Assessment of Csf Ada and Crp Levels in Differential Diagnosis of Meningitis in Adults

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Abstract

Background and Objectives: Infections involving the CNS, particularly meningitis and encephalitis are likely to arouse tremendous anxiety in both the physician and patients. Reliable, cost effective, rapid diagnostic tests which can be performed in any standard pathology laboratory could be of help in the differentiation of various types of meningitis in adults. In this regard, C - reactive protein level and Adenosine deaminase activity can be used as rapid tests in the differential diagnosis of meningitis. ADA estimation is useful in diagnosis of Tuberculous meningitis. CRP estimation has been documented to be helpful in diagnosing pyogenic meningitis. The levels of both ADA and CRP are low in cases of viral meningitis.


Methods: CSF samples were obtained from 50 patients who presented to the casualty and Outpatient department of Osmania General Hospital During September 2012 to September 2014 Diagnosis of meningitis was based on the clinical presentation and CSF analysis.

Results: In our study, out of a total of 50 patients, 25 patients were diagnosed as tubercular meningitis based on the clinical features and CSF analysis. The mean ADA activity was 14.36 in the Tuberculous meningitis group, the result being statistically significant (p<0.001). The sensitivity and specificity was 72% and 100% respectively when a cut-off value of ADA of 10U/l was used.

CSF-CRP is significantly higher in pyogenic meningitis compared to non-pyogenic meningitis. The sensitivity and specificity of the test was 90% and 100% respectively with an accuracy of 98%.

Interpretation and Conclusion: 2 rapid diagnostic tests-CRP and ADA activity in the CSF can help in the differential diagnosis of pyogenic from non-pyogenic and tubercular from viral meningitis respectively, CRP being elevated in pyogenic meningitis and ADA activity noted to be higher in tuberculous meningitis. The levels of ADA and CRP are low in viral meningitis. However, these tests should be interpreted judiciously in the light of the patients’ clinical manifestations and the results of CSF analysis.

Keywords: CSF; CRP; ADA; Pyogenic meningitis; Non-pyogenic meningitis; Tubercular meningitis

Abbreviations: ADA: Adenosine Deaminase; CNS: Central Nervous System; CPP: Cerebral Perfusion Pressure; CRP: C - reactive protein; CSF: Cerebrospinal Fluid; CT: Computed Tomography; EEG: Electroencephalogram; ELISA: Enzyme Linked Immuno sorbent Assay; ESR: Erythrocyte Sedimentation Rate; HSV: Herpes Simplex Virus; ICP: Intracranial Pressure; IL: Interleukin; LPS: Lipopolysaccharide; MRI: Magnetic Resonance Imaging; NPV: Negative Predictive Value; PCR: Polymerase Chain Reaction; PMNS: Polymorphonuclear Neutrophils; PPV: Positive Predictive Value; SAS: Subarachnoid Space; TNF: Tumor Necrosis Factor; WBC: White Blood Cells

Introduction

Infectious diseases remain a major cause of death and disability for millions of people around the world, despite decades of dramatic progress in their treatment and prevention. Each infectious agent can cause a spectrum of illnesses, which challenges the physician’s diagnostic skills. The central nervous system (CNS) may appear protected from perturbations in the environment by a blood brain barrier-a system of tight junction around capillaries that resist the entry of pathogens, inflammatory cells and macromolecules into the subarachnoid space and the brain. However, the barrier fails to resist the intensity of the microbial world and its presence also cause difficulty in the delivery of antimicrobial agents in adequate concentrations.

As vital tissues are involved, CNS infection can cause devastating sequelae and in some cases may result in both neurological and medical emergencies [1].

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Meningitis Definition
Meningitis is an infection within the subarachnoid space. It is associated with a central nervous system inflammatory reaction that may result in decreased consciousness, seizures, varied intracranial pressure and stroke. The meninges, the subarachnoid space and the brain parenchyma are all frequently involved in the inflammatory reaction. (Meningoencephalitis) [2].

Epidemiology Acute Bacterial Meningitis
The annual incidence of bacterial meningitis is more than 2.5 cases per 1,00,000 population in the United States. More than 2000 deaths due to bacterial meningitis are reported annually in the United States. The disease is more common and the mortality higher in the developing countries like India.

The epidemiology of bacterial meningitis has changed significantly in recent years reflecting a dramatic decline in the incidence of meningitis due to Haemophilus influenzae, and a smaller decline in that due to Neisseria meningitides, following the introduction and increasingly widespread use of vaccines for both these organisms [1].

The prognosis of bacterial meningitis is critically dependent on a rapid causal diagnosis and implementation of prompt treatment. However, clinical and biochemical parameters available within the few hours that follow patients admission are not reliable enough, except when bacteria are to be found in the cerebrospinal fluid under the microscope.

Therefore, the initial treatment of acute meningitis is most of the time presumptive. The definitive diagnosis, however difficult, is often established when the therapeutic management has already been initiated. The use of biological markers, especially lymphokines and acute-phase proteins, has been proposed to facilitate the accuracy of the initial diagnosis. Today, C-reactive protein (CRP) is the most widely used inflammatory marker in emergency departments with aim to discriminate bacterial from non-bacterial infections [3]. But CRP must be interpreted in the clinical context [4].

Tubercular Meningitis
Among the patients with meningitis, tubercular meningitis remains an important cause of morbidity and mortality in India. With the lack of early diagnosis, fatality remains high, sequelae may be distressing and disabling in the non-fatal cases. Adenosine deaminase activity has shown promising results in the diagnosis of tubercular pleural, peritoneal and pericardial effusion and tubercular meningitis.

Viral Meningitis
Viral meningitis is not a nationally reportable disease; however, it has been estimated that the incidence is ~75,000 cases per year. In temperate climates, there is a substantial increase in cases during the summer and early fall months, reflecting the seasonal predominance of enterovirus and arthropod-borne virus (arbovirus) infections.

Etiology
Bacteria causing meningitis
*Streptococcus pneumoniae* (pneumococcus): It is the most common cause of meningitis (50%) in adults > 20 years of age, accounting for nearly half the reported cases (1.1 per 1,00,000 persons per year) [1].

- N. Meningitis ~ 25%.
- Group B streptococci ~ 15%.
- Listeria monocytogens ~ 10%.
- H. influenza < 10%.

