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General Medicine

A STUDY OF PRESENTING SIGN-SYMPTOMS AND MRI CHARACTERISTICS IN CASES OF ACUTE MENINGOENCEPHALITIS IN IMMUNOCOMPETENT ADULTS IN A TERTIARY CARE HOSPITAL OF EASTERN INDIA

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ABSTRACT Meningoencephalitis is a life threatening illness that is prevalent worldwide and bacterial infection remains a major cause of death and long term neurological disabilities and thus hampers the quality of life.[1]. Patient is usually presented with photophobia, headache, or stiff neck, restless, irritability, confusion, convulsion, coma & death.[2].. Study conducted to study the morphological pattern of brain parenchymal lesions with Magnetic resonance imaging (MRI) of brain in Acute Meningoencephalitis. There are very few studies in India, especially from the eastern part of the country regarding evaluation of MRI findings in acute meningoencephalitis. The morphological features evident in MRI of brain in various etiological groups vary and an area that needs to be explored. Brain imaging in acute meningoencephalitis along with clinical features & CSF study is truly essential to formulate a proper management. Along with revelations of recent trends of infection responsible for meningoencephalitis, this study also shows that early confirmation of clinical suspicion with judgement of severity & neuroimaging (MRI with contrast) with CSF study is of great significance. Prompt diagnosis provides physicians with an opportunity to prevent undue mortality and morbidity.. Here lies the relevance of this study.

KEYWORDS : Acute Meningoencephalitis, Cerebrospinal Fluid, Mri Of Brain

INTRODUCTION:

The incidence of acute encephalitis in western countries is 7.4 cases per100,000 population per year. In tropical countries, the incidence is 6.34 per 100,000 per year. [3][4] Herpes simplex encephalitis has an incidence of 2–4 per million population per year.[5] . The common pathogens; which are encountered in adult bacterial meningitis are Streptococcus pneumonia (30-50%), Neisseria meningitides (10-35%), Staphylococci (5-15%), other Streptococcus species, Haemophilus influenzae (1-3%), Gram-negative bacilli (1-10%) and Listeria monocytogenes [6]. Prompt recognition, early diagnosis, efficient decision making followed by rapid institution of therapy plays a pivotal role in saving a large salvageable portion of the affected population and thus reducing mortality. Tuberculous meningitis (TBM) remains the most common presentation. In spite of advances in diagnostic technology and effective therapeutic options, it continues to pose significant management challenges. Despite anti-TB chemotherapy, 20-50% of the affected people die and many who survive have significant neurological deficits. The case fatality noted to be associated significantly with delay in diagnosis and treatment. Tuberculous meningitis (TBM) generally occurs in course of a sub acute or chronic case but TBM may have an acute presentation. Diagnostic evaluation includes various microbiological, pathologic, molecular, and biochemical investigations& imaging modalities. Imaging helps in early diagnosis and helps in preventing morbidity and mortality.[7] Imaging is essential in showing complications in addition to diagnosis.[8]

The plethora of magnetic resonance sequences available with the radiologist today provides a wealth of information; anatomical, pathological, physiological, functional and molecular aspects of the brain. It is most often; the procedure of choice and preferred over CT scan, due to its multilane and multi parametric imaging, and to its better contrast resolution.[9] It may detect the possible predisposing CSF leaks in par nasal sinuses, orbital cellulites, rhino sinusitis-the factors that may culminate into meningoencephalitis.

AIMS AND OBJECTIVES OF THESE STUDIES:

is to study the morphological pattern of brain parenchymal lesions with Magnetic resonance imaging (MRI) of brain in Acute Meningo encephalitis.

MATERIALS AND METHODS:

a) Patients, who admitted in between January 2013—August 2014 in the department of General Medicine of NRS Medical College and Hospital from rural and urban catchment area, were included in this study as simple random selection. 50 patients, aged>12years were included in this prospective observational study with Fever and Signs of Meningitis (Nuchal rigidity, vomiting, and headache) or Signs of meningoencephalitis: Meningeal signs with altered sensorium, focal neuro-deficits, and seizures. The following patients with Sepsis, Metabolic Encephalopathy, Dyselectrolytemia, Poisoning, Cerebrovascular Accident, Intracranial SOL, Neuro cysticercosis, Enteric Fever with meningism, Vascular Aneurysms producing local compressive effect, Acute disseminated Encephalomyelitis (ADEM) and Cerebral Malaria were excluded from the study. Clinical Characteristics-Glasgow Coma Scale (GCS) Scoring (3 to 15) as a marker of clinical severity on admission. According to the score calculated on admission, patients divided into three groups- Gr. A (GCS 3-5), Gr. B (GCS 6-9), Gr. C (GCS 10-15). **:** The macroscopic appearance of the CSF recorded. A routine CSF total and differential count; done by a haemocytometer by standard methods. The CSF samples subjected to a cytospin by using Shandon cytospin MODEL 001/ 002. CSF(500 microlitres) was added to the spin cups, spun for 10 minutes at 800 rpm and the resultant smear was Gram stained and examined microscopically. ZN staining, Bacterial culture, TB culture (BACTEC) and Cryptococcal staining(INDIA INK STAIN) were also done. Specific Viral analysis; done by CSF ELISA according to relevance, availability and feasibility. All CSF samples; cultured on Sheep blood agar, Chocolate agar, MacConkey's agar and Thioglycollate broth for specific diagnosis. MRI (Magnetic resonance imaging) with contrast (1.5 tesla machine) with Axial, Coronal and Saggital cuts were taken sometimes with Special Sequences like DWI (diffusion-weighted imaging), T1 and T2 FLAIR (fluid attenuated inversion recovery) and GRE(Gradient Echo) [As applicable-according to discretion of Radiologist. Neuroimaging may precede CSF study by lumbar puncture if there is any contraindication to the procedure like history suggestive of presence of Intracranial SOL, Papilloedema, focal neurodeficits, signs of increased intracranial tension or new onset seizures. We used laboratory methods available in the Hospital and NABL accredited private laboratory. It was a Simple observational study. History taking and Meticulous Clinical Examination & Haemato-Pathological and Biochemical Investigations: including complete blood count, Fasting and Post Prandial Glucose, Blood Urea and Creatinine, Serum Sodium and Potassium, Blood Culture study, HIV 1& 2, HbsAg and Anti HCV Antibody, Malaria dual antigen, Dengue Ns1 antigen and Dengue

specific IgG and IgM, Widal's Test, Leptospira specific IgM antibody. CSF was analysed for a) Cytology-Cell type and Cell count, b) Biochemistry- Glucose, Protein and Chloride and c) Microbiology- Gram staining, ZN staining, Bacterial culture, TB culture(BACTEC) and Cryptococcal staining (India Ink Stain) d) Specific Viral analysis by CSF ELISA according to relevance, availability and feasibility. Final Diagnosis Based on Set Criteria and Segregation of cases according to etiological groups from CSF and MRI findings. Descriptive statistical methods; used, utilizing the SPSS software for data analysis.

REVIEW OF LITERATURE:

Nearly one in four adults with acute bacterial meningitis will die, and many survivors sustain neurological deficits. The outcome has not changed since the early 1960s despite the introduction of potent antibiotics and specialised intensive care units. The prognosis is worse with a delay in management. [10] Bacterial meningitis in adults (those aged over 15 years) is a serious condition. The principles of prevention and treatment are easy to state but, unlike recommendations in guidelines for other conditions, the evidence base for many of our recommendations is lacking or a subject of controversy. Despite the existence of antibiotic therapies against acute bacterial meningitis, patients with the disease continue to suffer significant morbidity and mortality in both high and low-income countries.[11] Dilemmas exist for emergency medicine and primary- care providers who need to accurately diagnose patients with bacterial meningitis and then rapidly administer antibiotics and adjunctive therapies for this life-threatening disease. [7]

Marjolein J. Lucas,Matthijs C. Brouwer, et al in their study; published in 2014, assessed the incidence, clinical characteristics, and outcome of patients with bacterial meningitis presenting with a minimal score on the Glasgow Coma Scale from a nationwide cohort study of adults with community-acquired bacterial meningitis in the Netherlands from 2006 to 2012. Thirty of 1,083 patients (3%) presented with a score of 3 on the Glasgow Coma Scale. In 22 of 30 patients (73%), the minimal Glasgow Coma Scale score; explained by use of sedative medication or complications resulting from meningitis such as seizures, cerebral edema, and hydrocephalus. Systemic (86%) and neurologic (47%) complications occurred frequently, leading to a high proportion of patients with un-favourable outcome (77%). However, 12 of 30 patients (40%) survived and 7 patients (23%) had a good functional outcome, defined as a score of 5 on the Glasgow Outcome Scale. They concluded that patients with community-acquired bacterial meningitis rarely present with a minimal score on the Glasgow Coma Scale, but this condition is associated with high rates of morbidity and mortality. However, 1 out of 5 of these severely ill patients will make a full recovery, stressing the continued need for aggressive supportive care in these patients.[12]

