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Original Research Article

Clinical, Microbiological Presentation of Children with Acute CNS Infection

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Abstract:

Introduction: Meningitis is a common tropical infection which causes significant morbidity and mortality in children. Vaccination is available now-a-days for Haemophilus influenza and pneumococcus which are the common infection causing meningitis. Profile of acute Central Nervous System (CNS) infection in children varies with time to time as it depends on the organism, age, seasonal period, outbreaks, immunization and place. Based on this aim of our study is to evaluate the clinical, microbiological, radiological profile and outcome of children with acute CNS infection in a tertiary care teaching hospital.

Materials and Methods: This prospective observational study was done in the Department of Pediatrics, Tirunelveli Medical College for a period of one year. Total 50 children from one month to 12 years with features of acute CNS infection were included in the study. Clinical features, Cerebrospinal Fluid (CSF) and serology findings, Computed Tomography (CT) scan findings and outcome were taken for analysis.

Results: During the study period, 50 children were diagnosed with acute CNS infection. A total of 37 (74%) children were less than 3 years and 31 (62%) male children were commonly affected. Fever, seizures and altered sensorium were the common symptoms. Status epilepticus 40 (87%), shock 18 (36%), respiratory distress 16 (32%) were common findings. In CSF, elevated cell count, reduced sugar, elevated protein were seen in 21 (42%), 14 (28%) and 27 (54%), respectively. Pneumococcus, Japanese Encephalitis (JE), dengue, herpes, and scrub typhus were the common etiological agents for CNS infection. CT brain was abnormal in 8 (16%) children. Nine children died (18%) and rest 41 (82%) recovered.

Conclusion: In our study most of children were in 3 months to 3 years of age and predominantly male. Status epilepticus is most common seizure presentation. In electrolytes, hyponatremia was present in 12 cases and hypernatremia in 2 cases. Hypokalemia was seen in 7 cases and hyperkalemia was not seen in any case. CSF analysis was done and mostly were neutrophil predominant, followed by lymphocyte predominant. CT Brain was evaluated and findings like thalamic hypodensities, hydrocephalus, subdural hemorrhage and ganglionic hypodensities. Hence proper evaluation and knowing various clinico-etiological summary helps in management of children manifesting with acute CNS infection.

Keywords: CNS infection, encephalitis, clinical presentation.

Introduction

Meningitis is a clinical condition described by inflammation of meninges. The characteristic triad of meningitis contains fever, headache and neck stiffness [1]. Bacterial meningitis happens in about 3 per 100,000 people every year in western countries. Whereas viral meningitis is more common at 10.9 per 100,000 population [2].

Bacterial meningitis is a pyogenic inflammation of meninges and subarachnoid cerebrospinal fluid (CSF) and is characterized by neutrophilic pleocytosis in CSF [3]. Pnemococcal meningitis is instigated by streptococcus pneumonia, a gram-positive coccus and is the most common bacterial cause of meningitis. Meningococcal meningitis is caused by gram-negative diplococcus - Neiserria meningitides. Most patients improve completely if suitable antibiotic therapy is started on time. Tubercular meningitis is a very serious disease in terms of fatal consequence and permanent sequelae, requiring rapid diagnosis and treatment [4]. Tuberclous meningitis should be a solid thought when a patient presents with clinical picture of meningoencephalitidis, particularly in high risk groups. Death may occur as a consequence of missed diagnosis and deferred handling.

Global causes of viral meningitis include enterovirus, herpes, mumps, measles and HIV.

Enterovirus is the utmost common cause of viral meningitis. Aseptic meningitis is an illness characterized by serious inflammation of the meninges, generally with an associated CSF lymphocyte pleocytosis. Clinical indicators vary with headache and fever outweighing other signs. The illness is generally mild and runs its course without treatment, nevertheless some cases can be severe and life threatening. Notable recovery may be attained in some patients with viral meningitis who become even comatose. Strong supportive therapy and evading complications are very significant in handling these patients. Cryptococcal meningitis is instigated by Cryptococcus neoformans, particularly in individuals with malfunctioning cell mediated immunity. Swift antifungal therapy should be considered in these patients [5]. The prevalence of acute encephalitis in western countries is 7.4 per 100,000 populations per year. In tropical countries like India it is 6.4 per 100,000 per year.