Less common causes include:
- Staphylococcus aureus, coagulase negative staphylococci following invasive neurosurgical procedure.
- Enteric gram-negative bacilli in patient with chronic and debilitating diseases such as diabetes, cirrhosis, alcoholism, chronic urinary tract infections and can also complicate neurosurgical procedures, particularly craniotomy.
- Mycobacterium tuberculosis.
- Others - Borrelia burgdorferi, treponemapallidium, actinomyces, nocardia, brucella, leptospirosis, troperemawhippelii. (Table 1)

Fungal causes of meningitis
- Cryptococcus neoformans.
- Coccidioidesimmitis.
- Candida species.
- Histoplasmacapsulatum.
- Blastomycesdermatitidis.
- Aspergillus species.
- Sporothrixschenckii.

<table>
<thead>
<tr>
<th>Common</th>
<th>Less common</th>
<th>Rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enteroviruses</td>
<td>HSV -1</td>
<td>Adenoviruses</td>
</tr>
<tr>
<td>Arboviruses</td>
<td>LCMV</td>
<td>CMV</td>
</tr>
<tr>
<td>HIV</td>
<td>VZV</td>
<td>EBV</td>
</tr>
<tr>
<td>HSV-2</td>
<td>Influenza A,B</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Para influenza, Mumps, Rubella</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Viruses causing meningitis.
Protozoal causes of meningitis
- Toxoplasma gondii.
- Trypanosoma gambiense.
- Trypanosoma rhodesiense.

Helminthic causes of meningitis
- Cysticercosis.
- Gnathostoma spinigerum.
- Angiostrongylus cantonensis.
- Baylisascaris procyonis.

Non-infectious causes
- Malignancy.
- Chemical compounds.
- Primary inflammation - CNS sarcoidosis.
- Vogt Koyanagi Harada Syndrome.

Systemic Lupus Erythematosus.
Behcet’s syndrome.
Chronic benign lymphocytic meningitis.
Drug hypersensitivity.
Wegener’s Granulomatosis (Figure 1).

Clinical Presentation
- Meningitis can present as either an acute fulminant illness that can progress rapidly in a few hours, or as a sub-acute infection that progressively worsens over several days. The classic clinical triad of meningitis is fever, headache, and nuchal rigidity (“stiff neck”). Each of these signs and symptoms occurs in >90% of cases. Alteration in mental status occurs in >75% of patients and can vary from lethargy to coma. Nausea, vomiting, and photophobia are also common complaints. Nuchal rigidity is the pathognomonic sign of meningeal irritation and is present when the neck resists passive movement.

Figure 1: The pathophysiology of the neurologic complications of meningitis. SAS, subarachnoid space; Cerebrospinal fluid [1].
flexion. Kernig’s and Brudzinski’s signs are also classic signs of meningeal irritation.

- Seizures occur as part of the initial presentation of meningitis or during the course of the illness in up to 40% of patients. Focal seizures are usually due to focal arterial ischemia or infarction, cortical venous thrombosis with hemorrhage, or focal edema [1].

- The rash of meningococcemia begins as a diffuse erythematous maculopapular rash resembling a viral exanthem, but the skin lesions of meningococcemia rapidly become petechial. Petechiae are found on the trunk and lower extremities, in the mucous membranes and conjunctiva, and occasionally on the palms and soles.

- Raised intracranial pressure (ICP) is an expected complication of bacterial meningitis and is the major cause of obtundation and coma in this disease. More than 90% of patients will have a CSF opening pressure >180 mm H2O, and 20% have opening pressures >400 mm H2O. Signs of increased ICP include a deteriorating or reduced level of consciousness, papilledema, dilated poorly reactive pupils, sixth nerve palsies, decerebrate posturing, and the Cushing reflex (bradycardia, hypertension, and irregular respirations). The most disastrous complication of increased ICP is cerebral herniation. The incidence of herniation in patients with bacterial meningitis has been reported to occur in as few as 1% to as many as 8% of cases [1].

- Clinical features suggestive of tubercular meningitis include altered mental status, deteriorating level of consciousness, papilledema, dilated poorly reactive pupils, sixth nerve palsy, decerebrate posturing and focal neurological deficits like hemiplegia and cranial nerve palsies.

- Viral meningitis usually results in a benign and self-limiting illness requiring no specific therapy. It is a much less serious illness than bacterial or tubercular meningitis, unless there is associated encephalitis, which is rare. It occurs with acute onset headache and irritability. The headache is usually the more severe feature. Failure of a patient with suspected viral meningitis to improve within 48 hours should prompt a reevaluation [1].

### Diagnosis

- When the clinical presentation is suggestive of meningitis, blood cultures should be immediately obtained and empirical antimicrobial therapy initiated without delay. The diagnosis of meningitis is made by examination of the CSF. The need for cranial magnetic resonance imaging (MRI) or computed tomography (CT) prior to lumbar puncture remains a controversial issue and must be dealt with on a case-by-case basis. In a patient with a normal level of consciousness and a neurologic examination with no evidence of papilledema or focal deficits, is safe to perform lumbar puncture without prior neuroimaging studies. If lumbar puncture is delayed in order to obtain neuroimaging studies, empirical antibiotic therapy should be initiated after blood cultures are obtained. Antibiotic therapy for several hours prior to lumbar puncture will not significantly alter the CSF white blood cell count or glucose concentration, nor is it likely to sterilize the CSF so that the organism cannot be identified on Gram’s or AFB stain. Increased ICP should be treated in patients with clinical signs of increased pressure, and lumbar puncture performed with a 22- or 25-gauge needle. Only a minimum amount of CSF need be removed for analysis; ~3.5 ml of CSF is sufficient to obtain a cell count (1.0 ml), glucose and protein concentrations (1.0 ml), latex particle agglutination (LA) tests (0.5 ml), and Gram’s stain, AFB stain and bacterial cultures (1.0 ml). If possible, an additional 0.5 to 1.0 ml should be saved.

