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Original Research Article

Etiological Profile of Meningitis in a Tertiary Care Hospital of West India

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Abstract

Background and Objectives: There are few studies on meningitis in the adult population from the West India. Our objective was to study the etiological profile of community-acquired and health-care associated meningitis in a tertiary care hospital from West India. Additionally, we looked at laboratory profile which may help in recognizing subtypes of meningitis.

Methods: We carried out a retrospective study in a tertiary care neuroscience hospital in Gujarat. Case records of patients admitted from January, 2013 to December, 2017 were reviewed. We included patients who had clinical features and cerebrospinal fluid (CSF) analysis consistent with meningitis. We classified the patients as community-acquired and healthcare-associated meningitis. Further analysis was carried out by grouping patients with community-acquired meningitis into acute, subacute, and chronic meningitis.

Results: During the study period, 71 patients were diagnosed with meningitis. The causative agent was isolated in 21.4% of the patients with acute meningitis, 21.7% of the patients with subacute or chronic meningitis, and 44.4% of the patients with healthcare-associated meningitis. The patients with pyogenic meningitis had higher white blood cell counts, CSF cells, and CSF protein, compared to those with aseptic meningitis. Majority of the patients with subacute or chronic meningitis were presumed tuberculous meningitis based on clinicopathological features.

Conclusions: The yield of cerebrospinal fluid culture was low. Clinicians relied on clinical, laboratory, and radiological profile for treatment of meningitis. Leukocytosis and marked pleocytosis distinguished pyogenic meningitis, when there was overlap of clinical features with tuberculous meningitis.

Keywords: pyogenic meningitis, aseptic meningitis, tuberculous meningitis

Introduction

Meningitis and encephalitis stand for inflammation of the meninges and brain parenchyma, respectively. Evidence of inflammation is found in the form of pleocytosis in cerebrospinal fluid (CSF) analysis and intrathecal antibody synthesis. These inflammatory syndromes can be caused by infectious disorders, autoimmune disorders, neoplasia, drugs, and toxins [1,2].

A variety of bacteria, viruses, fungi, and parasites can cause acute, subacute, or chronic meningitis. Acute meningitis is commonly caused by viruses and bacteria,

and rarely by parasites. The most common causes of viral meningitis are enterovirus, Herpes simplex virus-2, and varicella zoster virus. The common bacterial agents include Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae, Listeria monocytogenes, and Staphylococcus aureus [3]. Clinical, laboratory and etiological profiles of subacute meningitis differ from acute meningitis [4]. Chronic meningitis, defined as meningitis lasting longer than a month without improvement, is caused by certain bacteria (for example, Mycobacterium tuberculosis, Borrelia burgdorferi, Treponema pallidum, etc.) and fungi [5]. Health-care associated meningitis may occur secondary to invasive neurosurgical procedures, complicated head trauma, or rarely, seeding of meninges in hospital-acquired bacteremia. These causative organisms are different than those seen in community-acquired meningitis [6].

There are few studies on the etiological profile of meningitis in the adult population from the West India. Most of the available data is from the pediatric age group. Knowledge of the etiological burden in a region helps the clinician in deciding empirical antibiotic therapy in acute meningitis which can lead to grave complications if there is delay in treatment initiation. In this study, we looked at the etiological profile of community-acquired and health-care associated meningitis in a tertiary care hospital from West India.

Methods

We conducted a retrospective study in a tertiary care neuroscience hospital in Gujarat. Data was collected from the records of patients admitted from January, 2013 to December, 2017. Case records and computerized log containing records of all the infections (culture reports) were reviewed. The approval of the Ethics Committee of the hospital was obtained prior to the start of the study. We included patients who had clinical features and CSF analysis consistent with meningitis or meningoencephalitis. Patients were excluded if they had autoimmune, neoplastic, or chemical meningitis. Community-acquired meningitis was classified by the duration of illness: acute if less than or equal to five days, subacute if more than 5 days, and chronic if more than one month [4,5]. Patients who developed meningitis after a neurosurgical procedure were labelled healthcare-associated meningitis [7].

