



Clinical Features of Suspected CNS Infection in A Tertiary Care Center

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Abstract

Background: Infections of the central nervous system are neurological emergencies requiring early recognition and efficient decision making. Clinical presentations are varied and non infective causes can also present with similar features.

Aim and Objectives: To study the causes of altered sensorium and to analyze the profile of patients presenting with CNS infection.

Methods: The study included 121 patients (73 males and 48 females) who met inclusion criteria (Age more than or equal to 18 years and suspicion of CNS infection) admitted in Sri Ramachandra Medical College Hospital from the year 2009 to 2011. Clinical presentations were analyzed by questionnaire and detailed examination including a fundoscopy done.

Results: Out of 121 patients, 90 had CNS infection. 15 patients had bacterial meningitis, 32 had tuberculous meningitis, 9 had aseptic meningitis, 30 had encephalitis and 4 had Cryptococcal meningitis. Viral encephalitis was seen more in younger age group. The most common presenting symptom was fever (105 patients), followed by altered sensorium (89), headache in (68), vomiting in (58) and seizures in 48 patients. Altered sensorium was universal in cryptococcal meningitis. 45.5% of patients with CNS infection presented with seizures while 35.5% had seizures in patients without infection. Mean duration of fever was 23 days for cryptococcal meningitis with TB meningitis having 15 days. 75% patients had neck stiffness and focal neurological deficits were seen in 9% patients. Fundus was abnormal in 28.1 % patients.

Conclusion: Clinical presentation of CNS infections is a changing scenario. Young patients had more incidence. Fever and altered sensorium were the most common symptom. Neck stiffness was not an universal feature.

Keywords- Altered sensorium, Fever, Meningitis, Neck stiffness, Seizures.

Introduction

Estimates of altered sensorium in hospitalized patients range from 14 to 56%, with higher rates

reported for elderly patients and patients undergoing hip surgery. Older patients in the ICU have especially high rates altered sensorium of

ranging from 70 to 87%. ¹Delirium has many clinical manifestations, but it is defined as a sudden decline in cognition that fluctuates over hours or days. The characteristic feature of delirium is a deficit of attention, though all cognitive domains—including memory, executive function, visuospatial tasks, and language—are variably involved. Associated symptoms may include altered sleep-wake cycles, perceptual disturbances such as hallucinations or delusions, affect changes, and autonomic findings including heart rate and blood pressure instability. ²Most of the CNS infections present with altered sensorium as do the non-infective causes which may lead to similar reduction in the level of consciousness. some of the common problems that will mimic acns infection can be electrolyte disorders like hyponatremia or hypernatremia which can present with delayed mentation and seizures. hypoglycemia can also present with altered sensorium. elevated blood sugar can also present with altered sensorium and coma. ³ Renal failure can also present with reduced consciousness as in uremic encephalopathy. very high or low temperature (hyperthermia and hypothermia) is also a very important differential diagnosis. traumatic head injuries like concussion, stroke, intracerebral hemorrhage are some of the common causes which present as altered sensorium. malignancy within the intracranial cavity can affect the consciousness similar to epilepsy and post seizure states. ⁴Pulmonary failure: hypoxemia and hypercarbia can also present with altered sensorium and coma. Liver failure/hepatic encephalopathy,. Other common metabolic etiologies include, vitamin deficiencies of thiamine and B₁₂, autoimmune disorders including CNS vasculitis, and endocrinopathies such as thyroid and adrenal disorders. ⁴ A common scenario involves the development of an acute cognitive decline in the setting of a urinary tract infection in a patient with preexisting dementia. Pneumonia, skin infections such as cellulitis, and frank sepsis can also lead to altered sensorium This is called septic encephalopathy, often seen in

the ICU patients and, is likely due to the release of proinflammatory cytokines and their diffuse cerebral effects. ⁵CNS infections such as meningitis, encephalitis, and abscess are -common etiologies of delirium; however, given the high mortality associated with these conditions when not treated quickly, clinicians must always maintain a high index of suspicion.

The present study was done to analyze the various clinical presentations of altered sensorium to aid in the early diagnosis.