- Almost all patients with bacterial meningitis will

<table>
<thead>
<tr>
<th>CSF Analysis</th>
<th>Bacterial meningitis</th>
<th>Tubercular meningitis</th>
<th>Viral Meningitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opening pressure</td>
<td>&gt;180 mm H2O</td>
<td>&gt;120 mm H2O</td>
<td>100-350 mmH2O</td>
</tr>
<tr>
<td>White blood cells</td>
<td>10- 10,000/microL, Neutrophil predominant</td>
<td>10- 1000/microL, Predominantly lymphocytic</td>
<td>25-500/microL, lymphocytic pleocytosis</td>
</tr>
<tr>
<td>Red blood cells</td>
<td>Absent in non traumatic tap</td>
<td>Absent in non traumatic tap</td>
<td>Absent in non traumatic tap</td>
</tr>
<tr>
<td>Glucose</td>
<td>&lt;40mg/dl</td>
<td>&lt;40mg/dl</td>
<td>Normal</td>
</tr>
<tr>
<td>Protein</td>
<td>&gt;45mg/dl</td>
<td>&gt;45mg/dl</td>
<td>20-80mg/dl</td>
</tr>
<tr>
<td>Gram's stain</td>
<td>Positive in &gt;60%</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>ZN Stain</td>
<td>Negative</td>
<td>May be positive in 37%</td>
<td>Negative</td>
</tr>
<tr>
<td>Culture</td>
<td>Positive in &gt;80%</td>
<td>Positive in 56%</td>
<td></td>
</tr>
<tr>
<td>Latex agglutination</td>
<td>Positive in S.pneumoniae, H influenzae type b, N meningitides, E coli, group B streptococci</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>PCR</td>
<td>Detects bacterial DNA</td>
<td>Positive</td>
<td>Positive for viral specific DNA/RNA like Enterovirus,HSV, EBV, VZV, CMV</td>
</tr>
<tr>
<td>Limulus lysate</td>
<td>Positive in gram negative meningitis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2: CSF Analysis.**
ultimately have neuroimaging studies performed. MRI is preferred over CT because of its superiority in demonstrating areas of cerebral edema and ischemia. In patients with bacterial meningitis, diffuse meningeal enhancement is often seen after the administration of gadolinium. Meningeal

- Enhancement is not diagnostic of meningitis but occurs in any CNS disease associated with increased blood-brain barrier permeability (Table 2).

Aims and Objectives

- To estimate the C reactive protein and Adenosine deaminase levels in CSF of patients with meningitis.
- To evaluate whether C-reactive protein and Adenosine deaminase levels could be used to differentiate the various types of meningitis in adults.

Review of Literature

C - reactive protein

Tillet and Francis, French investigators in 1930 described a substance that was present in the sera of acutely ill patients which was able to bind to the cell wall c-polysaccharide of streptococcus pneumoniae and agglutinate the organisms. In 1941, the substance was shown to be a protein and given the name C-reactive protein (CRP) [5].

CRP was subsequently shown to be an acute phase reactant and important in the nonspecific host defense against inflammation, especially infection and is routinely monitored as an indication of infection and autoimmune diseases. Using methods having detector limits of 3-8 mg/dl, CRP has also been shown to be predictive of future events in patients with acute coronary syndrome and in patients with stable angina and coronary artery stents. The use of CRP for these purposes requires use of hsCRP (highly sensitive CRP) assays having detection limits less than 0.3 mg/L. CRP production is a part of the nonspecific acute phase response to most forms of inflammation, infection and tissue damage and was therefore considered not to provide clinically useful information, indeed CRP values can never be diagnostic on their own and can only be interpreted in full knowledge of all other clinical and pathological results [5].

Biochemistry and Structure of Crp

CRP belongs to the pentraxin family of calcium dependent ligand-binding plasma proteins. The pentraxin family named for its electron micrographic appearance from the Greek pent (five), ragas (berras) [6].

The human CRP molecule is composed of five identical non-glycosylated polypeptide subunits which are non-covalently linked to form a disk shaped cyclic polymer with a molecular weight of ~115 KDa. It contains little or no carbohydrate. CRP is synthesized mainly in the liver [1]. CRP can be produced in neurons and lipopolysaccharides can induce CRP production in extrahepatic sites [7, 8]. Its production is controlled by interleukin-6 and it binds to polysaccharides present in many bacteria, fungi and protozoal parasites (Figure 2).

Functions of Crp

The function of CRP is related to its role in the innate immune system. Similar to immunoglobulin IgG, it activates complement, binds to Fc receptors and acts as an opsonin for various pathogens. Interaction of CRP with Fc receptors leads to the generation of proinflammatory cytokines that enhance inflammatory response. Unlike IgG, which specifically recognizes distinct antigenic epitopes, CRP recognizes altered self and foreign molecules based on pattern recognition. Thus, CRP is thought to act as a surveillance molecule for altered self and certain pathogens. This recognition provides an early defence and leads to a proinflammatory signal and activation of the humoral, adaptive immune system [9, 10].

Circulating Crp Concentrations

In healthy young volunteer blood donors, the median concentration of serum CRP is 0.8mg/l. CRP concentrations in the CSF are seven fold lower than those of serum. This difference is explained by direct hepatic release of CRP into plasma, which then undergoes ultra-filtration to reach the CSF. Meningeal irritation stimulates CRP production. Once it enters the CSF it binds to damaged tissue. Minimal CSF inflammation may be apparent in patients undergoing lumbar puncture very early in the course of the disease and with rapidly developing meningitis in which bacterial multiplication can outpace the ability of the liver to mount a CRP response [11].

Half-Life of Crp

Plasma half-life of CRP is about 19 hours. It is constant under all conditions of health and disease, so that the sole determinant of circulating CRP concentrations is the synthesis rate. When the stimulus for increased production completely ceases, the circulating CRP concentration falls rapidly at almost the rate of plasma CRP clearance [11].
Clinical Significance or Crp

The acute phase response

CRP was the first acute phase protein to be described. CRP named for its capacity to precipitate somatic C-polysaccharide of streptococcus pneumonia [12]. It is one of the most sensitive of the acute phase response with plasma levels rising up to 2000-fold after infection, myocardial infarction, stress, trauma, inflammation, surgery or neoplastic proliferation. Levels are in general much higher in bacterial than viral infections. The increase with inflammation occurs within 6 to 12 hours and peaks at about 48 hours. It is generally proportional to the degree of tissue damage. Because the increase is nonspecific, however, it cannot be interpreted without other clinical information [12].

Other acute phase proteins include proteinase inhibitors (alpha-1 antitrypsin, alpha-1 antichymotrypsin), coagulant proteins (fibrinogen, prothrombin, and factor VIII. plasminogen), complement component (C1s, C2, C3, C4, C5), transport proteins (haptaglobin, ceruloplasmin) and miscellaneous (albumin, serum amyloid A protein, fibronectin) [12].