Demographic, clinical, radiological, and laboratory data of the patients were charted. Surgical details were collected from cases of nosocomial meningitis. Comparison of data was done using the GraphPad Prism version 9.5.0 (730). Fisher's exact test was used for comparison of proportions. Student's t-test and Mann–Whitney U-test were used for normally distributed and nonnormally distributed numerical data, respectively. Kolmogorov and Smirnov method was used to determine if the data followed Gaussian distribution. $P < 0.05$ was considered statistically significant.

Results

During the study period, 71 patients were diagnosed with meningitis. The demographic and laboratory profiles of the patients are shown in table 1 and table 2. The microbiological profile is depicted in figure 1 and table 3.

Community-acquired meningitis

During the study period, there were 44 patients with community-acquired meningitis.

Acute meningitis: There were 21 patients with acute meningitis. Of these, 15 (71.4%) patients had leukocytosis. CSF profile was consistent with pyogenic meningitis (predominance of polymorphonuclear cells, low glucose, and raised protein in the CSF) in 14 (66.6%) patients. Six patients had relevant risk factors for acute meningitis: CSF rhinorrhea (four patients) and otitis media (two patients). The rest (33.4%) of the patients were labelled aseptic

meningitis. These patients had lower white blood cell counts (18806 ± 7317 per µL vs 11462 ± 4589 per µL; p = 0.0292), CSF cells (6548 ± 7138 per µL vs 154 ± 135.2 per µl; p = 0.0008), and CSF protein (293.1 ± 217.9 mg/dL vs 71.57 ± 40.90 mg/dL; p = 0.0163), compared to those with pyogenic meningitis. CSF culture could isolate the pathogenic agent in 3/17 (17.6%) of the patients (table 3).

Subacute or chronic meningitis: There were 23 patients with subacute or chronic meningitis. Median duration of illness was 14 days (range, 7 – 90 days). Most (86.9%) of the patients presented within three weeks of onset of symptoms. They had significantly less white blood cell counts and CSF cell counts, compared with patients with acute meningitis (table 1). About two-thirds of them had CSF lymphocytes more than 70%. Only five patients had microbiological confirmation (table 3): Mycobacterium tuberculosis in three patients (one had acid fast bacilli in the sputum and two had positive Xpert MTB/RIF in the CSF), Treponema Pallidum (detected by CSF Venereal Disease Research Laboratory test and Treponema pallidum hemagglutination assay) in one patient, and Aspergillus fumigatus (detected by fungal stain of nasal biopsy specimen) in one patient. Causative pathogen was not found in a patient with partially treated pyogenic meningitis. The rest (73.9%) of the patients were presumptively labelled tuberculous meningitis, based on clinical, radiological, and laboratory profiles. Six patients had radiological evidence of pulmonary tuberculosis (pneumonia and/or pleural effusion). Neuroimaging detected granulomatous brain lesions (tuberculomas) in five patients. One patient had recurrence of tuberculous meningitis after completing treatment several years ago. Ziehl–Neelsen staining of the CSF smears did not detect acid fast bacilli in any patient. Xpert MTB/RIF detected Mycobacterium tuberculosis in 2/10 (20.0%) of the patients.

Healthcare-associated meningitis

During the study period, there were 27 patients with meningitis following neurosurgical procedures (table 2). The median duration between the procedure and the onset of symptoms was 15 days (range, 5 – 145 days). CSF culture could isolate the pathogenic agent in 9/25 (36.0%) of the patients. In additional two patients, shunt tip culture and wound pus culture could identify the pathogenic patients. The neurosurgical procedures included craniotomy (23 patients) for excision of tumor, decompression and evacuation of intracranial hemorrhage, or decompression for Chiari malformation. Two of these patients had placement of an external ventricular drain. Four patients had intracranial hemorrhage following head injury. Other procedures included craniotomy and cysto-arachnoid shunt (one patient), ventriculoperitoneal shunt (two patients), and dorsal laminectomy for excision of a spinal cord tumor (one patient).