Schutte CM and van der Meyden CH in their study: found that, 88% of patients with a GCS value of > 12 had a good neurological outcome, while 88% of those with a GCS value of < or = 8 had a poor outcome. They found good correlation between both the GCS and CSF-protein level at admission and the outcome of patients with meningitis with the GCS value. GCS value was a better prognostic indicator than high CSF protein levels[13]. Mani R, Pradhan S et al in their study conducted in South India (NIMHANS) in 2007 [20] observed that, as compared to Western studies, the relative incidence of meningitis caused by H. influenzae, N. meningitides and Listeria is less in South-East Asia. On the contrary, gram negative bacilli such as Klebsiella pneumonia and Pseudomonas aeruginosa are increasingly being recognised as important pathogens of community-acquired as well as nosocomial meningitis. It is especially seen among the elderly and in patients with chronic debilitating diseases like cirrhosis, diabetes and malignancies.[14] As life expectancy is increasing, it may not be uncommon to see an increased incidence of community acquired acute bacterial meningitis in the elderly in the coming years. I. Steiner, H. Budka et al in their review of diagnosis and management recommendations in Viral encephalitis states that analysis of cerebrospinal fluid for protein and glucose contents, cellular analysis and identification of the pathogen by polymerase chain reaction (PCR) amplification (recommendation level A) and serology (recommendation level B). Neuroimaging, preferably by magnetic resonance imaging, is an essential aspect of evaluation (recommendation level B). Lumbar puncture can follow neuroimaging when immediately available, but if this cannot be obtained at the shortest span of time it should be delayed only in the presence of strict contraindications. Brain biopsy should be reserved only for unusual and diagnostically difficult cases. All encephalitis cases must be hospitalized with an access to intensive care units.[15]

Oliver Kastrup, Isabel Wanke, and Matthias MaschkeIn in their study **Neuroimaging of Infections**[16] states that cases of uncomplicated meningitis, cranial computed tomography (CT) appears to be sufficient for clinical management to exclude acute brainedema, hydrocephalus, and pathology of the base of skull. Magnetic resonance imaging (MRI) is superior in depicting complications like sub-/epidural empyema and vasculitic complications notably on FLAIR (fluid-attenuated inversion recovery)-weighted images. The newer technique of diffusion-weighted imaging (DWI) shows early parenchymal complications of meningitis earlier and with more clarity and is of help in differentiation of pyogenic abscess (PA) from ring enhancing lesions of other aetiology. Pfister HW, Feiden W, Einhäupl KM studied 86 patients with bacterial meningitis having central nervous system complications, including brain swelling, hydrocephalus, brain abscess, subdural empyema, or subdural effusion (using computed tomography) and cerebrovascular involvement (using cerebral angiography), systemic complications, including septic shock, disseminated intravascular coagulation, adult respiratory distress syndrome, or septic or reactive arthritis.[17]

Acute bacterial meningitis diagnosis is based on clinical and microbiological findings with neuroimaging in the form of MRI reserved for those with specific adverse clinical features or when an underlying cause such as mastoiditis is suspected. MRI is extremely useful for detecting and monitoring the complications of meningitis. [11] A study named - Viral aetiology and clinico-epidemiological features of acute encephalitis syndrome in eastern India conducted by Rathore SK, Dwibedi B et al during April 2011 to July 2012. Blood and CSF samples of 526 AES cases; investigated by serology and/or PCR. Viral aetiology was identified in 91 (17·2%) cases. Herpes simplex virus (HSV; types I or II) was most common (16·1%), followed by measles (2·6%), Japanese encephalitis virus (1·5%), dengue virus (0·57%), varicella zoster virus (0·38%) and enteroviruses (0·19%). Simultaneous infection of HSV-I with measles; observed in seven cases. This report provides the first evidence on viral aetiology of Acute encephalitis syndrome viruses from eastern India showing dominance of HSV that will be useful in informing the public health system. [18]

Panagariya A, Jain RS et al[19] in a study conducted in North West India with Herpes simplex encephalitis cases included patients admitted with provisional diagnosis of an encephalitic illness over a period of 30 months. Special investigations included CSF analysis, EEG, CT scan and MRI. Herpes simplex virus (HSV) antibody estimation in CSF and blood; done simultaneously using ELISA. 28 patients showed electroencephalographic, serologic and/or neuroradiological evidence of herpes simplex encephalitis. Males affected more than females. Age ranged from 4 years to 65 years. HSV encephalitis occurring worldwide, contributing to 10-20% cases of viral encephalitis.[20]Exact incidence of this disease (HSE) is the most difficult to estimate, because only few patients with common cause of fatal sporadic acute encephalitis with severe disease report to hospital whereas mild and self limiting cases usually go unrecognised. In India, HSE appears to be under diagnosed, probably due to lack of awareness and diagnostic facilities. Curiously, till 1992 only occasional case reports were available.[21] CT scan showed asymmetric fronto-temporal lesions with or without haemorrhage in 18 (64%) cases. MRI was characteristic with bilateral asymmetric fronto-temporal lesions in all the 16 patients, in whom it was done. Magnetic resonance imaging appears to be the most sensitive and specific neuroimaging method for HSE. It shows hyper intense signals on T2WI in medial temporal and inferior frontal areas bilaterally.[22]These characteristic MRI findings seen in their patients were similar to MR lesions seen in PCR confirmed HSE patients of another series.[40]MRI showed bilateral asymmetrical fronto-temporal lesions in 12 cases, while bilateral isolated temporal lesions were seen in 4 patients. All the four patients were below the age of 19 years. Demonstration of virus in the brain biopsy is 100% confirmatory test. However, brain biopsy is now rarely undertaken, because of risk of haemorrhage and other complications.[23]

HSE is the only form of sporadic encephalitis which has a specific antiviral therapy i.e. acyclovir. HSE is not very uncommon and carries a very high mortality and morbidity in absence of treatment. Acyclovir is quite innocuous as well as effective, if used early in the course, a

clinical criteria of diagnosis by exclusion and relevant supportive evidences with EEG, neuroradiology and CSF examination may prove to be practical in initiating treatment in most of the centres in Indian conditions.

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S.K. Handiquea, R.R. Das et al [25]conducted a study named- **Temporal Lobe Involvement in Japanese Encephalitis: Problems in Differential Diagnosis**. In this study they selected sixty-two patients with JE who underwent CT or MR imaging or both. On MR imaging and CT, Japanese encephalitis (JE) shows lesions in the thalami, substantia nigra, basal ganglia, cerebral cortex, cerebellum, brain stem, and white matter, whereas temporal lobe involvement; characteristically seen in Herpes simplex encephalitis (HSE). Temporal lobe involvement in JE may cause problems in differentiating it from HSE. They undertook this study to show the temporal lobe involvement pattern in JE and highlight differentiating features from temporal lobe involvement in HSE. Eleven (17.7%) patients showed temporal lobe involvement with abnormal MR imaging in all. They concluded that the temporal lobe involvement pattern is characteristic and mostly involves the hippocampus, usually sparing the rest of the temporal lobe. This and the concurrent involvement of the thalami, substantia nigra (SN), and basal ganglia allow differentiation from HSE. If the temporal lobe involvement is more severe, laboratory tests may be the only way to differentiate it from HSE