Encephalitis presents as diffuse or focal neuropsychological dysfunction even though it primarily encompasses the brain, it often includes the meninges as well (meningoencephalitis). From an epidemiological and pathophysiologic view encephalitis is dissimilar from meningitis, however on clinical assessment both can be present, with signs and symptoms of meningeal inflammation. The prodrome characteristically comprises of fever, headache, nausea, vomiting, lethargy and myalgias. The clinical appearance is encephalopathy with diffuse or focal neurological symptoms together with behavioural and personality changes, with reduced level of consciousness, neck pain/stiffness, photophobia, lethargy, generalized or focal seizures, acute confusion or amnestic states and flaccid paralysis [8]. There are no much studies done till now showing the clinical, etiological and outcome in patients with meningitis and meningoencephalitis.

Distinguishing the aetiologies also aids in terms of both reducing antibiotic usage and hospital bed occupancy and comforting contacts of cases and health care staff of a non-bacterial cause. As there are fewer progresses in therapies for viral meningitis and there remain no effective therapies for most pathogens, this study is done to emphasise the importance of early diagnosis, so that prompt management is given at appropriate time in paediatric age group. Based on this aim of our study is to find the aetiology of acute CNS infection based on clinical, microbiological & radiological profile in children admitted in a tertiary care centre.

Material and Methodology

This study was done as a prospective observational study among inpatient pf pediatric department of Tirunelveli medical college for a period of one year. Children from 1 month to 12 years of age presenting with signs & symptoms of acute CNS infection will be included in this study. While babies < 1 Month of age, Children > 12 years, Complex febrile seizure, who were partially treated acute CNS infection cases and patients who are not willing were excluded.

Statistical analysis was done using IBM SPSS 24.0 software. The patients with clinical features of acute CNS infection will be enrolled after obtaining informed/ written consent from parents /guardians. With strict aseptic precautions blood samples [5ml] is collected by venipuncture & transferred in sample collection tubes. Lumbar puncture is done for all suspected cases after stabilization & getting informed consent, CSF is tested for cells, glucose, protein, gram stain, bacterial culture & sensitivity and viral serology. Supportive radiological investigations like chest x-ray, CT brain, abdominal ultrasound, MRI Brain will be done wherever required & findings noted.

Results

During the study period, 50 children were admitted with features of acute CNS infection with male preponderance 31 (62%). 22 (44%) children were in the age group of three months to three years, 15 (30%) children were in the age group of 1-3 months and 13 (26%) children were in the age group of 3-12 years.

Demographic and clinical features were analyzed and in our study 22 (44%) children were in the age group of three months to three years, 15 (30%) children were in the age group of 1-3 months and 13 (26%) children were in the age group of 3-12 years. Seizures, fever and altered sensorium were the common presentations seen in 46 (92%), 42 (84%) and 31 (62%) children, respectively. Many children with CNS infection presented with fever (84%) and seizures (92%) in present study. Status epilepticus was the common type of seizure seen in 40 (87%) of 46 seizure cases.

Table 1: Demographic and Clinical features

Variables	N (%)
Age	
1-3 months	15 (30)
>3 months - 3 years	22 (44)
>3 years - 12 years	13 (26)
Sex	

Male	31 (62)
Female	19 (38)
Symptoms	
Seizures	46 (92)
Fever	42 (84)
Altered sensorium	31 (62)
Irritability	24 (48)
Vomitting	19 (38)
Shock	18 (36)
Respiratory distress	16 (32)
Meningeal signs	7 (14)
Glasgow Coma Scale (GCS) <6	6 (12)
Bulging fontanel	4 (8)
Headache	3 (6)
Kernig sign	1 (2)
Brudzinski sign	1 (2)
Types of seizures (n=46)	
Status epilepticus	40 (87)
Non convulsive status epilepticus	4 (8.7)
Focal seizures	2 (4.3)

Meningeal signs were seen in only 7 (14%) children. Kernig and Brudzinski signs were seen in one children each. GCS was less than 6 in 6 (12%) children. Shock and respiratory distress were seen in 18 (36%) and 16 (32%) children, respectively. Due to delayed presentation, many children presented with respiratory distress (32%).