Material and methods

This study was a longitudinal study of 121 consecutive patients presenting with altered sensorium conducted at Sri Ramachandra Medical College in the Department of Medicine from 2009 - 2011, after approval of Hospital ethics committee. All patients fulfilling inclusion criteria (Age more than or equal to 18 years and suspicion of CNS infection by the admitting physician or team) were screened and investigations done. Patients with age less than 18 years, onset of symptoms after hospital stay for more than 48 hours, recent hospital stay in less than 1 week, recent neurosurgical procedure in less than 1 week, history of head trauma with CSF leak preceding the onset of symptoms, patients with localised infection of CNS such as brain abscess, patients who died, absconded or left against medical advice before the complete workup including CSF analysis was done and patients with SOL in the brain were excluded from the study. The suspicion of CNS infection was made by the admitting physician or team based on the clinical features which broadly included fever or prodromal flu-like illness, headache, new onset seizures, focal neurological weakness, confusion/ altered behaviour, decreased Glasgow coma score (GCS), signs of meningism or rash. Patients with suspected Nosocomial or Post traumatic CNS infections were excluded as per the exclusion criteria based on CDC guidelines. Detailed history was recorded in predesigned proforma which included presenting complaints, symptoms of

meningeal irritation, relevant past history, history of risk factors. Patients were examined in detail and details were recorded in pre designed proforma which included general examination and detailed neurological examination. Special emphasis was made on examination of signs of meningeal irritation such as neck rigidity, Kernig's sign and Brudzinski sign. Fundus was examined in every patient. Laboratory investigations like Complete blood count, Random blood sugar, Urine analysis, Renal and Liver function tests and Serum electrolytes were done in all cases. Mantoux, Sputum for AFB, ESR, and Chest X ray, Blood culture, Pus swab culture, was done in selected cases. CSF samples were collected through lumbar puncture in all cases, after informed consent. Samples were examined for cell count, glucose, protein, chloride, Gram stain, bacterial culture, AFB smear, culture of AFB and viral markers like HSV. CSF for PCR TB and HSV was done in suspected case of Tuberculous and Viral etiology respectively. Neuro imaging CT or MRI brain was done in selected patients based on the clinical features like fundus changes. Treatment given to the patients was decided by the concerned physician based on hospital protocols. Patients

were divided into CNS infections and Non CNS infections based on the presenting features, CSF Analysis and Imaging findings. CNS infections were further divided into Bacterial Meningitis, Tubercular Meningitis, Aseptic meningitis, Encephalitis and Cryptococcal meningitis based on the case definitions mentioned earlier. Each group was analysed in detail. Patients were again re-examined at the time of discharge to look for any neurological sequelae.

Results were expressed as mean for continuous variables. For categorical data univariate analysis was performed using Pearson Chi-square test. A 'p' value of <0.05 is considered to be statistically significant. Statistical analysis was done using SPSS windows version 17.0 software

Results

The study included 121 patients (73 males and 48 females). 90(74.3%) were diagnosed to have CNS infection and 31(25.7%) were diagnosed to not have CNS infection. 37(31%) belonged to the age group of 18-30 years, 22(18%) to 31-40, 24(22%) to 41-50, 13(11%) to 51-60, 11(9%) to 61-70 and 14(11%) belonged to the age group of above 70 years. The various observations are summarised in the following tables.

Table 1- The study group

	18-30	31-40	41-50	51-60	61-70	>70	TOTAL
BACTERIAL MENINGITIS	3	3	4	4	0	1	15
TUBERCULOUS MENINGITIS	7	4	11	5	3	2	32
ASEPTIC MENINGITIS	5	4	0	0	0	0	9
ENCEPHALITIS	13	7	5	1	2	2	30
CRYPTOCOCCAL MENINGITIS	2	1	1	0	0	0	4
ALL CASES	37	22	24	13	11	14	90

Table 2 – The presenting features

SYMPTOM	NO OF PATIENTS (PERCENTAGE) N=121
FEVER	105 (86.7%)
HEADACHE	68 (56.1%)
ALTERED SENSORIUM	89 (73.5%)
SEIZURES	48 (39.7%)
VOMITING	58 (47.9%)
PHOTOPHOBIA	12 (9.9%)
DIPLOPIA	6 (5%)
DIMINISHED / LOSS OF VISION	4 (3.3%)

Table 3 – Clinical presentation of Headache

DIAGNOSIS	HEADACHE PRESENT	HEADACHE ABSENT	TOTAL	P-VALUE
CNS INFECTION	59 (65.6%)	31 (35.4%)	90	<0.001
NOT CNS INFECTION	9 (29%)	22 (71%)	31	
ALL CASES	68 (56.2%)	53 (43.8%)	121	

Table 4 – Profile of altered sensorium

DIAGNOSIS	ALTERED SENSORIUM PRESENT	NO ALTERED SENSORIUM	TOTAL	P VALUE
CNS INFECTION	62 (68.9%)	28 (31.1%)	90	0.059
NOT CNS INFECTION	27 (87.1%)	4 (12.9%)	31	
ALL CASES	89 (73.6%)	32 (26.3%)	121	