Table 1: Demographic and laboratory profile of community acquired meningitis

Characteristic	Acute meningitis (n = 21)	Subacute/chronic meningitis (n = 23)	p
Age in years, mean ± SD	41.76 ± 20.46	34.83 ± 13.96	0.2745
Males, n (%)	12 (57.14)	10 (43.49)	0.5467
WBC count per µL, mean ± SD	16358 ± 7328	10699 ± 5376	0.0029
CSF cell count per µL, mean ± SD	4416 ± 6532	387 ± 492	0.0443
CSF lymphocytes > 70%, n (%)	6 (21.57)	17 (73.91)	0.0059
CSF: serum glucose < 0.6, n (%)	19 (90.48)	22 (95.65)	0.5988
CSF ADA > 5 U/L, n (%)	3/6 (50.0)	7/9 (77.8)	0.3287
CSF culture no growth	14/17 (82.3)	10/10 (100.0)	-

Table 2: Demographic and laboratory profile of hospital acquired meningitis

Characteristic	Hospital acquired meningitis (n = 27)
Age in years, mean ± SD	42.00 ± 15.33
Males, n (%)	15 (55.5)
WBC count per µL, mean ± SD	14201 ± 5543
CSF cell count per µL, median (range	500 (60 – 25000)
CSF lymphocytes > 70%, n (%)	5 (18.5)
CSF: serum glucose < 0.6, n (%)	27 (100)
CSF culture no growth	16/25 (64.0)

Table 3: Microbiological profile of meningitis

Characteristic	Acute meningitis	Chronic meningitis	Hospital acquired meningitis
	n = 21	n = 23	n = 27
CSF culture, n (%)	17 (80.95)	10 (43.48)	25 (92.59)
No growth, n (%)	14/17 (82.35)	10/10 (100)	16/25 (64.00)
Confirmed etiology			
Streptococcus pneumoniae, n	2	-	-
Streptococcus viridans, n	-	-	1
Staphylococcus aureus, n	1	-	7
Klebsiella pneumoniae, n	-	-	2
Enterococcus faecalis, n	-	-	1
Acinetobacter baumannii, n	-	-	1
Treponema pallidum	-	1	-
Mycobacterium tuberculosis	-	2	-
Aspergillus fumigatus, n		1	-
Herpes simplex virus-2	1	-	-