Suyash Mohan, Krishan K. Jain Et al describes in their study- **Imaging of Meningitis and Ventriculitis** describes how imaging helps in non-invasive differentiation of infective from the non-infective conditions and helps in better clinical decision-making. In acute meningitis; meningeal enhancement is located over the cerebral convexity, whereas in chronic meningitis it is most prominent in the basal cisterns. The role of neuroimaging is to confirm suspected meningitis, rule out meningitis mimics, evaluate for complications, and rule out increased intracranial pressure before lumbar puncture.[26] Magnetic resonance imaging is critical in evaluating complications of meningitis (eg. ventriculitis, extra-axial collections, cerebritis and abscess, herniations, cranial neuropathy, and vasculopathy). A study aimed at evaluating the clinical and radiological outcome of tuberculous meningitis (TBM) patients with pulmonary miliary tuberculosis was done by Kalita and Misra in which MRI was abnormal in 7 out of 8 patients(revealed hydrocephalus, granuloma, exudates and infarction) and 3 of these patients had normal CT scan. This study shows the Superiority of MRI over CT Scan in detecting Brain pathology of Tuberculous aetiology.[27] During the last two decades, the clinical presentation of TBM has changed, Atypical presentations include acute meningitis syndrome simulating pyogenic meningitis, progressive dementia, status epilepticus, psychosis, stroke syndrome, locked-in-state, trigeminal neuralgia, infantile spasm and movement disorder[28]

P Kamra, R Azad et al performed a study- **Infectious meningitis: prospective evaluation with magnetization transfer MRI**. The study was performed in lucknow (India) with the aim of prospectively characterizing infectious meningitis of different aetiology using magnetization transfer (MT) MRI. Spin-echo (SE) T1, T2 and pre- and post-contrast T1 weighted MT images in 100 patients with aetiologically proven meningitis were evaluated for the visibility and enhancement of the meninges on pre- and post-contrast T1 weighted MT images, respectively. The MT ratio (MTR); calculated from the thickened meninges in tuberculous meningitis. In addition, the percentage difference in the mean signal intensity (SI) of the meninges and adjacent brain parenchyma was calculated and compared between different groups. Visibility of the meninges on pre-contrast T1 weighted MT images may be considered highly suggestive of tuberculous meningitis.[30]

Wakai M1, Hayashi M et al report a case of acute onset of tuberculous meningoencephalitis presenting with symmetric linear lesions in the bilateral thalamus**.** It shows at the severest stage of the disease, a brain MRI revealing symmetric, linear lesions without the effect of Gd-enhancement in the bilateral thalamus, which thereafter disappeared along with the healing of the illness. They conclude with the remarks with; Thalamic and other parenchymal lesions must be kept in mind in dealing with acute tuberculous meningo-encephalitis [31]**.** Ete T, Mondal S, Sinha D, Siddhanta S et al reported; in their case of Miliary tuberculosis and tuberculoma of brain presenting like meningitis in immunocompetent patient[32]**.** Deepak Patkar, JayantNarang Et al in their study- Central Nervous System Tuberculosis Patho-physiology and Imaging Findings outlines that Imaging, particularly magnetic resonance imaging, is a cornerstone in the diagnosis as well as follow-up of central nervous system (CNS) tuberculosis. Imaging appearance of CNS TB is becoming more and more complex and atypical with the onset of multidrug-resistant tuberculosis. Early, accurate diagnosis can help in preventing morbidity and mortality. Newer imaging techniques like magnetic resonance spectroscopy help to improve characterization and thus aid in diagnosis of atypical CNS TB.[33]

It is concluded that MRI could have an important role in the early screening for infectious meningitis, provided a gadolinium-enhanced FLAIR sequence is used.

RESULTS AND ANALYSIS

All immune-competent patients aged 12yrs or more were selected randomly over a period of 19 months for this observational study as per the clinical inclusion criteria.18 cases(36%) were male and 32cases(64%) were female. Patients ranging from ages 12 yrs to 77 yrs: selected and divided into age groups. Maximum number of patients (26%) belonged to 12-20 yrs age group. (See figure 7)

The patients were clinically examined and classified into three groups according to the Glasgow coma scale.15 cases (30%) belonged to group A (GCS 3 to 5), 22 cases (44%) Belonged to Gr. B (GCS 6 to 9) while 13 cases (26%) belonged to Gr. C (GCS 10 to 15) on admission, 30% patients had a very poor clinical condition (GCS 3 to 5) during admission as evident from the GCS category distribution while majority of patients belonged to group B. Patients were subjected to MRI of brain with contrast (appropriate sequences were used) followed by CSF examination. CSF culture and VIRAL ELISA: performed as applicable and as per feasibility and availability. In some cases, CSF study: done prior to MRI of brain for the sake of the patient before initiating therapy. After obtaining the investigation results, the cases: segregated into etiological groups and Re classified according to the GCS groups and gender. Majority of cases had a viral aetiology (56%) followed by tuberculous (28%) and bacterial aetiology (16%). Pyogenic meningitis cases had a Male predilection (62.5%) while tuberculous and viral meningitis had female predilection in incidence, 57.14% and 75% respectively. (See Figure-8)

Majority of pyogenic meningitis cases (37.5%) belonged to 31-40yrs age group while maximum number of tuberculous meningitis cases (35.71%) and viral Meningoencephalitis cases (28.57%) belonged to 12-20 yrs age group. Out of 50 cases 8 cases(16%) were diagnosed as **pyogenic meningitis**[5males(62.5%) and 3 females(37.5%)] 1case was in gr A(GCS 3 to 5), 5 cases in gr B(GCS 6 to 9) and 2 cases were in gr C(GCS 10 to 15). So, 12.5% cases presented in a clinically severe state (GCS 3 to 5) during admission. 14 cases (28%): diagnosed as tuberculous meningitis [6males (42.86%) and 8 females (57.14%)]. Among them, 6cases were in gr A (GCS 3 to 5), 6 cases in gr B (GCS 6 to 9) and 2 cases were in gr C (GCS 10 to 15). 42.86% cases presented in a clinically poor condition (GCS 3 to 5) on admission, 28 cases(56%) were diagnosed as viral meningoencephalitis[7males(25%) and 21females (75%)] 8 cases were in gr A(GCS 3 to 5), 11 cases in gr B(GCS 6 to 9) and 9 cases were in gr C(GCS 10 to 15).28.57% cases presented in a clinically poor state(GCS 3 to 5) on admission. After comparative analysis of three etiological groups and their GCS categories it was found that tuberculous meningitis cases(42.8%) presented in a more severe state followed by cases of viral meningoencephalitis(28.57%) and pyogenic meningitis(12.5%).
CSF Findings

CYTOLOGY:

In cases that were later diagnosed as **pyogenic meningitis**, the cell counts ranged from 120 to 5900 cells/cumm with a mean count of 950.5± 3748.84 cells/cumm and neutrophil predominance. In cases with a final diagnosis of **tuberculous meningitis**, the cell counts ranged from 60 to 460 cells/cumm with a mean count of 225.86±217.22 cells/cumm, with lymphocyte predominance. In cases categorized as **viral meningoencephalitis**, the cell counts ranged from 30 to 510 cells/cumm with a mean count of 128.607±276.86cells /cumm and a predominantly lymphocytic picture.

BIOCHEMISTRY & ADA LEVELS:

Pyogenic meningitis cases revealed a mean CSF glucose of 19±18.9mg/dl, mean protein levels of 62.375±48.52mg/dl, mean chloride levels of 112.88± 12.48 meq/Lt with mean ADA level of

8.025±24.14. This picture was consistent with hypoglycorrhachias expected in pyogenic meningitis.

Tuberculous meningitis cases revealed a mean CSF glucose of 35.79±22.9 mg/dl, mean protein levels of 268.86±368.12 mg/dl, mean chloride levels of 112.714±12.54 mEq/Lt with mean ADA level of 16.29±16.14 U/L. Protein levels: markedly increased with ADA levels also higher than normal range along with low glucose levels consistent with the diagnosis.

Viral meningoencephalitis cases revealed a mean CSF glucose of 60.11± 32.28 mg/dl, mean protein levels of 96.96±91.98 mg/dl, mean chloride levels of 113.45±14.32 mEq/Lt with mean ADA level of 3.76±4.38U/L. The protein levels were higher with normal glucose levels.

CSF CULTURE, STAINING AND VIRAL PCR:

According to affordability of the patient and availability of appropriate facilities in Eastern India CSF culture and staining, CSF viral antibody detection by ELISA(when suspected) were sent with the routine samples. Some cases were diagnosed accurately from CSF culture and ELISA that were corroborating with the clinical assumptions and radiological imaging findings.

PYOGENIC MENINGITIS ETIOLOGIES:- (N=8)

CSF gram staining and culture revealed Streptococcus pneumoniae in 4(50%) cases, Neisseria meningitides in 1(12.5%) case, Staphylococcus aureus in 1(12.5%) case and culture negative in 2(25%) cases. This shows that majority of the culture positive cases were positive for Streptococcus pneumonia followed by equal incidence of Neisseria meningitides and Staphylococcus aureus. 25 % cases that were culture negative had classical symptoms which resolved with empiric antibiotics.

