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Original Research Article

The Association of Meningitis with Altered Sensorium and CSF Inflammation in HIV-Positive Patients

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ABSTRACT

Background: Meningitis is a serious infection in HIV patients claiming millions of lives across the world. Comparative studies of meningitis in HIV positive and negative patients are scarce.

Methods: We studied the comparative clinical profile of a 116 HIV seropositive and 218 HIV seronegative patients with meningitis at a tertiary care hospital in India.

Results: High proportion of altered sensorium [84.7% vs. 70.5%], relatively higher median CSF white blood cell count [100 cells/mm3 vs. 35 cells/mm3] and higher median CSF protein content [170 mg/dl vs. 90 mg/dl] were seen in HIV positive patients.

Conclusions: Our study shows that meningitis in HIV positive individuals is clinically more severe with more inflammation in the CNS. This can partly explain the high case fatality rates of meningitis in HIV positive patients.

Keywords: HIV positive, meningitis, TB meningitis, CSF

INTRODUCTION

According to the WHO 2015 report there are 36.7 million HIV seropositive persons in the world with 2 million more being newly infected every year.[1] These individuals are at a high risk for life threatening infections due to their weakened immunity. Meningitis is a serious infection in HIV positive patients with very high mortality. Many reports of meningitis in HIV positive individuals show this pattern. Large case series[2] of HIV positive meningitis report a case fatality rate as high as 68%. HIV infection is an established risk factor for poor outcome in meningitis.[3,4] Taken together HIV infection and meningitis form a deadly alliance.

Detailed comparative analysis of the clinical features between meningitis in HIV positive and negative individuals is scarce.[5,6] This type of analysis is very essential to understand the factors which result in the high death rate seen in HIV patients with meningitis. The potentially fatal nature of the disease requires careful study of these factors. Informed public health policies targeting HIV patients can only be planned with accurate factual data. Moreover in resource limited settings, clinical suspicion and algorithms for diagnosis also depend on concrete knowledge on the clinical profile of the disease. In this background, we describe the clinical profile of HIV positive and negative meningitis at a tertiary hospital.

METHODS

The study design was cross sectional and observational. Over four years 423 Adult patients [>14 years] diagnosed with meningitis hospitalized at the Govt. General Hospital, Guntur [a tertiary care centre in South India with 1200 beds and a catchment population of 20 million] were considered for inclusion in the study.

Clinical diagnosis of meningitis was based on neck stiffness and signs of meningeal irritation with any of fever, headache, altered sensorium and focal neurological deficit. Diagnostic confirmation of meningitis[7-9] and HIV seropositive status[10] was done as per standard guidelines. Demographic, clinical and laboratory features were compared between HIV positive versus HIV negative patients. Statistical analysis was performed using IBM SPSS version 20. Categorical data is summarized with percentages; quantitative data by mean and SD. Non parametric quantitative data is presented by median and inter quartile range [IQR]. Comparison of qualitative data was made using the chi-square test and quantitative variables using the student independent t test. To compare non parametric data Mann Whitney U test was applied. A two sided p value < 0.05 was considered statistically significant. In addition a difference of 10% between the groups was considered clinically relevant. The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from each patient or from the next of kin for patients who were too ill to communicate.

RESULTS

From May 2022 to June 2022, 423 patients were diagnosed with meningitis. 334 patients were included in the study after exclusion due to insufficient data or patient disinclination to consent. 116 patients were HIV seropositive and 218 were HIV seronegative [Table 1].

In our study, tuberculous meningitis was the most common diagnosis in both the groups [82.6% and 68.5%]. Altered sensorium was more common [84.7% vs. 70.5%] in HIV positive patients than in HIV negative patients [Table 2].

CSF analysis [Figure 1] of HIV positive individuals showed more evidence of inflammation. These patients had higher median white blood cell count [100 cells/mm3 vs. 35 cells/mm3] and higher median protein content [170 mg/dl vs. 90 mg/dl]. More proportion of patients with HIV had turbid CSF [68% vs. 56.2%] than seronegative patients.

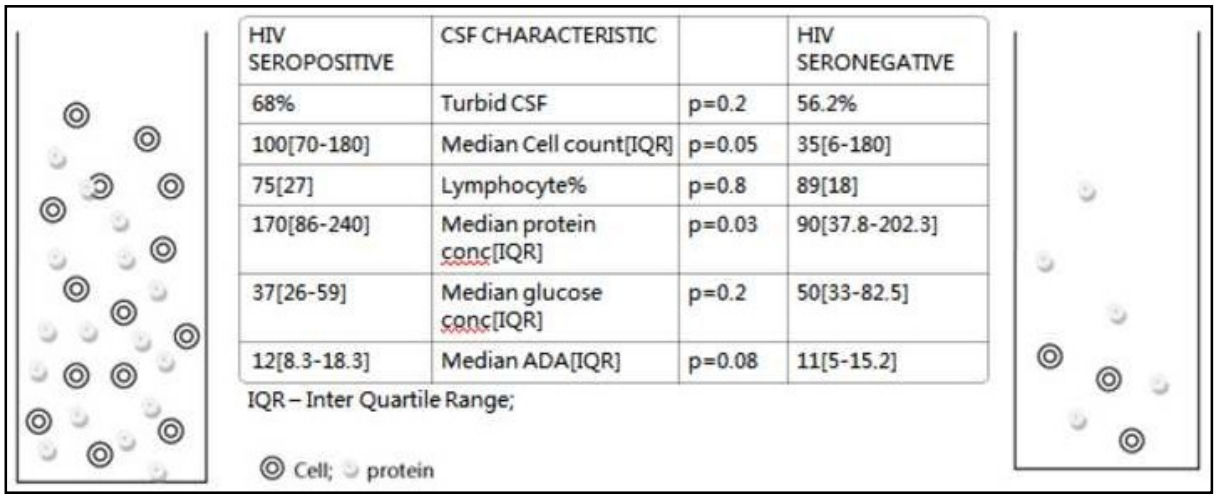
Table 1: Comparison of demographic features