Table 5 - Fundoscopy

	NORMAL	PAPILLOEDEM A	RETINOPATH Y	OPTIC ATROPY
ALL CASES (N - 121)	87 (71.9%)	13 (10.7%)	15 (12.4%)	6 (5%)
NOT CNS INFECTION (N - 31)	18 (58%)	2 (6.4%)	11 (35.4%)	0 (0%)
BACTERIAL MENINGITIS (N – 15)	14 (93.3%)	0 (0%)	1 (6.7%)	0 (0%)
TUBERCULOUS MENINGITIS (N – 32)	14 (43.8%)	9 (28.1%)	3 (9.4%)	6 (18.7%)
ASEPTIC MENINGITIS (N – 9)	9 (100%)	0 (0%)	0 (0%)	0 (0%)
ENCEPHALITIS (N – 30)	28 (93.3%)	2 (6.7%)	0 (0%)	0 (0%)
CRYPTOCOCCAL MENINGITIS (N – 4)	3 (75%)	1 (25%)	0 (0%)	0 (0%)

Out of the 90 patients diagnosed to have CNS infection 15(16.7%) had Bacterial Meningitis, 32(35.5%) had Tuberculous meningitis, 9(10%) had Aseptic meningitis, 30(33.3%) had Encephalitis, and 4(4.5%) had Cryptococcal Meningitis. Out of 15 patients diagnosed to have bacterial meningitis 10(66.6%) were males and 5(33.7%) were female. Among Tuberculous meningitis, 11(34.3%) were male and 21(65.7%) were females. Among Aseptic meningitis, 6(66.7%) were males and 3(33.3%) were females. Among Encephalitis, 25(83.3%) were males and 5(16.7%) were females. Among Cryptococcal meningitis, 3(75%) were males and 1(25%) was female. Bacterial meningitis was found to be more or less equally distributed among the age groups below the age of 60 and only one patient above 60 yrs was found to have bacterial meningitis in this study. Tuberculous meningitis was found to be more common among the age group 41-50

accounting for 11(34.4%) out of 32 cases diagnosed. Aseptic meningitis was found to be confined to the young age with all the patients were found to be below the age of 40 years. Among Encephalitis the majority of patients were found to be below the age of 50 years with 13(43.3%) belonging to the age group of 18 -30 years. Out of four cases of Cryptococcal meningitis in this study 2 were among 18-30 age group and one each belonged to the age groups of 31-40 and 41-50.

The most common presenting symptom was fever accounting for 105(86.7%) followed by altered sensorium in 89(73.5%), headache in 68(56.1%), vomiting in 58(47.9%), seizures in 48(39.7%), photophobia in 12(9.9%), diplopia in 6(5%) and diminished or loss of vision in 4(3.3%). Fever was present in 85(94.4%) of patients diagnosed to have CNS infection and 20(64.5%) of patients diagnosed not to have CNS infection. Statistical

analysis showed a significant P value for the association of fever with CNS infection. Fever was present in 100% cases of Bacterial meningitis, 96.8% cases of Tubercular meningitis, 88.9% cases of Aseptic meningitis, 90% cases of Encephalitis and 100% cases of Cryptococcal meningitis. Headache was present in 59(65.6%) of patients diagnosed to have CNS infection and 9(29%) of patients diagnosed not to have CNS infection. Statistical analysis showed a significant P value for the association of headache with CNS infection. Among CNS infections headache was present in 73.3% cases of Bacterial meningitis, 59.4% cases of Tubercular meningitis, 77.8% cases of Aseptic meningitis, 60% cases of Encephalitis and 100% cases of Cryptococcal meningitis. Altered sensorium was present in 62(68.9%) of patients diagnosed to have CNS infection and 27(87.1%) of patients diagnosed not to have CNS infection. Statistical analysis did not show a significant P value for the association of altered sensorium with CNS infection. Among CNS infections altered sensorium was present in 60% cases of Bacterial meningitis, 59.4% cases of Tubercular meningitis, 10% cases of encephalitis, 100% cases of Cryptococcal meningitis and patients with aseptic meningitis had no altered sensorium. Seizures was present in 37(41.1%) of patients diagnosed to have CNS infection and 11(35.5%) of patients diagnosed not to have CNS infection. Statistical analysis did not show a significant P value for the association of seizures with CNS infection. Among CNS infections seizures was present in 20% cases of Bacterial meningitis, 21.9% cases of Tubercular meningitis, 83.3% cases of Encephalitis and 50% cases of Cryptococcal meningitis. Patients with aseptic meningitis had no seizure. Among other symptoms, Vomiting was found to be present all CNS infections and non CNS infection more or less in equal distribution. Photophobia was found to be present in 60% of cases of Bacterial meningitis. Diplopia and Diminished or Loss of vision were found to be present in 18.7% and 12.5% of cases of TB meningitis respectively while not found at all in other CNS infections.

