhold antibiotics when viral meningitis is suspected. In our institution, all cases of meningitis would be admitted for inpatient evaluation. It may be possible to discharge a patient with viral meningitis to an early outpatient follow-up, with advice to return to the ED immediately if unwell[15]. However, risk assessment must be performed and discussed with the patient and/or family.

Adjunctive therapies of meningitis included acyclovir and dexamethasone. Acyclovir was indicated when there was concern for concomitant encephalitis due to herpes simplex virus. Dexamethasone should be given for meningitis due to Streptococcus pneumonia as it would reduce inflammation in the brain and subsequently the incidence of permanent neurologic sequelae such as hearing loss or focal neurological deficit[16-20]. However, dexamethasone was not shown to reduce mortality[21]. Interestingly, the use of adjunctive dexamethasone did not show significant benefit in developing regions. This was attributable to poor nutrition, delayed presentation, presence of chronic diseases such as HIV, or the inadvertent inclusion of cases of tuberculous meningitis[22,23]. The administration of dexamethasone in our study was only done for 3.6% of admissions suspected of meningitis. We postulated that this could be a reflection of the uncertainty surrounding the diagnosis of meningitis. Further efforts at quality improvement in care delivery would be necessary to ensure that dexamethasone was given along with antibiotics when meningitis was suspected in the ED.

Neurosurgical intervention was rare and may be indicated for monitoring or relieving raised intracranial pressure in patients with meningitis[24]. In our study, only 1 patient required an emergent right frontal extra-ventricular drain insertion for relieving and monitoring of raised intracranial pressure. Although uncommon, ED physicians should be aware of the indications for neurosurgical referral. Raised intracranial pressure and hydrocephalus should be promptly detected so that timely neurosurgical referral could be made for placement of an extra-ventricular drain or ventriculo-peritoneal shunt to improve clinical outcomes for patient[25,26].

Study Limitations

Our study was based on a single centre's experience and therefore would not be able to give a full perspective of meningitis in ED with a different setting and beyond the ED. Furthermore, aspects of clinical management were guided by institutional practices which may not be applicable in other centres, thus affecting generalizability of our results. A major

variation should be highlighted – lumbar puncture was not performed at the ED but at the inpatient unit. Therefore, all patients with an ED diagnosis of meningitis would be admitted to the hospital. Consequently, it was not necessary to differentiate between the various causes of meningitis at the ED as this would be further evaluated at the inpatient unit. Nonetheless, we believed that the results of our study had provided a glimpse into challenges of diagnosing meningitis in the ED. This knowledge would be useful for ED physicians in their assessment of patients with suspected meningitis.

Next, a retrospective study was carried out as meningitis was not a common condition with only about 17 cases a year in our context. Therefore, we could only identify patients at the ED who were diagnosed with meningitis and not patients who were assessed not to have meningitis. This thus precluded us from reviewing case records, performing phone follow up, sending out letters or checking the registry of deaths to ascertain the outcome for this group of unidentified patients. We have hence limited the definition of accuracy to the number of patients who had meningitis among all who were diagnosed with meningitis at the ED. We attempted to address this limitation by identifying 13 patients who had a second attendance to the ED which prompted a diagnosis of meningitis.

Also, due to the retrospective nature of this study, data was collected based on the documentation of various medical personnel in the ED record instead of forms with predefined data fields. The robustness of the data would be affected by inconsistency in documentation as well as missing and incomplete information. For instance, details about comorbidities and other risk factors such as diabetes mellitus, alcoholism, human immunodeficiency virus and other immunocompromised states could not be obtained for an accurate presentation and meaningful discussion.

Conclusion

Meningitis was difficult to diagnose accurately in the ED setting. Given the lack of clinical features which could be used to differentiate meningitis from other conditions, a high index of suspicion would be required so that interventions may be promptly initiated to reduce mortality and morbidity.

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