Major Acute Phase Responses [13]

CRP is increased in following conditions

1) Infections

Highest levels are found in acute bacterial infections compared to acute viral, fungal, and tubercular infection.

2) Inflammatory disorders

Rheumatoid Arthritis, Rheumatic fever, seronegativearthritides (Reiters syndrome) vasculitis syndrome (e.g. Hypersensitivity vasculitis).

Inflammatory bowel disease - higher in Crohns than in ulcerative colitis.

3) Tissue injury and necrosis

- Acute myocardial infarction.
- Ischemia and infarction of other tissues.
- Rejection of kidney, marrow transplant.
- Trauma - surgery, burns, fractures.

4) Malignancy

Especially breast, lungs, GI tract. Not increased in:

- SLE, mixed connective tissue disease, dermatomyositis, scleroderma.
- Pregnancy, strenuous exercise.

Methods to Assess Levels of Crp [5]

- RID (Radial immuno diffusion).
- RIA (Radio immuno assay).
- IN (Immunonephelometry).
- IT (Immunoturbidimetry).
- Homogeneous enzyme immunoassay.

Crp as a Predictor of Cardiovascular Events

Recent reports indicate that inflammation may be associated with atherosclerosis. Myocardial infarction is frequently at the end of a long process of inflammation-mediated atherosclerosis. Thus, the inflammation is believed to have a role in pathogenesis of cardiovascular events measurement of markers of inflammation has been proposed as a method to improve the prediction of these events.

Myocardial Infarction

Myocardial infarction is invariably associated with a major CRP response. The peak value of CRP occurs about 50 hours after the onset of pain in myocardial infarction and correlates closely in magnitude, though clearly not in timing, with the peak serum level of cardiac isoenzymes such as creatine kinase MB [14].

Angina

Angina without infarction and invasive investigation, such as coronary arteriography do not stimulate CRP production, whereas some other causes of chest pain such as pulmonary embolism, pleurisy or pericarditis are usually associated with raised CRP levels.

Acute Pancreatitis

Serum CRP levels closely reflect the severity and progress of acute pancreatitis providing a better guide to intra-abdominal events than other markers such as leukocyte counts, ESR and temperature [15].

Trauma

The CRP concentration always rises after significant trauma, surgery or burns, peaking after 2 days and then falling towards normal with recovery and healing.

After Surgery

CRP usually increases more than 100 mg/litre by 48 to 72 hours. In the absence of complications, values decline thereafter and reach normal concentrations 3 to 7 days later.

In Extensive Burns

CRP increases significantly in patients with extensive burns versus those with minor burns. A second peak of CRP develops if infection occurs as a later complication of the burns suggesting the value of CRP to monitor the course of healing [16].

Malignancy

Most malignant tumours, especially when they are extensive and metastatic, induce an acute phase response. This is particularly so with those neoplasms which cause systemic symptoms such as fever and weight loss, for example, Hodgkin’s disease and renal cell carcinoma. However, given the non-specific nature of the acute phase response, a definite role of CRP measurements in the management of cancer
patients, other than in cases of intercurrent infection has not yet been established [17].

**Adenosine Deaminase**

Adenosine deaminase is an enzyme of purine salvage pathway that catalyses the hydrolytic deamination of adenosine to inosine and ammonia.

**ADA**

\[
\text{Adenosine + H}_2\text{O} \rightarrow \text{Inosine + Ammonia}
\]

ADA has 2 principle isoenzymes ADA1, ADA2 which have different optimal pH, Michaeli’s constant and relative substrate specificity patterns.

ADA1 has roughly equal affinities for adenosine and 2’ deoxyadenosine and is found in many tissues.

ADA2 is the major component (73%) of the activity of total ADA in the serum of healthy persons. ADA2 has much greater affinity for adenosine and found only in macrophages and monocytes, which release it when stimulated in the presence of live organisms [18].

**Expression of Ada in Organisms**

In humans, the highest ADA activity is found in thymus and other lymphoid tissues (~800IU/mg) and the lowest in erythrocytes (~1IU/mg).

Among non-lymphoid tissues in human, relatively high levels of ADA are found in the villi of epithelial cells lining the duodenum, levels are lower in the other portions of the gastrointestinal tract. Tissues such as muscle, liver, kidney, brain and blood have low activity in most species.

The activity of ADA is subject to changes depending upon the degree of activity of the cell i.e. whether differentiation or proliferation occurs [19].

**Physiological Roles of Ada and Adenosine**

Additional to the key role in purine metabolism, ADA has other important physiological roles. These are:

**Enzymatic Activity of Ada**

First the physiological role of ADA can be seen in connection with adenosine, the concentration of which can be modulated by enzymatic action of ADA. The responses of adenosine include coronary vasodilation, reduction in heart rate and contractile force, inhibition of platelet aggregation, mast cell degradation, inactivation of eosinophil migration, renal vasoconstriction, regulation of ion channel activity, membrane potential and neurotransmitter and hormone release [20].

**Severe Combined Immunodeficiency Disease (SCID)**

ADA deficiency is the cause of one form of SCID in which there is dysfunction of both the B and T lymphocytes with impaired cellular immunity and decreased production immunoglobulin. ADA deficiency accounts for about one half of cases of autosomal recessive SCID.

In addition, neurological abnormalities, mesangial sclerosis in renal tissue, pulmonary insufficiency and liver abnormality have also been seen in ADA patients.

**Clinical Applications in Serum Ada**

**Ada in Pleural Effusion**

Several studies have suggested that an elevated pleural fluid ADA level predicts tuberculosispleuritis with a sensitivity of 90-100% and specificity of 89-100% when the Giustic method is used. The reported cut off value for ADA varies from 47 to 60 U/L [21].

**Ada in Pericardial Effusion**

Recent reports in patients with tuberculous pericarditis have shown the ADA levels in pericardial fluid are useful in early diagnosis. Using a cut off value of 40 U/L, the specificity and sensitivity of ADA testing in the series of 9 patients with proven and 5 patients with suspected tuberculous pericarditis were 93% and 97% respectively [22]. In another series, there was a positive correlation between high pericardial ADA levels and the subsequent development of constrictive pericarditis [23].

**Ada in Peritoneal Fluid**

Ascitic fluid ADA activity has been proposed with a specificity and sensitivity of 99-100% and 100% respectively using a cut off value of >32 U/L [24, 25].