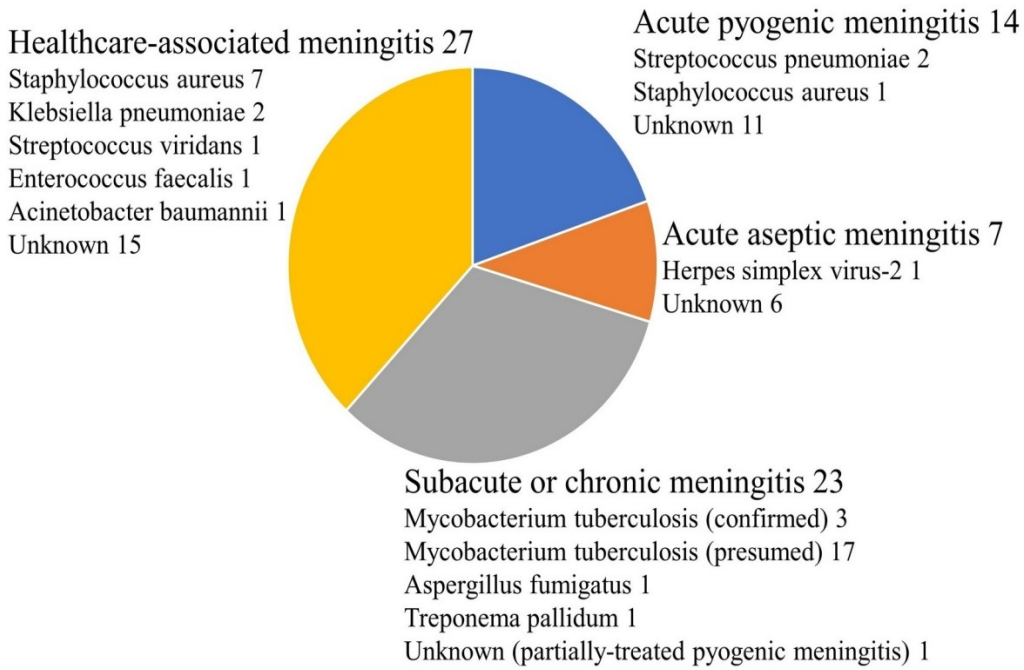

Figure 1: Microbiological profile of patients with meningitis

Discussion

CSF culture could identify the pathogenic agent in 21.4% (3/14) of the patients presenting with community-acquired acute pyogenic meningitis. The isolates included Streptococcus pneumoniae sensitive to penicillin and vancomycin, and Staphylococcus aureus resistant to methicillin. CSF smear showed Gram-positive cocci in another patient, but CSF culture did not yield a growth. The low yield of CSF culture in several studies has been attributed to fastidious nature of pathogen, prior antibiotic treatment, delay in transport of specimens to the laboratory, and non-availability of media for certain pathogens in the emergency setting [8-10]. Prompt bed-side inoculation of CSF samples on culture media improves detection of the pathogenic agent [11]. CSF FilmArray meningitis/encephalitis panel (BioFire) detected Herpes simplex virus-2 in a patient with acute meningitis. BioFire is a multiplex polymerase chain reaction platform that checks several common meningitis pathogens simultaneously. Rest of the patients who had aseptic meningitis did not undergo further evaluation because of financial constraints.

Causative agent (Mycobacterium tuberculosis) was detected in only 15.0% (3/20) of the patients treated with anti-tuberculous drugs. Diagnosis of tuberculous meningitis is challenging because of low sensitivity of the available diagnostic modalities and long turnaround time of the gold-standard mycobacterial culture; quite often the clinician has to initiate anti-tuberculous therapy based on the clinical, radiological, and laboratory features [12]. Sometimes it is difficult to discriminate pyogenic from tuberculous meningitis when there are overlapping clinical features, especially when the later presents with short duration of illness. CSF adenosine deaminase levels did not differ significantly between them; rather, we found that leukocytosis and markedly elevated CSF cell count (with predominance of polymorphonuclear cells) distinguished pyogenic meningitis.

Causative agents were identified in 12/25 (48.0%) of the patients with healthcare-associated meningitis, and included Staphylococcus aureus, Streptococcus viridans, Klebsiella pneumoniae, Enterococcus faecalis, and Acinetobacter baumannii. Microorganisms causing meningitis in the hospitalized patients vary according to the pathogenesis and timing of infection after the predisposing event [6]. A higher proportion of these patients, compared to community-acquired meningitis, have meningitis caused by Gram-negative bacilli [13]. Cutaneous Gram-positive bacteria such as coagulase-negative staphylococci and Staphylococcus aureus are common causes of meningitis following neurosurgical procedures [14,15]. Technically, microorganisms may gain access to the central nervous system even before hospitalization. The yield of CSF culture is low, and some patients perhaps have meningeal reaction to traumatic brain injury and intracranial hemorrhage [15].

Our study has some limitations inherent to retrospective nature and secondary to financial constraints and referral bias. Several patients did not undergo complete set of investigations that could lead to identification of the etiological agent, such as blood culture, serology, and molecular studies. Most of the patients were already on empirical antibiotics before being referred to our center. Additionally, due to referral bias, we did not have immunocompromised patients (secondary to human immunodeficiency virus infection) and perhaps missed patients with severe co-morbid systemic illness.

Conclusion

The yield of CSF culture was low in community-acquired and healthcare-associated meningitis. Clinicians often have to rely on clinical, laboratory, and radiological profile in managing patients

with meningitis. We found that leukocytosis and marked CSF pleocytosis distinguished pyogenic meningitis; these can be used to guide treatment in patients who have overlapping clinical features with tuberculous meningitis. The accessibility to certain investigations, such as molecular diagnostics, need to be improved to enhance identification of the etiological agent in meningitis.

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