Characteristic	HIV Sero-positive	HIV Sero-negative	P value
Mean Age (SD)	35 (9)	30 (17)	0.003
Females (%)	29.6	42.5	0.02
Diagnosis			<0.001
TB Meningitis (%)	82.6	68.5	
Aseptic Meningitis (%)	10.4	24	
Cryptococcal Meningitis (%)	5.2	1	
Bacterial Meningitis (%)	1.7	6.5	

Table 2: Comparison of clinical features

Characteristic	HIV Sero-positive	HIV Sero-negative	P value
Altered Sensorium (%)	84.7	70.5	0.01
Focal Neurological Deficit (%)	28.2	26.8	0.9
Cranial Nerve Deficit (%)	11.9	24.1	0.04

Figure 1: Comparison of CSF parameters in HIV positive and negative meningitis



DISCUSSION

In this study comparing 116 HIV positive and 218 HIV negative meningitis patients, tuberculous meningitis was the commonest cause in both the groups, the clinical presentations were different between the groups and CSF inflammation was higher in the HIV seropositive group. There are many factors that might have contributed to these results.

Aetiology

Tuberculosis is endemic in India, with about 1285 million patients in 2015. The state of Andhra Pradesh in South India has a very high prevalence of the disease.[11] This might contribute to the high proportion of tuberculous meningitis in our patients.[12] As corroborated by other studies,[13] this seems to be the common aetiology of meningitis in areas of high prevalence of tuberculosis.

Clinical presentation

84.7% of HIV positive meningitis patients in our study had a confused state. Similar studies from Africa,[13] Indonesia[6] and Uganda[14] also report a high degree of altered sensorium in these patients varying from 35% to 75%. Certain attributes of HIV infection and its pathogenesis could explain this observation. HIV infected patients are prey to many secondary infectious agents. They have a higher frequency of multiple infections[15,16] and multi organ involvement.[17,18,19] Chronic infections are also more common[20] in these patients. Non communicable diseases are also high in this group.[21] This results in poor functional reserve of various organs. Therefore any added insult can easily tip the balance and result in severe disease. Any number of factors responsible to maintain a stable metabolic milieu for normal sensorium is affected easily. As such altered sensorium – a result of any such derangements or encephalopathy per se should be more common in HIV patients. Our study reflects this higher incidence of mental disorientation in the HIV positive group. The higher degree of metabolic disturbances[22] common in HIV positive individuals might also underlie the comparatively higher proportion of altered sensorium in this group. The higher degree of inflammation of the CNS in HIV positive patients as evidenced by the CSF parameters in this study may also have contributed to this difference. Clinical studies of bacterial,[23] tuberculous[24] and fungal meningitis[25] have shown that altered sensorium is an unequivocal risk factor for high mortality.

CSF analysis

HIV patients have a weakened immune system. Pathogenic organisms[26-29] isolated from HIV seropositive patients are more virulent and cause more severe disease in these patients. This can result in higher cell count and protein load in the

cerebrospinal fluid in CNS infections. An Autopsy study comparing infectious meningitis between HIV and non HIV brain tissue reported a significantly higher inflammation of the brain and meninges in HIV seropositive patients.[30] Thus HIV positive meningitis is associated with extensive inflammation of the CNS. The rapid multiplication of pathogenic organisms[26-29] in the immunocompromised state consequent to HIV infection may induce the high protein load in the CSF. This high CSF protein content and WBC have been noted previously in many clinical studies of HIV positive meningitis.[31,32] There are certain limitations to our data. Selection bias of a single hospital study might affect our results.

CONCLUSIONS

Our study comparing HIV-positive and HIV-negative meningitis patients reveals that tuberculous meningitis is the predominant cause in both groups. Clinical presentations differ, with a higher incidence of altered sensorium in HIV-positive patients, potentially linked to the immunocompromised state and increased virulence of pathogens. Elevated CSF inflammation in HIV-positive cases suggests a more severe disease course. Our findings highlight the pronounced clinical severity and CNS inflammation in HIV-associated meningitis, contributing to higher mortality in this population.

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