**Serum Ada**

Serum ADA levels have been studied by many workers in the differential diagnosis of jaundice, diagnosis of typhoid fever in Mediterranean spotted fever and in chronic lymphocytic leukaemia with variable results [26-28].

**Ada in Csf**

A review of literature has shown that CSF ADA levels could differentiate various types of meningitis. Over the last decade or so, various investigators have shown that the cut-off levels of ADA could be sensitive and specific for tubercular meningitis. Ribera et al proposed a cut-off value 9U/l and showed a high sensitivity of (1.0) and specificity (0.99) [29]. The enzymatic activity, as well as progression of the disease was studied in 32 patients with tuberculous meningitis. A significant rise in levels of enzymes was observed during the first 10 days of therapy, was followed by a gradual decline, and reached normal values after 3 to 4 months of treatment.

**Methodology**

**Source of data**

CSF samples were obtained from 50 patients who presented to the casualty and Out Patient Department of Osmania General Hospital, Hyderabad during the period of September 2012 to September 2014.

**Collection of data**

*Criteria for diagnosis of meningitis*
• Triad of fever, headache, nuchal rigidity.
• Altered mental status.
• Nausea, vomiting and photophobia.
• Seizures.
• Signs of meningeal irritation.
• 50 patients were included in the study

Criteria for diagnosing different types of meningitis

Group 1: Included 9 cases of pyogenic meningitis based on clinical features - usually acute in onset, may be associated with sinusitis, otitis media, and signs of meningeal irritation.

CSF analysis
• Pleocytosis of $> 250$ cells/mm$^3$ predominantly neutrophils.
• Proteins $> 45$ mg/dl.
• Sugar $< 40$ mg/dl or less than 40% of the blood glucose concentration.
• Gram stains and culture positivity.
• Neuroimaging - Diffuse meningeal enhancement, abscesses or parameningeal focus

Group 2: Included 25 cases of tubercular meningitis based on:
Clinical features - usually insidious in onset, may be associated with tuberculosis of other organs, signs of meningeal irritation.

CSF Analysis
• Pleocytosis of $> 10$ cells/mm$^3$ predominantly lymphocytes.
• Proteins $> 45$ mg/dl.
• Sugar $< 40$ mg/dl or less than 40% of blood glucose concentration.
• ZiehlNeelson may be positive for AFB.
• Neuroimaging: Meningeal enhancement, basal exudates and/or tuberculoma.

Group 3: Included 16 cases of viral meningitis based on:

Clinical presentation: Usually acute in onset with signs of meningeal irritation

CSF Analysis
• Lymphocytic Pleocytosis of $> 25$ cells/mm$^3$.
• Proteins $> 45$ mg/dl.
• Sugar normal.
• Neuroimaging - diffuse meningeal enhancement.

Group 4: 0 cases of fungal meningitis

CSF Analysis
• Cell Count: 20-1000/mm, lymphocytic predominant.
• Protein: 50-1000mg/dl.
• Sugar: 10-40mg/dl.
• KOH: Positive for Candida

Inclusion criteria
• Age $> 18$ years.
• Clinical features suggestive of meningitis

Exclusion criteria
• Age $< 18$ years.
• A patient with acute infections at sites other than central nervous system.
• Patients in whom lumbar puncture is contraindicated.
• Associated severe hepatic dysfunction.
• Females on oral contraceptives and intrauterine device
• Severe dyslipidemia.
• Patients on steroids

Results

Study design: A prospective clinical evaluation study is undertaken to study the predictive value of CRP and ADA in relation to various types of meningitis.

Statistical Methods used

Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean±SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. Binomial proportion test and Fisher Exact test has been used to find the significance of association of CRP and ADA levels with type of meningitis. (Table 3, 4)

The following statistics can be defined:

Sensitivity: Probability that a test result will be positive when the disease is present (true positive rate, expressed as a percentage). $= a / (a+b)$.

\[
\begin{array}{ccc}
\text{Class 1} & \text{Class 2} & \text{Total} \\
\hline
\text{Sample 1} & A & b & a+b \\
\text{Sample 2} & C & d & c+d \\
\text{Total} & a+c & b+d & n \\
\end{array}
\]

Table 3: Fisher Exact Test.

\[
\begin{array}{ccc}
\text{Disease} & \text{Test} & \text{Present} & \text{n} & \text{Absent} & \text{n} & \text{Total} \\
\hline
\text{Positive} & \text{True positive} & a & b & c & a+c \\
\text{Negative} & \text{False Negative} & B & d & c & b+d \\
\text{Total} & a+b & c+d \\
\end{array}
\]

Table 4: Fisher Exact Test Statistics=$P=(a+b)!(c+d)!(a+c)!(b+d)!/n!(a+b+c+d)!.
Specificity: Probability that a test result will be negative when the disease is not present (true negative rate, expressed as a percentage). = d / (c+d).

Positive predictive value: Probability that the disease is present when the test is positive (expressed as a percentage). = a / (a+c).

Negative predictive value: Probability that the disease is not present when the test is negative (expressed as a percentage). = d / (b+d).

Accuracy is the sum of true positive and true negative divided by number of cases.

Diagnostic values based on accuracy
0.9-1.0 - Excellent test
0.8-0.9 - Good test
0.7-0.8 - Fair test
0.6-0.7 - Poor test
0.5-0.6 - Fail

Significant Figures
+ Suggestive Significance 0.05<P<0.10
*Moderately Significant 0.01<P<0.05
**Strongly Significant P<0.01

Statistical Software
SPSS 15, STATA 8.0, MED CALC9.0.1 and systat 11.0 were used for analysis of data Microsoft word and excel used to generate graphs, tables etc (Figure 3-5) (Table 5, 6).

Age Distribution of Meningitis
Tuberculosis meningitis is more common in young age group. 90% in age group of 18 to 20 years.

Pyogenic meningitis was more common in extremes of age group. Viral meningitis was more common in age group of 21 to 40 years.

Gender Total cases TBM Fungal Meningitis Pyogenic Viral
Male 39 21 0 6 12
Female 11 4 0 3 4
Total 50 25 0 9 16

Table 5: for analysis of data Microsoft word and excel used to generate tables.

<table>
<thead>
<tr>
<th>Types of Meningitis</th>
<th>No of Cases</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBM</td>
<td>25</td>
<td>50</td>
</tr>
<tr>
<td>Fungal Meningitis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pyogenic Meningitis</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>Viral Meningitis</td>
<td>16</td>
<td>32</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 6: Types of Meningitis.