Table 2: Blood and CSF pareameters

Parameters	**N (%)**
Blood	
Anaemia	34 (68)
Leucocytosis	18 (36)
Hypoglycaemia	9 (18)
Hypocalcaemia	15 (30)
Hyponatraemia	12 (24)
CSF	
Elevated cell count	21 (42)
Predominant neutrophil	10 (47.6)
Predominant lymphocyte	11 (52.4)
Reduced sugar	14 (28)
Elevated protein	27 (54)

Pneumococcus was isolated in 3 (6%) children. IgM ELISA in CSF was positive for JE in 8 (16%) children. Dengue was the etiological agent in 5 (10%) children who presented with severe thrombocytopenia (<20000/mm^3) and IgM ELISA for dengue was positive. CSF-PCR was positive for herpes in 4 (8%) children. The other common tropical fever scrub typhus (etiological agent- Orientia tsutsugamushi) with characteristic eschar presented withCNS manifestation in 2 (4%) children.

Table 3: Microbiological and radiological findings

Profile	**N (%)**	**Diagnosis**
Organism		
Japanese encephalitis virus	8 (16)	IgM ELISA
Dengue virus	5 (10)	IgM ELISA
Herpes simplex virus	4 (8)	Polymerase chain reaction
S. pneumoniae	3 (6)	CSF culture
Orientia tsutsugamushi (Scrub typhus)	2 (4)	IgM ELISA
CT Brain findings		Disease
B/L Thalamic hypodensities	2 (4)	Japanese encephalitis
Temporal lobe changes	2 (4)	Herpes simplex encephalitis
Subdural haemorrhage	2 (4)	Organism not identified.
Hydrocephalus	1 (2)	Organism not identified.
Gangliocapsular hypodensities	1 (2)	Organism not identified.
Normal	42 (84)	-

The CT brain was abnormal in 8 (16%) cases and normal in 42 (84%) cases. Bilateral thalamic hypodensities was seen in JE and temporal lobe changes were seen in HSV causing meningitis. In this study, 9 (18%) children died and rest recovered completely.

Discussion

This is a prospective study which will include pediatric patients with features of acute CNS infection. All children from 1 month to 12 years of age presenting with signs & symptoms of acute CNS infection will be included in this study.

We started analyzing with age distribution among our patients, in our study 15 infants were below three months of age, similarly 13 children were above 3 years of age. While rest 22 patients were 3 months to 3 years of age. Prevalence rate amongst below one-year age group has been reported as 77%, 65% and 75% and 61% by various authors.[6] Children in this age group are more susceptible to infection due to their underdeveloped immune system and therefore disease is likely to occur when exposed to bacteria or pathogens. This is in similar with a study done in Australia on meningococcal disease that reported the average age of infection is between 0-4years of age [7].

Coming to sex distribution in our study 31 were male children and 19 were female children. Males outnumbered the females by a ratio of 1.63:1 indicating male preponderance of ABM in our study in accordance with other studies8. Relative resistances to infection in females are related to certain factors regulating the synthesis of gamma globulin on X chromosome, thus explaining the preponderance for meningitis and septicemia amongst males. A study in Australia that reported that males contract meningitis more regularly than their female counterparts.[7]

In our study only three children had delayed developmental milestones, where other children had normal developmental milestones. Our results are in accordance with other studies showing developmental delay in 23% and 31%.

Coming to presentation of symptoms seizures was the most common symptom presenting in 46 cases followed by fever in 42 patients, altered sensorium was seen in 31 patients and vomiting in 19 cases. The number of patients presenting to the emergency with symptoms suggestive of meningitis far exceeds the number of patients who actually have the disease. The classic symptom triad of fever, neck stiffness, and altered mental status is present in only a minority of patients. [9] Other associated symptoms may include nausea and vomiting, cranial nerve abnormalities, rash, and seizure. Infants can also present with non-specific symptoms such as lethargy and irritability. Therefore, if the patient presenting with acute headache does not have neck stiffness or fever and is mentating normally, it is extremely unlikely that they have meningitis.[10] A prospective study of children ages 2 months to 16 years from Israel also demonstrated the non-discriminatory value of symptoms in diagnosing meningitis.[11]

Status epilepticus was the most common type of seizure seen in our study, which was observed in 40 children. Central nervous system infections are an important cause of epilepsy in developing countries. There is a paucity of studies on the causes, patterns, and outcomes of status epilepticus in developing countries. In a study from India, electroencephalography (EEG) monitoring revealed nonconvulsive status epilepticus in 10.5% of patients in the neurointensive care unit. In an Indian hospital-based study, central nervous system infection and single enhancing lesions on computed tomography scan were associated with status epilepticus in 62.5% of patients.