The mean duration of fever at the time of presentation was found to be maximum 23 days for Cryptococcal meningitis, followed by 15 days in Tuberculous meningitis, 6 days in Encephalitis, 5 days in both Bacterial and Aseptic meningitis. The mean duration of fever was found to be lesser (3 days) in patients who were diagnosed not to have CNS infection. 82% patients had a normal fundoscopy. 11% patients had focal neurological deficits with lateral rectus palsy being the most common. Neck stiffness was present in 75.6% of patients with CNS infection and 32.2% of patients without CNS infection. Statistical analysis showed a significant P value for the association of neck stiffness with CNS infection. Among CNS infections neck stiffness was present in 66.7% cases of Bacterial meningitis, 87.5% cases of Tubercular meningitis, 77.8% cases of Aseptic meningitis, 63.3% cases of Encephalitis and 50% cases of Cryptococcal meningitis. Kernigs sign was found to be positive only in 21% of cases diagnosed as CNS infection. Brudzinkis sign was found to be positive only in 11% of patients diagnosed as CNS infection.

Discussion

In the present study out of 121 patients suspected to have CNS infection 90 patients (74%) were diagnosed to have CNS infection and 31 (26%) were diagnosed as not CNS infection. Out of 31 patients diagnosed not to have CNS infection, 8 patients had Urosepsis, 6 had Malaria, 3 had Viral fever, 3 had Community acquired Pneumonia, 2 had hyponatremia induced Seizures, 2 had CVA and one each had CVT, Typhoid fever, Leptospirosis, Migraine, Normal pressure Hydrocephalus, Alcohol withdrawal seizures and Alprazolam overdose. In a similar study by Michael et al⁶; out of 217 patients with suspected CNS infection 44 (20%) had CNS infection and 173 (80%) were found to not have CNS infection. In our study out of 90 patients with CNS infection 15(17%) had Bacterial meningitis, 32(36%) had Tuberculous meningitis, 9(10%) had Aseptic meningitis, 30 (33%) had Encephalitis and 4 (4.5%) had cryptococcal meningitis. Micheal et al⁶

reports the relative incidence as 13 patients(30%) purulent meningitis, 18 patients (40%) aseptic meningitis, and 13 patients (30%) encephalitis. The relative incidence of Tuberculous and Cryptococcal meningitis was not looked upon in this study. The relative proportion of cases who were diagnosed to have CNS infection among the suspected cases were more in our study compared to Micheal et al⁶. The difference was probably because of the higher prevalence of Tuberculous meningitis in Indian subcontinent, which was not included by Micheal et al⁶ and probable differences in the inclusion methods.

The mean age of patients in this study was 44 years ranged from 18 to 89 years. Micheal et al⁶ reports the mean age of patients as 41 years ranging from 16-87 years among suspected CNS infections. Various studies by Durand et al⁷, Thwaites et al⁸, Wani et al⁹, Elisabeth et al¹⁰, Mailles et al¹¹, Wada-Isoe et al¹², Baradkar et al¹³ have observed the age differences in patients with meningitis.

In the present study 73(60%) of all the patients were males and 48(40%) were females. Micheal et al⁶ reports the sex distribution as 99 (46%) males and 118 (54%) females among 217 patients. In our study out of 15 patients with Bacterial meningitis 10(66.6%) were males and 5(33.3%) were females. Studies done in the Indian subcontinent by Wani et al⁹ show Tuberculous meningitis to be more prevalent among females as observed in our study in contrast to studies done in the west.