Sex Distribution of Meningitis
Tubercular, pyogenic, viral meningitis were more common in males than females. out of 50 cases 39 were males 11 were females.
Distribution of Various Meningitis

Most common meningitis in the group is Tubercular Meningitis with 50%, followed by Viral Meningitis, being 32%, Pyogenic Meningitis being least 18% (Figure 6-18) (Table 7-12).

Table 7: Tubercular and pyogenic meningitis had decreased sugar levels.

<table>
<thead>
<tr>
<th>Type of Meningitis</th>
<th>Number</th>
<th>ADA Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubercular</td>
<td>25</td>
<td>14.36</td>
</tr>
<tr>
<td>Pyogenic</td>
<td>9</td>
<td>4.77</td>
</tr>
<tr>
<td>Viral</td>
<td>16</td>
<td>1.018</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td></td>
</tr>
</tbody>
</table>

Table 8: ADA Levels are Elevated in Tubercular Meningitis.
Figure 12: CRP levels are elevated in pyogenic meningitis.

Figure 13: ADA Levels are Elevated in Tubercular Meningitis.

Figure 14: P Value of CRP is Significant in Pyogenic Meningitis.

Figure 15: P value of ADA in Tubercular Meningitis is Significant Sensitivity and specificity of Pyogenic Meningitis.

Figure 16: SENSITIVITY and SPECIFICITY of pyogenic meningitis in-relation to CRP levels are 90% and 100% respectively. NPV is 97.8% which implies that pyogenic meningitis could be ruled out if CRP is negative. ACCURACY of CRP is 98% The result is statistically significant P VALUE being<0.001.

Figure 17: SENSITIVITY and SPECIFICITY of tubercular meningitis are 72% and 100% respectively. P value is<0.001 which is very significant.

Type of Meningitis | Number | P value of CRP   
:-----------------|--------|----------------- 
Tubercular       | 25     |                 
Pyogenic          | 9      |<0.001          
Viral             | 16     |                 
Fungal            |        |                 

Table 9: P Value of CRP is Significant in Pyogenic Meningitis.
Discussion

Infections involving the CNS, particularly meningitis and encephalitis are likely to arouse tremendous anxiety in both the patients and physician. Perhaps this to be expected considering the high mortality rates associated with these infections and the neurologic sequelae that may linger in those who recover.

The initiation of treatment in suspected cases of meningitis can often be delayed due to the lack of confidence in the presently available laboratory tests. Reliable, cost effective, rapid diagnostic tests which can be performed in any standard pathology laboratory could be of help in the differentiation of various types of meningitis in adults.

In this regard, C reactive protein level and Adenosine deaminase activity can be used as rapid tests in the differential diagnosis of meningitis. ADA estimation is useful in diagnosis of tuberculous meningitis and their use has been suggested to help differentiate tuberculous meningitis from viral and bacterial meningitis [33].

Sang-Ho Choi et al studied ADA activity in CSF of 182 patients with meningitis. The mean ADA level in the tuberculous meningitis group was 12.7±7.5 U/l and it was significantly higher than the other groups (3.10±2.9 U/l; p<0.001). The sensitivity and specificity was 0.83 and 0.95 respectively when a cut-off value of 7 U/l was used [34].

Pettersson et al reports sensitivity of 1.0 and specificity of 0.99 when a cut-off value of 20 U/l was used, but in that study there were only 3 enrolled tuberculous meningitis patients [35].

Chotmongkol V et al identified a CSF ADA level of 15.5 U/l as the best cut-off value to differentiate tuberculous meningitis.
and non-tuberculous meningitis, with a sensitivity of 75% and specificity of 93%. When tuberculous meningitis was compared with aseptic and carcinomatous meningitis, a CSF ADA level of 19.0 U/l was the best cut-off value for differentiation, with a sensitivity of 69% and a specificity of 94% [36].

In our study, a total of 25 patients were diagnosed as tubercular meningitis based on the clinical features and CSF analysis. The mean ADA activity was 14.36 U/l in the tuberculous meningitis group; 4.77 in the pyogenic meningitis group; 1.018 in the viral meningitis group. Comparing the ADA activity in the 3 groups, the difference was found to be statistically significant (p<0.001) in the tuberculous meningitis group compared to the other groups. The sensitivity and specificity was 72% and 100% respectively when a cut-off value of ADA of 10U/l was used.

Malan C et al showed that in both bacterial and TBM groups, the mean ADA level in the CSF was significantly higher than in aseptic meningitis (p<0.001), but a significant difference was not shown between bacterial meningitis and TBM groups [37]. Similar results were noted in our study where the mean ADA value in viral meningitis was 1.018 which was well below the cut-off value.

However, the value of ADA in the differential diagnosis of bacterial meningitis and fungal meningitis is controversial and there has been no cut-off value of CSF ADA activity [34].

In our study, we found that the value of CSF ADA was 4.77 in pyogenic meningitis. Some studies have reported a lower efficacy of this test and show an overlap between tuberculous meningitis and bacterial meningitis, so we used the higher cut-off value of 10 U/l in order to increase the sensitivity of ADA and overcome this lacuna [38].

Martinez et al reported that CSF ADA activities were not significantly different between the group with tuberculous meningitis and the group with cryptococcal meningitis in AIDS patients [39]. According to a study by Lopez, CSF ADA levels were raised in cases of neurobrucellosis and cryptococcal meningitis [40]. It has been postulated that the selective increase of ADA depends on the degree of stimulation of T lymphocytes rather than the total numbers. Ena et al reported CSF ADA elevation in tuberculous meningitis patients with significant T cell depleted AIDS [41].

Gambhir IS et al found that the mean CSF ADA levels in TBM patients was 9.61±4.10 U/l and was significantly elevated as compared to viral encephalitis and enteric encephalopathy cases; but the difference was insignificant in comparison to pyogenic meningitis and cerebral malaria [42].

ADA exists as 2 isoenzymes, ADA (1) and ADA (2). It appears that ADA (2) isoenzyme originates mainly from monocytes and macrophages. ADA isoenzyme analysis by Schutte CM et al concluded that the ratio of ADA (2) / ADA (Total) was >0.8 in patients with tuberculous meningitis [43]. The level of ADA (2) was tested in our study.