TUBERCULOUS MENINGITIS:- (N= 14)

All the cases suspicious of tuberculous aetiology were ZN smear negative. CSF culture was negative in 10 cases (71.4%) while culture could not be done in 4 cases(28.6%). Diagnosis had to established on clinical features, CSF cytology, CSF biochemistry, brain imaging and therapeutic response to antitubercular drugs.

***VIRAL MENINGOENCEPHALITIS:-* (N=28)**

Patients with CSF cytology indicating a viral infection revealed the following viral etiologies in CSF Elisa(IgG). 10 cases(35.72 %) were positive for Herpes simplex, 3 cases(10.72%) were positive for Varicella zoster,4 cases(14.28%) were positive for Japanese B while 11 cases (39.28%) were negative or indeterminate.

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MRI FINDINGS:

(With contrast and appropriate sequences as relevant and applicable.)

The MRI findings as observed and analysed with the expert opinion of the radiologists not only strengthened our diagnosis but revealed different patterns of lesions varying with MRI sequences (T1, T2, FLAIR and DWI with gadolinium contrast) and involving certain anatomical regions of brain and the meninges. They not only revealed the morphological spectra of the primary pathology but also the sequelae, complications and associated features. The pattern of involvement in MRI Brain has been described below. They are classified into groups which were in some cases coexistent and had a considerable overlap in different cases in varying combinations.

Cases diagnosed as Pyogenic Meningitis revealed.

PATTERN OF LESION:

Cerebritis with hypo-intensities on T1 and hyper-intensities on T2 Flair sequences seen in 4 cases(50%). Meningeal enhancement on T2 weighted images in 4 cases(50%), Ventriculitis with intra-ventricular fluid collections in 3 cases(37.5%), Lacunar infarcts evident on DWI sequence in 2 cases(25%), Middle cerebellar peduncle involved with patchy signal intensities and mild restricted diffusion along with patchy enhancement of right cavernous sinus (suggestive of cavernous sinus thrombo-phlebitis) in 1 case(12.5%). Maxillary sinusitis was found in 1 case(12.5%) and 2 cases(25%) had a normal MRI.

ANATOMICAL AREAS INVOLVED

4(50%) cases showed meningeal involvement, 2(25%) cases involved the peri-ventricular area, 1case(12.5%) showed basal ganglia lacunar infarct, 1(12.5%) case revealed patchy altered signal intensities involving the middle cerebellar peduncle with mild restricted diffusion and 1(12.5%) case involved centrum semiovale region.

CASES WITH A FINAL DIAGNOSIS OF TUBERCULOUS MENINGITIS REVEALED—

PATTERN OF LESION :

Mildly dilated ventricles or hydrocephalus in 9 cases(64.29%). Meningeal enhancement on T2 weighted images in 7 cases (50%). Ring enhancing or nodular lesions scattered in various parts of brain in 6 cases(42.86%). Perifocal or peri-lesional edema in 5 cases(35.71%), Infarcts in different areas of brain in 4 cases(28.57%), Granulomatous lesions in 3 cases(21.43%) and normal MRI in 1 case

ANATOMICAL AREAS INVOLVED :

Ventricles dilated in 9 cases(64.29%), Meningeal enhancement in 7 cases (50%), Basal ganglia in 6 cases(42.86%), Thalamic involvement in 5cases(35.71%), Parietal area in 5 cases(35.71%), Brainstem in 3 cases(21.43%), Cerebellum in 3 cases(21.43%),Occipital region involved in 2 cases

CASES CATEGORIZED AS VIRAL MENINGOENCEPHALITIS AFTER DIAGNOSIS REVEALED—

T2 hyper intensities in Temporal region in 7 cases(25%) ,Thalamic involvement in 7 cases(25%), Periventricular area in 6 cases (21.43%) with lacunar infarct in periventricular and basal ganglia region in 1case out of the 6 cases. Hypo intense on T1 weighted images with Hyper intensities on T2 FLAIR images were seen in Parietal area in 5 cases (17.86%)and Basal ganglia or Midbrain involvement seen in 4 cases each(14.29%). Frontal area along with parietal or temporal involvement (haemorrhagic component)were found in 2 cases(7.14%). Cerebellar hyper intensities with effaced folia seen in 1 case (3.57%) and Corpus callosal (splenium) hyperintensity seen in 1 case (3.57%). 11 cases(39.29%) had a normal MRI. 10cases(35.72%) were established as Herpes simplex encephalitis as confirmed on CSF ELISA and they had similar MRI findings. Hypo to iso intense on T1 weighted images while hyper intensities on T2 FLAIR images were observed in temporal areas with fronto-parietal or temporo-parietal spread along with basal ganglia, thalamus and midbrain involvement in varying combinations in different cases. 4 cases (14.28%) with positive clinical suspicion were diagnosed as cases of Japanese B encephalitis on CSF serology (positive IgG for Jap B). They had similar MRI findings when analysed after obtaining the serology results. 75% of the four cases had bilateral thalamic hyper intensities along with midbrain involvement in 2cases and basal ganglia with periventricular involvement in 1case. While 25% of the 4 cases had MRI simulating Herpes virus encephalitis. The MRI revealed hyper intensities on T2 Flair images in bilateral temporo-parietal region, basal ganglia, thalamic and paraventricular area. 3(10.72%)cases with history of varicella zoster virus infection shared similar MRI feature of periventricular T2 hyper intensities in all and lacunar infarcts in 2(7.14%) out of the 3 cases. 11(39.28%)cases were etiologically inconclusive due to negative CSF ELISA. The MRI revealed bilateral thalamic involvement with corpus callosal hyper intensities in 1case (3.57%), 1case (3.57%) had cerebellar hyper intensities, 1 case(3.57%) had periventricular T2 enhancement and another case showed bilateral thalamic, basal ganglia and midbrain involvement. 63.64% of these cases had a normal MRI of brain. 2 (7.14%) cases had a positive history of measles in recent past and 3(10.72%) cases were suffering from dengue along with meningoencephalitis. All 5 cases had a normal MRI of brain. Now whether the measles or dengue infection culminated into meningoencephalitis in those cases or they were distinctly coexistent and totally unrelated to each other, could not be exactly infer.

COMPARISON OF MRI FINDINGS IN DIFFERENT ETIOLOGICAL GROUPS

Analysing the MRI findings of different etiological groups following findings were noticed.

In pyogenic meningitis cases meningeal involvement was seen in 50% cases while brain parenchymal involvement were relatively less as compared to other etiological groups. Ventriculitis was seen in 37.5% cases and infarcts seen in 25% cases could be attributed to a sequelae of cerebritis and cerebral vasculitis.

In tuberculous meningitis cases, various anatomical areas were

affected with pattern of brain parenchymal and ventricular involvement consistent with the diagnosis. The MRI's played a pivotal role in confirmation of diagnosis with identification of the sequelae and complications of tubercular infection. Majority of cases (64.29%) revealed hydrocephalus. Ring enhancing lesions (42.86%) and granulomas (21.43%) confirmed by MR Spectroscopy (in situations of diagnostic dilemma). Meningeal enhancement was marked in 50% cases. Infarcts were noted in 28.57% probably due to cerebral arteritis and ischemia because of tubercular infection. The MRI findings on retrospective analysis corroborated with the maximum clinically severe cases (as per GCS category) during presentation in this etiological group.

Viral meningoencephalitis cases showed cerebral hyper intensities (on T2W, Flair images) in majority of cases (60.71%), attributable to the seizure episode at or before presentation. Most of those cases which turned out to be inconclusive in CSF ELISA, had a normal MRI (39.29%) and belonged to Group C (GCS 10 – 15) during admission. Thus, it was marked that patients who were relatively better clinically and had negative viral ELISA had normal brain imaging or minimal findings in MRI.

DISCUSSION

PYOGENIC MENINGITIS

Acute bacterial meningitis is more common in resource-poor than resource-rich settings. Survival is dependent on rapid diagnosis and early treatment, both of which are difficult to achieve when laboratory support and antibiotics are scarce.