Commonly symptoms usually start with fever and can progress to irritability, refusal to eat, headache, neck pain, and sometimes seizures as in our study group. In infants, findings are commonly as vague as somnolence, irritability, high-pitched cry, diffuse hyper-reflexia, or a full or bulging fontanel and symptoms of poor feeding and vomiting.

Meningeal signs were seen only in few children like, neck stiffness was seen in five patients and Kernig and Brudzinski sign in one patient each. Meningeal irritation was defined as presence of Brudzinski sign I or II, Kernig sign, tripod phenomenon, or neck stiffness in children older than 1 year. In children 1 year or younger, signs of meningeal irritation were the signs mentioned herein or irritability during manipulation of head or legs by the pediatrician or a bulging fontanel.

We also analyzed hemogram where anemia was present in 34 children and leukocytosis in 18 children. We analyzed all other parameters total count was abnormal in 21 children. Anemia is a common finding in critically ill pediatric and adult patients. In both populations, the majority of patients are often anemic at presentation. Moreover, increasing anemia develops soon after admission to a pediatric intensive care unit (PICU), and most of the red blood cells (RBCs) administered is used within the first 48 hours to reverse hypoxia and improve oxygen delivery. We evaluated electrolytes level in detail, and hyponatremia was present in 12 cases and hypernatremia in 2 cases. Many studies have demonstrated that patients with acute CNS diseases have significantly lower levels of serum sodium,

osmolality and glucose compared to the control group, while patients with acute CNS diseases have significantly higher levels of urea and osmolality compared to the control group. This is similar to Bussmann et al [12] and Von-vigier et al [13] who demonstrated low serum levels of sodium and osmolality. Hypocalcemia was present in 15 children. Hypoglycemia was present in 9 cases in our study.

Tone and posture were abnormal in almost 45 children in our study and rest was normal. Severe brain damage may occur in the course of many metabolic and infectious diseases affecting the brain in infants and young children in whom the acute stage of brain injury may be manifest clinically as convulsions, coma, and states of decerebrate and decorticate rigidity.

CSF analysis was done in and in 21 patient's findings was there, among which 10 were neutrophil predominant, 10 were lymphocyte predominant and in one children RBC was seen. Cell count was positive in 21 children. CSF protein was elevated in 27 children. Sugar levels were reduced in 14 children. Similarly, CSF culture was positive in only one case. The gold standard for diagnosing viral and bacterial meningitis is a CSF culture.[14] CSF obtained from a lumbar puncture is used to culture cells, glucose level, protein, cell count, and differential, and to begin a Gram stain. The viruses that cause meningitis are easily determined by analysis of cell protein and glucose in the CSF.[14] In four patients organisms were isolated, it was streptococcus in two patient, dengue in five patients, and Japanese encephalitis in four patients. Etiology: bacterial (organisms are age-dependent), viral (can be seasonal), fungal (most common in immunocompromised population), parasitic (rare) and aseptic. In our study the diagnostic facilities were minimal and sample size were too low to find more causative organisms.

CT Brain was evaluated in all patients and it was normal in 42 children, only 8 children had some sort of findings like thalamic hypodensities, hydrocephalus, sub dural hemorrhage and ganglionic hypodensities. CNS infections require quick diagnosis and treatment to prevent life threatening complications, with imaging playing a crucial role in the workup of children. In our study around half of children required more than 20 days hospitalization, 24 children required more than 20 day in hospital whereas 14 children required less than 10 days hospitalization, 12 children required stay in hospital between 10 to 20 days.

Finally coming to outcome, in our study 11 children died and rest recovered and discharged. The case fatality rate in developing nations including India has been reported between 10-30% by various authors.[15] approximately one third mortalities occurred during first 48 hours reflecting the critical condition of the patients at admission. Even in developed nations with best available facilities case fatality rate is around 10 %. It is around 22% in our study which is influenced by multiple factors.

Conclusion:

In our study most of children were in 3 months to 3 years of age and predominantly male. Status epilepticus is most common seizure presentation. In electrolytes, hyponatremia was present in 12 cases and hypernatremia in 2 cases. Hypokalemia was seen in 7 cases and hyperkalemia was not seen in any case. CSF analysis was done and mostly were neutrophil predominant, followed by lymphocyte predominant. CT Brain was evaluated and findings like thalamic hypodensities, hydrocephalus, subdural hemorrhage and ganglionic hypodensities. Hence proper evaluation and knowing various clinico-etiological profile helps in management of children manifesting with acute CNS infection.

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