It has been suggested by Piras and Gakis that ADA levels in CSF may help differentiate TBM from viral meningitis and further that TBM and bacterial meningitis ‘differ clearly from one another as regards the relationship of ADA to the number of cells’ [33].

As in previous studies, it is apparent from the results of our study that the level of ADA in CSF was considerably elevated in tuberculous meningitis compared with viral meningitis. This conclusion has proved to be extremely beneficial in the treatment of viral meningitis where patients have been started inadvertently on prolonged courses of anti-tubercular medication with the misdiagnosis of tubercular meningitis.

We found that the ADA levels correlated with the severity of clinical presentation. Patients who presented with altered sensorium, cranial nerve involvement and hemiperesis were noted to have higher ADA values. However, there was no clear correlation with the outcome (Table 13).

The test for ADA in CSF is simple and can be carried out in a central laboratory with a rapid diagnosis, thus reducing unwarranted or harmful therapy for patients.

Further, C reactive protein can help differentiate pyogenic from non-pyogenic meningitis [44-47]. Large number of studies conducted around the world suggests that CRP levels in the CSF are higher in pyogenic meningitis compared to non-pyogenic meningitis and hence aid in the differential diagnosis and management of meningitis [48-52]. But there are very few Indian studies.

A number of recent studies strongly suggest that measurements of CRP in CSF could reliably discriminate between pyogenic

<table>
<thead>
<tr>
<th>Study</th>
<th>Number of patients diagnosed with TBM</th>
<th>ADA cutoff level</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rajendra Prasad et al [44]</td>
<td>29</td>
<td>3.3</td>
<td>100%</td>
<td>97.87%</td>
</tr>
<tr>
<td>Kashyap et al [45]</td>
<td>117</td>
<td>11.39</td>
<td>82%</td>
<td>83%</td>
</tr>
<tr>
<td>Gautum N et al [46]</td>
<td>20</td>
<td>6.97</td>
<td>85%</td>
<td>88%</td>
</tr>
<tr>
<td>Pettersson et al [35]</td>
<td>3</td>
<td>20</td>
<td>100%</td>
<td>99%</td>
</tr>
<tr>
<td>Chotmongkol et al [36]</td>
<td>16</td>
<td>15.5</td>
<td>75%</td>
<td>93%</td>
</tr>
<tr>
<td>Choi et al [34]</td>
<td>36</td>
<td>7</td>
<td>83%</td>
<td>95%</td>
</tr>
<tr>
<td>Riberia et al [29]</td>
<td>32</td>
<td>100%</td>
<td>99%</td>
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</tr>
<tr>
<td>Lopez et al [40]</td>
<td>14</td>
<td>9</td>
<td>48%</td>
<td>100%</td>
</tr>
<tr>
<td>Rohani MY et al [47]</td>
<td>25</td>
<td>10</td>
<td>72%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Table 13: Showing the various studies on ADA with the cut-off values used and sensitivity and specificity obtained.
and non-pyogenic meningitis, implicitly recommending their routine clinical application [48-52].

The finding of our study is that CSF-CRP is significantly higher in pyogenic meningitis compared to non-pyogenic meningitis. This result remained statistically significant with p<0.001. The sensitivity and specificity of the test was 90% and 100% respectively with an accuracy of 98%.

Previous studies conducted by GoranRajs et al, have observed that CSF-CRP levels are higher in gram-negative pyogenic meningitis compared to gram positive pyogenic meningitis suggesting that infection with gram-negative bacteria probably enhances permeability of CRP through the blood brain barrier [53, 54].

A recent meta-analysis by Gerdes LU et al suggested that a negative CRP test in either CSF or serum can be used with a very high probability to rule out bacterial meningitis. In a study conducted by Vaishnavi C et al, CRP in CSF was significantly higher in patients with pyogenic meningitis compared to tubercular meningitis. Authors concluded that the estimation of CRP in the differential diagnosis of meningitis might be made to give a preliminary diagnosis of meningitis [55-57].

Riberio MH et al estimated the levels of CRP in CSF from 33 patients with bacterial meningitis, 21 patients with lymphocytic meningitis and 54 controls. 100% of these patients with bacterial meningitis were correctly classified on the basis of measurement of CRP levels in CSF. No more than 4% of patients were incorrectly classified as belonging to the bacterial group on the basis of CRP levels in CSF. In conclusion authors recommend the estimation of CRP in CSF in the differentiation of bacterial from non-bacterial meningitis [58].

Hemavani V et al evaluated the role of CRP in CSF in differentiation of meningitis. The study included 499 CSF samples from cases of viral, pyogenic, tuberculous and fungal meningitis and 580 normal CSF samples. CRP positive by qualitative latex agglutination test was seen in 73.3% of CSF samples from partially treated pyogenic meningitis and 92% among pyogenic meningitis cases. All suspected cases of tuberculosis meningitis were negative for CRP in the CSF while only 1 out of CSF samples for bacteriologically confirmed tuberculous meningitis was positive. CRP was raised in 27.2% and 12.5% of CSF samples from candidal and cryptococcal meningitis cases respectively while none of the 102 samples from suspected viral meningitis and 580 non-meningitis cases was positive for CRP in the CSF. The study concludes that CSF CRP determination can be of value to differentiate pyogenic versus other microbial meningitis etiology. However, it cannot differentiate between tuberculosis, fungal and viral meningitis [50].

In our study, the CRP in CSF of patients with pyogenic meningitis, tubercular meningitis and viral meningitis were; 31.44mg/dl, 0.86mg/dl and 1.01mg/dl respectively. Another study conducted by Rajamani et al, had 100% sensitivity in patients with pyogenic and tubercular meningitis both, but had 0% sensitivity with viral meningitis. 100% of patients of pyogenic and tubercular meningitis has serum CRP above 12 mg/dl but patients of pyogenic meningitis has levels above 96mg/L. CSF-CRP sensitivity was found in 83.33% cases of pyogenic and none from tubercular meningitis or viral meningitis. CSF - CRP level in pyogenic meningitis were very high (104±90.21 mg/dl) but within normal range in tubercular meningitis, viral meningitis and controls (< 6mg/dl) [52].

Tankhiwale SS et al investigated 75 clinically, biochemically and microscopically diagnosed cases of pyogenic meningitis including 28 adults and 47 pediatric patients. 31 out of 75 cases (42.66%) were positive for CSF-CRP while 34 were positive for only serum CRP. Thus, total of 66 patients showed raised CRP levels in either in serum or CSF while only 27 yielded bacterial growth in culture. The difference was statistically significant. Hence, the authors concluded that estimation of CRP in CSF and serum help as an early marker for rapid diagnosis of pyogenic meningitis [59].