SyamalModi and Amit Kumar Anand in their study **Phenotypic Characterization and Antibiogram of CSF Isolates in Acute Bacterial Meningitis** done in a tertiary care hospital Patna (India) found that 62.3% patients were males and 37.7% were females. The gender distribution and male preponderance in disease incidence was also marked (62.5 % males and 37.5% females) in our study done in Eastern India. In our study sample, size was smaller in comparison to theirs. This male predilection reported in several previous studies [33]. Similar to the study by Marjolein J. Lucas, Matthijs C. Brouwer et al (2014)[12]. patients using immunosuppressive drugs and those with asplenia, diabetes mellitus, alcoholism, or infection with immunodeficiency virus: considered immunocompromised and excluded from our study.

The Glasgow coma scale (GCS) is an objective measurement of a patient's level of consciousness and has prognostic implications in traumatic head injuries. Morbidity and mortality of patients with meningitis have related amongst others to level of consciousness, hypoglycorrhachia, extremes of age, and high CSF protein values. Schutte CM, van der Meyden CH in their study found patients with a GCS value of > 12 had a good neurological outcome, while those with a GCS value of ≤ 8 had a poor outcome. They concluded that the GCS value was a better prognostic indicator than high CSF protein levels[13]. In our study we adapted GCS as the criteria for clinical severity. Group A (GCS 3 to 5) considered as most severe clinical category. Pyogenic meningitis accurately and rapidly diagnosed by gram staining. Some studies have reported: sensitivities- 60-90% and specificities >97% of CSF on gram staining in diagnosis of ABM .[34] .In our study 50% cases were diagnosed as Streptococcus pneumonia induced meningitis, followed by equal incidence of Neisseria meningitides and Staphylococcus aureus cases (12.5% each) on CSF gram staining and culture 25percentage cases did not reveal any organism on CSF culture. Negative CSF cultures are estimated to occur in 11%–20% of patients with bacterial meningitis.[35] However, the clinical presentation of patients with culture-positive bacterial meningitis and patients with culture- negative bacterial meningitis was reported to be similar. R Mani, S Pradhan et al in their study conducted in South India (NIMHANS): found that streptococcus pneumoniae was the most common etiological agent of community acquired meningitis in all age groups accounting for 238 (61.8%) cases in their study, reflecting a similar trend reported in an earlier study from their institute (1978-1988).[36] Most Indian studies have also reported a high incidence of pneumococcal meningitis [37]. In our study also Streptococcus pneumonia was the most common organism isolated from CSF culture(50% cases). Analysis of the CSF is essential, and simple techniques can enhance the yield of diagnostic microbiology. Penicillin-resistant and chloramphenicol-resistant bacteria are a considerable threat in resource-poor settings that go undetected if CSF and blood cannot be cultured.

Magnetic resonance imaging (MRI) is not routinely required in cases of uncomplicated bacterial meningitis. It helps to visualize meningeal enhancement more clearly. Potential sources of infection include fractures of the paranasal sinus or petrous bone as well as inner ear infection and mastoiditis. Pyogenic ventriculitis is an uncommon but very severe intracranial infection requiring rapid diagnosis and therapy because of its high mortality. Neuroimaging is the only tool to reliably diagnose this life-threatening condition. MRI is more sensitive and shows periventricular high signal on FLAIR images, ependymal Enhancement.[16] Pyogenic and aseptic meningitis may cause leptomeningeal enhancement. Meningitis also may cause venous thrombosis with hyper-densities on the surface of the brain or along venous sinuses on brain MRI. Magnetic resonance venography (MRV) : used to confirm venous thrombosis.

In our study a case showed cavernous sinus thrombophlebitis in MRI and was considered a complication and consequence of the bacterial meningitis. 50% cases showed meningeal involvement, 25% cases involved the periventricular area, 12.5% showed basal ganglia lacunar infarct,12.5% case revealed patchy altered signal intensities involving the middle cerebellar peduncle with mild restricted diffusion and 12.5% case involved centrum semiovale region. Infarcts: considered, a sequelae of cerebritis and vasculitis. MRI of patients suffering from pyogenic meningitis were somewhat nonspecific in some cases and did not contribute much to the confirmation of diagnosis. The future rests with the provision of effective conjugate vaccines against S pneumoniae, Haemophilus influenzae, and Neisseria meningitides to children in the poorest regions of the world.[39]

VIRAL MENINGOENCEPHALITIS

Cranial MRI is superior to CT in early detection of signs of this necrotizing encephalitis, which can be demonstrated within the first 48 h on T2-weighted (T2WI) or FLAIR images.39 In infants and neonates, DWI appears to be more sensitive than T2WI or FLAIR imaging in early detection of the cytotoxic cortical edema.[40]

A study named - Viral aetiology and clinico- epidemiological features of acute encephalitis syndrome in eastern India conducted by Rathore SK, Dwibedi B et al during April 2011 to July 2012.[18] Blood and CSF samples of 526 AES cases were investigated by serology and/or PCR. Viral aetiology was identified in 91 (17·2%) cases. Herpes simplex virus (HSV; types I or II) was most common (16·1%). Simultaneous infection of HSV I with measles was observed in seven cases. This report provides the first evidence on viral aetiology of acute encephalitis syndrome viruses from eastern India showing dominance of HSV that will be useful in informing the public health system. In our study, there were majority of HSV cases. In CSF Elisa (IgG). 10 cases(35.72 %) were positive for Herpes simplex, 3 cases(10.72%) were positive for Varicella zoster,4 cases(14.28%) were positive for Japanese B while 11 cases(39.28%)were negative or indeterminate. Therefore, there is a similarity and etiological preponderance of HSV in both western and eastern India.

In our study MRI brain in cases with herpes simplex encephalitis revealed predominant temporal lobe and inferior frontal lobe involvement along with T2 hyper intensities in parietal lobes too. This neuroimaging finding is characteristic of herpes simplex encephalitis as described in various literatures and other studies.

Japanese encephalitis (JE) is the leading cause of encephalitis in Southeast Asia, where 30,000–50,000 cases are recorded annually (Tsai, 1997).[41] The World Health Organisation estimated nearly 14,000 deaths due to JE in the year 2002. Of these, 8,500 occurred in Southeast Asia, 3,000 in the western Pacific region and about 2,000 in the eastern Mediterranean region. Typical MRI features consist of either mixed intensity or hypo intense lesions on T1WI and hyper intense or mixed intensity lesions on T2WI predominantly in the thalami, but also in the basal ganglia, brainstem, cerebellum, and cortical areas[16]. This was also congruous to our neuroimaging findings that guided our investigations to reach an early diagnosis. 14.28% cases were positive for Japanese B in our study.

During analysis of the study a solitary case had concurrent involvement of temporal lobes with bilateral thalamus and basal ganglia, simulating herpes encephalitis. It was confirmed as Japanese B encephalitis (JE) on CSF serology. As cited by S.K. Handique, R.R. Das in their study, this pattern of involvement although not that common, may be seen in JE creating a diagnostic dilemma with herpes

encephalitis. So an early MRI of brain with characteristic findings may provide an important clue to the diagnosis in situations where antibody estimation for JE is not readily available.

The incidence of neurologic complications associated with varicella is estimated to be 1–3 per 10,000 cases [42]. The central nervous system (CNS) manifestations that occur most frequently with varicella are cerebellar ataxia and encephalitis [42]. The most serious CNS complication of varicella, has an incidence of 1–2 episodes per 10,000 varicella cases, with the highest incidence in adults and infants.[43] The CSF findings are usually abnormal with elevated opening pressure, a mild-to-moderate lymphocytic pleocytosis (usually <100 cells/μL), mildly elevated protein (50–100 mg/dL), and normal glucose levels. CNS imaging studies may show edema and areas of low attenuation consistent with demyelination [44]. In our study 10.72% cases with history of varicella zoster had positive CSF Elisa. Their neuroimaging revealed periventricular hyper intensities and focal white matter signal changes similar to that seen in demyelination. So in this context it may be taken into consideration that in developing countries like India, MRI may prove to be an important noninvasive diagnostic tool in cases of meningoencephalitis.