In our study the most common presenting symptom was fever accounting for 105(86.7%) followed by, altered sensorium in 89(73.5%), headache in 68(56.1%), vomiting in 58(47.9%), seizures in 48(39.7%), photophobia in 12(9.9%), diplopia in 6(5%) and diminished or loss of vision in 4(3.3%). Fever was found in 64.6% of patients diagnosed not to have CNS infection. Micheal et al⁶ reports the symptomatology as fever in 48%, Altered Sensorium in 36 %, Headache in 75%, Vomiting in 43%, Photophobia 41%, Seizures in 18%, and Rash in 14% of patients diagnosed with CNS infection. Durand et al⁷ reports the symptomatology in Bacterial Meningitis as Fever

in 95%, Altered sensorium in 78%, Seizures in 23%, Rash in 11%. Van de Beek et al¹⁴ reports Fever in 77%, Altered sensorium in 69%, Headache in 87%, Seizures in 5%, Rash in 26% of patients with Bacterial meningitis. Wani et al⁹ reports the symptomatology of Tuberculous meningitis as Fever in 84.2%, Headache in 78.9%, Altered sensorium in 44.7%, Seizures in 5.3%, and Vomiting in 63.1%. Nowak et al¹⁵ reports Fever in 100%, Headache in 100% and Seizures in 9% of patients with Aseptic Meningitis. Carol et al¹⁶ reports Fever in 81%, Seizures in 29% of patients with Viral Encephalitis. Mailles et al¹¹ reports Altered sensorium in 95% and Seizures in 25% of patients with Encephalitis. Baradkar et al¹³ reports Fever, Headache and Altered sensorium in 100% of patients with Cryptococcal meningitis.

In our study neck stiffness was present in 75.6% of patients with CNS infection and 32.2% of patients without CNS infection. Micheal et al⁶ reports neck stiffness in 36% of CNS infections and 34% of Non CNS infections. Neck stiffness was reported in 54% of Bacterial meningitis, 44% of Aseptic Meningitis, 8% of Encephalitis in this study. Thwaites et al⁸ reports Neck stiffness in 84% of Bacterial meningitis and 91% of Tuberculous Meningitis. Moghtaderi et al¹⁷ reports Neck stiffness in 94% of Bacterial meningitis and 90% of Tuberculous meningitis. Wani et al⁹ reports Neck stiffness in 78.9% of patients with Tuberculous meningitis.

Van de Beek et al¹⁴ reports Neck stiffness in 83% and Durand et al⁷ reports Neck stiffness in 88% of Bacterial Meningitis. Nowak et al¹⁵ reports Neck stiffness in 35% of Aseptic meningitis. Baradkar et al¹³ reports Neck stiffness in 90% of Cryptococcal meningitis. Except a few studies, all studies including the present one reports neck stiffness in majority of patients with CNS infection. The classic triad of Fever, Altered sensorium and Neck stiffness was present in 44.4% of patients diagnosed to have CNS infection. Only one patient without CNS infection had the classic triad. The classic triad was present in 26.7% of Bacterial Meningitis, 50% of Tuberculous meningitis, None in Aseptic

meningitis, 60% of Encephalitis, and 50% of Cryptococcal meningitis. Van de Beek et al¹⁴ reports the classic triad in 44% of Bacterial meningitis.

In our study 71.9% of all the patients and 76% of patients with CNS infection had normal fundus study. Among Bacterial meningitis Van de Beek et al¹⁴ reports papilloedema in 3% and Durand et al⁷ reports papilloedema in 4%. Wani et al⁹ reports papilloedema in 36.8% of Tuberculous meningitis. Optic atrophy was reported in 27% of patients with Tuberculous Meningitis by Kumar et al¹⁸. Fundus changes were found to be more common in Tuberculous meningitis compared to others. The major changes observed were papilloedema and optic atrophy.

In our study focal neurological deficits was observed in 8 (9%) out of 90 patients with CNS infection and 4 (12.9%) of Non CNS infection. Micheal et al⁶ reports focal deficits in 14% of cases with CNS infection and in 18% without CNS infection. Wani et al⁹ reports Cranial N palsy in 36.8% and Limb weakness in 18.4% of Tuberculous Meningitis. Thwaites et al⁸ reports Cranial N palsy in 22% and Hemiplegia in 8% of Tuberculous Meningitis and in 8% and 4% of Bacterial meningitis respectively. Moghtaderi et al¹⁷ reports Cranial N palsy in 36.8% and Hemiplegia in 33.8% of Tuberculous Meningitis and in 28.5% and 25.2% of Bacterial meningitis respectively. Van de Beek et al¹⁴ reports 3rd Cr N palsy in 4%, 6th Cr N palsy in 3%, 7th Cr N palsy in 2%, 8th Cr N palsy in 7% and Hemiparesis in 7% of Bacterial meningitis. The incidence of focal neurological deficits was lesser in our study compared to other studies.

Conclusion

CNS infections have varied aetiology and clinical presentations. The classical triad of meningitis is not observed in all patients. The present study focuses on the specific clinical presentations of various CNS infections and non-infectious causes have to be judiciously excluded.

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