Patients with hepatic dysfunction, dyslipidemia, females on oral contraceptives, patients on steroids were not included in the study as each of these factors independently affect CRP levels [60, 61]. We suggest a protocol for the early differential diagnosis of meningitis using CSF ADA activity and CRP levels. In case of a patient with unexplained fever, headache, nausea/vomiting, a spinal tap with blood cultures is indicated. Before a spinal tap, a brain computed tomography (CT) may be needed in case of altered mental status or papilledema, or of focal neurologic deficits. If CSF analysis shows polymorphonuclear leukocyte dominant pleocytosis (CSF WBC>1500/mm³), it is almost always pyogenic meningitis.

CRP can be used as a rapid confirmatory test since elevated CRP levels are highly suggestive of pyogenic meningitis. Send the gram stain and CSF culture and start antibiotics for pyogenic meningitis. If CSF analysis shows pleocytosis<1500/mm³, with or without polymorphonuclear leukocyte dominant, since tuberculosis meningitis may first be manifested as a polymorphonuclear leukocyte dominant pattern, check the CSF AFB smear/culture, fungus smear/culture, Cryptococcus latex agglutination test, viral PCR and CSF ADA. In cases with a lymphocyte dominant pattern CSF ADA can be used to determine the possibility of tuberculous meningitis versus viral meningitis.

Early confirmatory diagnosis and aggressive management can help prevent serious CNS complications. 2 rapid diagnostic tests-CRP and ADA activity in the CSF can help in the differential diagnosis of pyogenic from non-pyogenic and tubercular from viral meningitis respectively. CRP being elevated in pyogenic meningitis and ADA activity noted to be higher in tuberculous meningitis. The levels of ADA and CRP are low in viral meningitis. However, these tests should be interpreted judiciously in the light of the patients’ clinical manifestations and the CSF characteristics.

**Conclusion**

1. Most common meningitis is present study is Tubercular meningitis.
meningitis, followed by Viral Meningitis.
2. Tubercular meningitis is seen mostly in younger Age group, whereas pyogenic meningitis in extremes of age group.
3. Males are affected than females in are 3 types of Meningitis in present study.
4. Fever & headache was present in all cases of Meningitis (100%). 70% presented with altered sensorium.
5. Average cell count is more in pyogenic meningitis least in viral meningitis
6. Tubercular & Pyogenic meningitis had raised protein levels and decreased sugar levels.
7. CSF ADA activity was higher in patients with tubercular meningitis when compared to pyogenic and viral meningitis.
8. CSF –CRP levels were higher in pyogenic meningitis than in non-pyogenic meningitis.
9. ADA levels correlated with clinical presentation but not with the outcome of tubercular meningitis.
10. All deaths occurred in Tubercular meningitis group.

Summary

Meningitis is the most common form of supportive central nervous system (CNS) infection which occurs throughout the world. The prognosis of meningitis is critically dependent on a rapid causal diagnosis and implementation of immediate treatment. However, clinical and biochemical parameters available within the few hours that follow patients admission are not reliable enough, except when bacteria are to be found in the cerebrospinal fluid under the microscope. Therefore, the initial treatment of meningitis is most of time presumptive. A number of recent studies strongly suggest that ADA activity in CSF is elevated in tubercular meningitis. CSF CRP levels can reliably discriminate between pyogenic and non-pyogenic meningitis. Thus, 2 rapid diagnostic tests- CSF ADA activity and CRP levels can help in the differential diagnosis of tubercular, pyogenic and viral meningitis. However, they should be interpreted judiciously in the light of the patients’ clinical manifestations and the CSF characteristics.

In our study, a total of 25 patients were diagnosed as tubercular meningitis based on the clinical features and CSF analysis. The ADA activity was 14.36 U/l in the tuberculous meningitis group; 4.77 in the pyogenic meningitis group; 1.018 in the viral meningitis group. Comparing the ADA activity in the 3 groups, the difference was found to be statistically significant (p<0.001) in the tuberculous meningitis group compared to the other groups. The sensitivity and specificity was 72% and 100% respectively when a cut-off value of ADA of 10U/l was used.

ADA levels did correlate with the severity of clinical manifestations. However, it did not show any correlation in terms of mortality.

We found that CSF-CRP is significantly higher in pyogenic meningitis compared to non-pyogenic meningitis. This result remained statistically significant with p<0.001. The sensitivity and specificity of the test was 90% and 100% respectively with an accuracy of 98%.

Proforma
Sl No. Name: Age: Sex: IP No:

History
Fever: Y / N
Duration (Days):
Headache: Y / N
Duration (Days):
Vomiting: Y / N
Duration (Days):
Seizures: Y / N
No. of Episodes: Partial / Generalized
Altered Sensorium:
Drowsy/ Irritable/ Stupor/Coma:
Neurological Deficits:

Any other Relevant History:

Physical Examination
Vitals: Bp: Pr: Rr: Temp:
Others:
CNS Examination
HMF Cranial Nerves
Motor System
Plantars
Sensory System
Cerebellar Signs
Neck Stiffness: Y / N
Kernigs Sign: Y / N
Brudzinski’s Sign: Y / N
CVS: RS: PA:

Investigations
CBC: Hb %: TLC: N= L= M= B= E =
LFT:
RBS:
CXR:
CT Scan Brain Plain:
HIV Test:
CSF Analysis:

Appearance:

Cell Count:

Cell Type: N = L=

Protein: Mg/Dl

Sugar: Mg/Dl

Gram Stain

AFB Stain

C Reactive Protein: Md/Dl

Adenosine Deaminase: U/L

Diagnosis

Treatment

Outcome

To Master Chart

ADA - Adenosine Deaminase, AFB - Acid Fast Bacilli, ATT - Anti-tubercular Treatment, CRP - C-reactive protein

CXR- Chest X-Ray, ESR - Erythrocyte Sedimentation Rate, F- Female, FM - Fungal Meningitis, Hb%- Haemoglobin %, IP. No. - In-patient No, L - Lymphocytes, M - Male, N - Neutrophils, PM - Pyogenic Meningitis, TBM - Tubercular Meningitis, TLC- Total Leucocyte Count, VM - Viral Meningitis

References