Dengue encephalopathy is a well-recognized and common entity, the incidence ranging from 0.5 to 6.2 %.[45] Dengue is not classically a neurotropic virus, although there is recent evidence of direct neuronal injury. Dengue encephalitis must be thought of in differentials of encephalopathy, in patients with dengue. In such cases, neuroimaging and CSF analysis should be done whenever possible. The virus or antibody can be isolated from the serum, but the CSF samples may be negative. The dengue encephalitis is thought to be benign, but can be fatal at times.[46]

We found 3 such cases in our study with feature of encephalopathy who were diagnosed cases of IgM positive dengue with CSF analysis indicating a viral aetiology and a normal MRI . Dengue specific IgM antibody (ELISA) was negative in 2 and could not be done in 1 case. In light of our knowledge regarding dengue encephalopathy, a negative CSF antibody cannot refute its presence. So whether the encephalopathy was due to some other viral pathogen or as consequence of dengue could not be confirmed. All 3 patients survived without any residual neuro deficit or CNS complications.

Infection of the CNS with the measles virus (MV) may result in 1) acute post-infectious encephalitis, 2) acute progressive encephalitis, and 3) SSPE. Data about imaging findings in acute measles encephalitis are sparse. T2WI may reveal cortical edema and bilateral symmetric hyper-intense lesions within the putamen and caudate nuclei as well as within the centrum semiovale.[47] Sometimes patients also present bilateral thalamic lesions and signal abnormalities within the corpus callosum. We found 2 cases with a recent history of measles who subsequently developed features of encephalopathy. The disease was self limiting and their MRI were normal.

We would sum up in accordance to I. Steiner, H. Budka et al and their review of diagnosis and management recommendations in Viral encephalitis.[21] A holistic approach to diagnosis should be based on medical history, examination followed by analysis of cerebrospinal fluid for protein and glucose contents, cellular analysis and identification of the pathogen by **polymerase chain reaction (PCR) amplification (recommendation level A)** and **serology (recommendation level B)**. Neuroimaging, preferably by magnetic resonance imaging, is an essential aspect of evaluation (recommen dation level B**).**

Lumbar puncture can follow neuroimaging when immediately available, but if this can not be obtained at the shortest span of time it should be delayed only in the presence of strict contraindications. All encephalitis cases must be hospitalized with an access to intensive care units. Supportive therapy is an important basis of management. Specific, evidence-based, anti-viral therapy**, acyclovir, is available for herpes encephalitis (recommendation level A)**. **Acyclovir might also be effective for varicella-zoster virus encephalitis**, gancyclovir and foscarnet for cytomegalovirus encephalitis

TUBERCULOUS MENINGITIS

J Kalita, UK Misra in their study evaluated the clinical and radiological outcome of tuberculous meningitis (TBM) patients. In this study, most of the patients were females who were anemic.MRI revealed hydrocephalus, exudates, infarction and multiple granuloma and the majority of the patients improved following antitubercular therapy. In our study there was a female predilection (57.14%). Under nutrition and anaemia may be a result or risk factor for development of tuberculous meningitis. We came across a wide range of clinical spectra and various morphological patterns of brain involvement with complications as evident on brain MRI. Adults with tuberculous meningitis (TBM) can often present with the classic meningitis symptoms of fever, headache and stiff neck along with focal neurological deficits, behavioral changes, and alterations in consciousness [48]. A history of tuberculosis is elicited in only approximately 10% of patients [48]. The presence of active pulmonary tuberculosis on chest X- ray ranges from 30 to 50%. TBM may have an acute presentation. The duration of presenting symptoms may vary from 1 day to 9 months, although several cases may present with symptoms of less than 2 weeks duration. In our cases patients had a history of less than 2 weeks duration prior to admission.

Cerebrovascular complications of tuberculous meningitis that occur typically as multiple or bilateral lesions in the territories of the middle cerebral artery perforating vessels are termed as tuberculous vasculopathy. Vessel pathology appears to be a consequence of its immersion in the local inflammatory exudate. Infiltrative, proliferative and necrotising vessel pathologies have been described, leading to luminal thrombosis. There is some evidence that vasospasm may mediate strokes early in the course of the disease and proliferative intimal disease later strokes [49]. In this study we encountered 28.57% cases with cerebral infarcts.

Contrast enhanced MRI, generally considered as the modality of choice. It is useful for assessment of the location of lesions and their margins, as well as ventriculitis, meningitis and spinal involvement (sensitivity 86%, specificity 90%) [50]. A large lipid, lactate peak has been used to specifically identify tuberculomas by magnetic resonance spectroscopy[93].In TBM, MRI shows diffuse, thick, meningeal enhancement. Cerebral infarcts can be seen in nearly 30% of cases [51]. A study from South Africa reported that the combination of hydrocephalus, basal enhancement and infarction was 100% specific and 41% sensitive for the diagnosis of TBM, although the authors suggested pre-contrast hyper density in the basal cisterns as the best predictor of TBM. [52] Our cases had classical findings indicating TBM. Ring enhancing lesions, perifocaledema, granulomatous lesions and infarcts (due to vasculopathy or vasospasm as described above) in various anatomical locations. Hydrocephalus and meningeal enhancement were also seen in the MRI's of our cases.

SUMMARY

This observational study was done in a tertiary care hospital of Eastern India. 50 consecutive hospital admitted patients (>12 yrs) fulfilling the inclusion criteria were randomly selected over a period of 19 months. A male preponderance was marked in Pyogenic meningitis cases while a female preponderance was noted in tuberculous meningitis and viral meningoencephalitis cases.

An increased propensity of disease occurrence was seen in age groups 31-40 yrs in pyogenic meningitis and younger age groups (12- 30 yrs) were more affected in tuberculous and viral meningoencephalitis. Individual patients assessed by clinical status on admission and divided into three GCS groups. 15 cases(30%) belonged to group A(GCS 3 to 5), 22 cases(44%) belonged to gr B(GCS 6 to 9) while 13 cases(26%) belonged to gr C(GCS 10 to 15) on admission. 18 cases(36%) were male and 32 cases(64%) were female. Patients ages ranging from 12 yrs to 77 yrs were selected and divided into age groups. CSF study and MRI brain was done and etiologically the cases were reclassified.

Out of 50 cases 8 cases (16%) were diagnosed as pyogenic meningitis [5 males (62.5%) and 3 females (37.5%)], 14 cases (28%) were diagnosed as tuberculous meningitis [6males (42.86%) and 8 females (57.14%)] and 28 cases (56%) were diagnosed as viral meningoencephalitis [7males (25%) and 21females (75%)]. CSF study revealed neutrophilic picture with hypoglycorrhachia in bacterial meningitis with CSF culture studies revealing Streptococcus pneumoniae as the most commonly isolated pathogen (50% cases). Tuberculous meningitis revealed CSF lymphocytic pleocytosis with significantly increased protein and ADA levels. CSF ZN staining in all cases were negative, CSF culture for tuberculosis was negative

in71.4% cases and could not be done in 28.6% cases although the diagnosis was established on other parameters and imaging evidence.

The CSF samples of viral meningoencephalitis revealed lymphocytic picture and increased protein with majority of cases being positive for Herpes simplex antibody (in CSF by ELISA method) in 35.72%. 14.28% cases were positive for Japanese B antibody. 10.72% cases were diagnosed as Varicella zoster cases. Serological confirmation of diagnosis was not possible in other cases due to non-availability of the specific test (Viral PCR) or a negative serology in 39.28%.

MRI Brain was done with gadolinium contrast, using appropriate sequences(T1W, T2W, FLAIR, GRE, DWI, Spectroscopy).The morphological patterns as evident on MRI Brain were studied in each patient. Cases with suspicion of pyogenic meningitis had features of cerebritis, patchy hyper intensities of middle cerebellar peduncle (12.5%),T2 hyper intensities of meninges and ventriculitis. Maxillary sinusitis was noted in 12.5%, lacunar infarcts were noted in 25% cases as sequelae. One case was complicated with cavernous sinus thrombophlebitis (patchy enhancement) clinically presenting with ophthalmoplegia.25% cases had a normal MRI.

The pattern of lesions identified in brain MRI in tuberculous meningitis cases were- Hydrocephalus(64.29%), meningeal enhancement(50%), ring enhancing or nodular lesions(42.86%), granulomatous lesion(21.43%) with perifocaledema(35.71%). The pattern of radiological abnormalities identified in different anatomical regions of brain and found in varying combinations. Apart from one case out of 14 cases in this group, all the MRI's were abnormal and helped immensely in confirmation of diagnosis.

In viral meningoencephalitis cases T2 hyper intensities were seen in inferior frontal and temporal lobes (extension into parietal lobes in some cases) with or without haemorrhagic component, consistent with the diagnosis of Herpes Simplex encephalitis. Bilateral thalamic T2 hyper intensities (25%cases) with enhancement of basal ganglia region: consistent with the diagnosis of Japanese B encephalitis. 1 case had concurrent involvement of temporal lobes with bilateral thalamus and basal ganglia, simulating herpes encephalitis. It was confirmed as Japanese B encephalitis (JE) on CSF serology. This pattern of involvement although not that common may be seen in JE creating a diagnostic dilemma with herpes encephalitis. Periventricular hyperintensities(21.43% cases) and lacunar infarct(7.14%) were seen in MRI's. Definite serological confirmation was not possible inm these cases but periventricular hyperintensities suggest a possibility of CMV encephalitis.

Lacunar infarcts and haemorrhages may be seen as asequelae of secondary CNS vasculitis and focal white matter signal changes (similar to demyelinating lesions) consistent with varicella encephalitis. 39.28% cases had a normal MRI out of which 2 cases(7.14%) had a history of measles immediately prior to the development of neurological symptoms and 3 cases (10.72%) were suffering from Dengue during the episode of encephalopathy. 35.72% cases were etiologically inconclusive without any suggestive history of possible viral pathogen.

In pyogenic meningitis cases brain parenchymal involvement was relatively less as compared to other etiological groups. In tuberculous meningitis cases the MRI findings on retrospective analysis corroborated with the maximum clinically severe cases (as per GCS category) during presentation. Viral meningoencephalitis cases showed cerebral hyper intensities (on T2W, Flair images) in majority of cases (60.71%), attributable to the seizure episode at or before presentation. Thus, it was marked that patients who were relatively better clinically and had negative viral ELISA also had normal brain imaging or minimal findings in MRI. The MRI has played a pivotal role in confirmation of diagnosis with identification of the sequelae and complication.

LIMITATIONS OF THE STUDY

Sample size is small (N= 50). This study was done over a certain catchment area, hence not a multicentric study. As the study was done in a tertiary care hospital, the mean values may not properly reflect the actual population mean. Empiric therapy had to be started in most of the cases prior to confirmation of diagnosis, for the sake of the patients. Some of the patients who fulfilled the inclusion criteria, had to be excluded due to economic constraints.

CONCLUSION

In this Eastern India based study viral aetiologies' were more frequently detected (56%) followed by tubercular (28%) and pyogenic(16%) causes of disease. There was an overall female preponderance (64%) with maximum number of patients belonging to younger age groups. Male predilection in pyogenic meningitis (62.5%) and a female predilection (57.14%) in tuberculous meningitis was noted, which was similar to several other studies done in other parts of the world. Most of the tuberculous meningitis cases (42.8%) were clinically more severe according to the GCS category during admission followed by viral meningoencephalitis (28.57%) and pyogenic meningitis (12.5%). CSF cytology revealed neutrophillic picture in pyogenic and lymphocytic pleocytosis in tuberculous and viral meningoencephalitis. CSF biochemistry revealed hypoglycorrhachia in pyogenic and tuberculous meningitis and high protein levels in viral and grossly high protein content in tuberculous meningitis cases. ADA levels were also high in tuberculous meningitis. CSF gram staining, culture and serology results showed Streptococcus pneumoniae as the most common pathogen causing pyogenic meningitis(50%) and Herpes simplex as most common viral pathogen(35.72%) causing meningoencephalitis. MRI findings were highly informative, reliably contributed in diagnosis and helped in retrospective analysis of symptom complex and sequelae. Brain parenchymal involvement was more marked in viral meningitis in the form of T2 hyperintensities in various anatomical sites, predominantly in the temporal lobe in herpes simplex encephalitis and bilateral thalamic involvement with basal ganglia involvement in Japanese B encephalitis. Infarcts were noted in Varicella zoster encephalitis. Brain Imaging(MRI) of tuberculous meningitis cases unveiled a wide spectrum of parenchymal affection in the form of ring enhancing lesions, cerebral granulomas, infarcts and edema along with hydrocephalus. These two etiological groups comprised of more number of cases presenting with seizures and altered sensorium as compared to pyogenic meningitis cases. MRI of patients suffering from pyogenic meningitis were somewhat nonspecific in some cases and did not contribute much to the confirmation of diagnosis. This is a potential area of research and rightfully demands attention in the near future. India being a resource poor nation, improvisation of the specific diagnostic modalities and implementation with regard to affordability should be prioritised. Especially in this part of the world, there is a dearth of multi centric prospective studies on meningoencephalitis. More studies to be conducted based on correlation of clinical aspects with brain imaging; prognostication and taking into account the long-term outcomes.

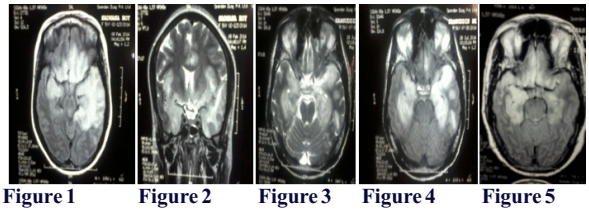

Figure 1 **Figure 2** **Figure 3** **Figure 4** **Figure 5**

FIG 1& FIG 2: Bilateral temporal and inferior frontal hyper intensities on T2 Flair images. Suggestive of Herpes simplex encephalitis. FIG 3 & 4- Viral haemorrhagic encephalitis suggestive of herpes simplex encephalitis. FIG 5- Herpes Encephalitis showing temporal enhancements

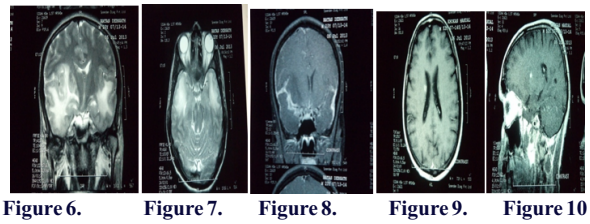

Figure 6. **Figure 7.** **Figure 8.** **Figure 9.** **Figure 10**

FIG 6 & FIG 7- Bitemporal T2 Hyperintensities favouring Herpes encephalitis. FIG 8- Showing meningeal enhancement post contrast in the same patient. FIG 9 & 10- Right periventricular infarct in T2 Flair image as a sequelae of pyogenic meningitis.

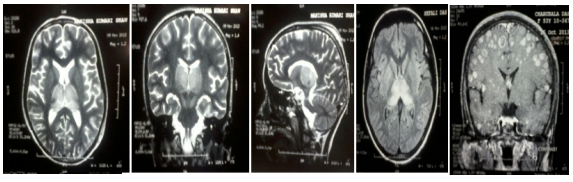

Figure 11. **Figure 12.** **Figure 13.** **Figure 14.** **Figure 15**

FIG 11, 12,13,14- Bilateral thalamic T2 hyperintensities in a case of Japanese B encephalitis. FIG 15- Extensive rim enhancing nodular focal lesions of various sizes with mild perilesional edema scattered in both cerebral hemispheres (Tuberculomas). A case of TB Meningitis.

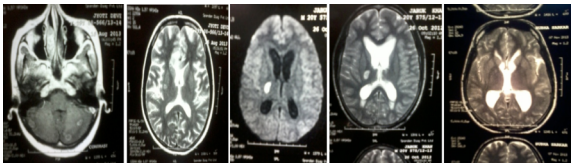

Figure 16. **Figure 17.** **Figure 18.** **Figure 19.** **Figure 20.**

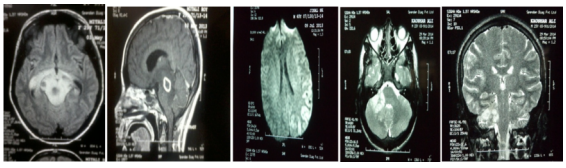

Figure 21. **Figure 22.** **Figure 23.** **Figure 24.** **Figure 25**

FIG 16 & 17: Ring enhancing and granulomatous lesion suggestive of TB Meningitis.

FIG 18 & 19: Right cerebral infarct with periventricular ischaemia and hydrocephalus conspicuous in post contrast T2 Flair image. A case of TB Meningitis. FIG 20: Hydrocephalus in a case of TB Meningitis. FIG 21 & 22: Brainstem hyperintensities with ring enhancing lesion in a case of TB Meningitis. FIG 23: Left parieto occipital T2 Hyperintensities in a case of viral meningoencephalitis. FIG 24& 25- Shows patchy altered signal intensities in right cerebellar peduncle with evidence of mild restricted diffusion. Patchy contrast enhancement of right sided cavernous sinus. (Right cavernous sinus thrombo phlebitis).

CHARTS

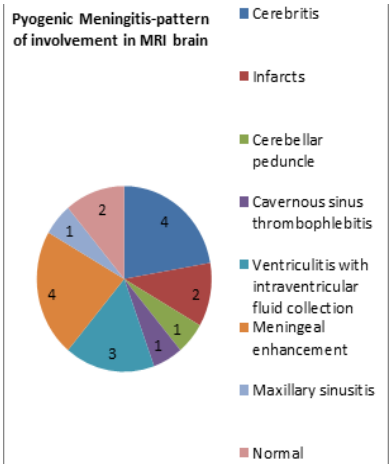

Chart 1: Pattern of lesion in Pyogenic Meningitis

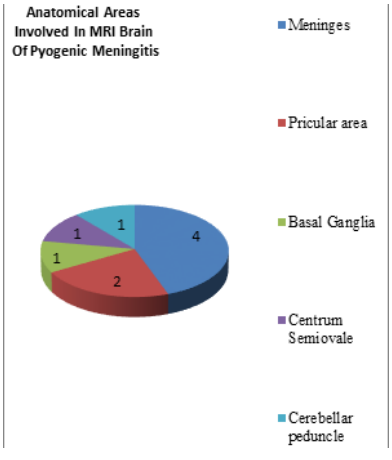

Chart 2: Anatomical areas involved in Pyogenic Meningitis

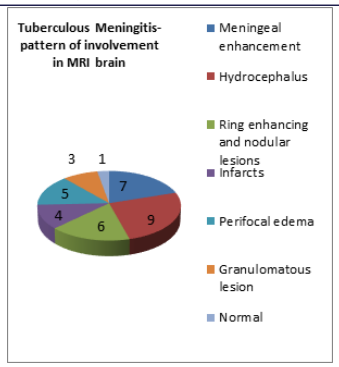

Chart 3: Tuberculous Meningitis: Pattern of lesion

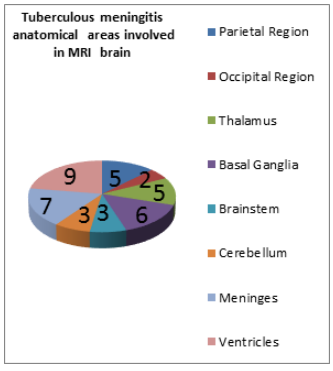

Chart 4: Tuberculous Meningitis: Anatomical areas involved:

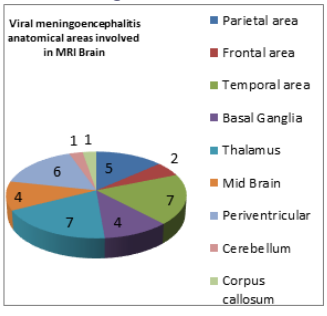

Chart 5: Viral Meningoencephalitis: Anatomical areas involved

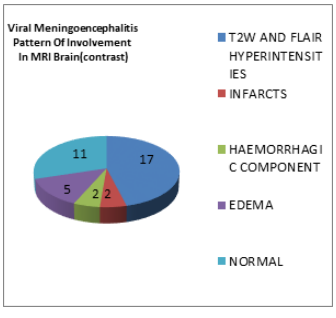

Chart 6: Viral Meningoencephalitis: Pattern of lesion:

FIGURES

Figure 1	
Pyogenic Meningitis-pattern of involvement in MRI brain	No. of Cases
Cerebritis	4
Infarcts	2
Cerebellar peduncle	1
Cavernous sinus thrombophlebitis	1
Ventriculitis with intraventricular fluid collection	3
Meningeal enhancement	4
Maxillary sinusitis	1
Normal	2

Figure 2	
Anatomical areas involved in MRI brain of pyogenic meningitis	No of Cases
Meninges	4
Pricular area	2
Basal Ganglia	1
Centrum Semiovale	1
Cerebellar peduncle	1

Figure 3	
Tuberculous Meningitis- pattern of involvement in MRI	No of Cases
Meningeal enhancement	7
Hydrocephalus	9
Ring enhancing and nodular lesions	6
Infarcts	4
Perifocal edema	5
Granulomatous lesion	3
Normal	1

Figure 4	
Anatomical area of Brain involved in MRI in Tubercular Meningitis	No. of cases
Parietal Region	5
Occipital Region	2
Thalamus	5
Basal Ganglia	6
Brainstem	3
Cerebellum	3
Meninges	7
Ventricles	9

Figure 5	
Anatomical areas involved in MRI brain in Viral meningoencephalitis	No of Cases
Parietal area	5
Frontal area	2
Temporal area	7
Basal Ganglia	4
Thalamus	7
Mid Brain	4
Periventricular	6
Cerebellum	1
Corpus callosum	1

Figure-6	
VIRAL MENINGOENCEPHALITIS CASES- PATTERN OF INVOLVEMENT IN MRI BRAIN(CONTRAST)	No. of case
T2w And Flair Hyperintensities	17
Infarcts	2
Haemorrhagic Component	2
Edema	5
Normal	11

DISTRIBUTION ACCORDING TO AGE GROUPS figure-7	
AGE GROUPS (IN YEARS)	NUMBER OF PATIENTS (N=50)
12 to 20	13
21 to 30	12
31 to 40	12
41 to 50	07
51 to 60	05
61 to 70	0
>71	01

Figure 8				
ETIOLOGY	TOTAL NUMBR	MALES (N=18)	FEMALES (N=32)	PERCENTAGE (%)
PYOGENIC MENINGITIS	8	5	3	MALES- 62.5 FEMALES- 37.5
TUBERCULOUS MENINGITIS	14	6	8	MALES- 42.86 FEMALES-57.14
VIRAL MENINGOENCEPHALITIS	28	7	21	MALES- 25 FEMALES- 75

Figure-9 CLASSIFICATION ACCORDING TO GCS IN DIFFERENT ETIOLOGICAL GROUPS				
Clinical Groups (Glasgow Coma Scale/ Gcs)	Number Of Patients According To Clinical Severity On Admission	Pyogenic Meningitis (N= 8)	Tuberculous Meningitis (N= 14)	Viral Meningoencephlitis (N = 28)
Group - A (Gcs: 3 To 5)	15	1	6	8
Group - B (Gcs: 6 To 9)	22	5	6	11
Group – C (Gcs: 10 To 15)	13	2	2	9

Aetiological group	**CSF - total cell count(mean)**	**Neutrophils (mean)**	**Lymphocytes (mean)**
Pyogenic meningitis	**950.5 ± 3748.84**	**85.88 ± 25.18**	**14.13 ± 25.18**
Tuberculous meningitis	**225.86 ± 217.22**	**13.14 ± 32.8**	**86.86 ± 32.8**
Viral meningoencephalitis	**128.61 ± 276.86**	**14.93 ± 25.14**	**85.07 ± 25.14**

Figure10 ORGANISMS ISOLATED IN CSF CULTURE OF PYOGENIC MENINGITIS CASES			
Sl.No.	Organisms isolated in CSF culture in Pyogenic Meningitis	Number of case (N= 8)	Percentage (%)
1.	Streptococcus pneumoniae	4	50
2.	Neisseria meningitidis	1	12.5
3.	Staphylococcus aureus	1	12.5
4.	Undetermined /Negative	2	25

Figure 11: CSF BIOCHEMISTRY AND ADA LEVELS IN DIFFERENT ETIOLGICAL GROUPS				
Etiological Group	**CSF Glucose (Mean)**	**CSF Protein (Mean)**	**CSF Chloride (Mean)**	**CSF ADA Levels (Mean)**
Pyogenic Meningitis	**19 ± 18.9**	**62.375 ± 48.52**	**112.88 ± 12.48**	**8.03 ± 24.14**
Tuberculous Meningitis	**35.79 ± 22.9**	**268.86 ± 368.12**	**112.71 ± 12.54**	**16.29 ± 16.14**
Viral Meningoencephalitis	**60.11 ± 32.28**	**96.96 ± 91.98**	**113.45 ± 14.32**	**3.76 ± 4.38**

Figure-12		
Etiology confirmed on CSF ELISA	Number of patients (N=28)	Percentage(%)
HERPES SIMPLEX	10	35.72
JAPANESE B	04	14.28
VARICELLA ZOSTER	03	10.72
NEGATIVE/INDETERMINATE	11	39.28

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