ORIGINAL ARTICLE

Treatment of Tuberculous Meningitis and Its Complications in Adults

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ABSTRACT

Objective: To determine the frequency of complications of Tuberculous Meningitis and review its treatment.

Methods: This cross sectional study was conducted in the department of medicine unit-III, PMC Hospital Nawabshah from January 2016 to December 2016, on 122 patients who were admitted with complaints of headache, fever, neck stiffness or unconsciousness were studied. After taking history and examination, the baseline investigations were sent along with x-ray chest, contrast CT Brain was done where needed. After fundoscopy and imaging Lumber Puncture was done and CSF was sent for detailed examination. Diagnosis of tuberculous meningitis was made on 32 cases by presence of mycobacteria in CSF by Staining and / or Culture or clinical meningitis with headache, fever, meningismus, CSF showing increased protein, decreased glucose, and pleocytosis with Lymphocyte predominance and response to anti tuberculous drugs. Patients were examined daily. If patients developed new complication then CT or MRI brain was repeated.

Result: 32 patients with tuberculous meningitis were identified. More than half of the cases were presented with one or more complications. Hydrocephalus was found in 8.7 %, stroke in 15.6 %, cranial nerve palsy in 21.8 %, visual impairment in 9.3 %, seizure in 18.6 % and death occurred in 18.7 %.

Conclusion: Tuberculous meningitis is associated with significant risk of complication and death.

Key words: Hydrocephalus, Tuberculous Meningitis, Tuberculoma

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INTRODUCTION:

Tuberculous meningitis (TBM) is caused by mycobacterium Tuberculosis. It is one of common infection of central nervous system. Despite the anti-tuberculous therapy 20 % to 50 %[1] of patients die and many survivors are left with neurologic sequelae. Death and complication from TB meningitis are strongly associated with delay in diagnosis and treatment.[1]

WHO guidelines suggest treatment of TBM with two months of Rifampsin, Isoniazid (INH), Pyrazinamide and ethambutol followed by Rifampsin, and INH for 10 Months[2]. Some centers use all three drugs Rifampsin, INH and PZA for full duration of therapy. According to WHO guideline treatment of MDR - TBM is combinations of at-least five effective drugs including one quinolone and one injectable second line drugs for 18 to 24 months[3].

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Complications and their supportive therapy:

Inflammatory exudates within subarachnoid space or venticular system lead to Hydrocephalus. Hydrocephalus may be communicating due to abnormal flow throw basal cisterns or non-communicating due to blockage at level of fourth ventricle.

Communicating Hydrocephalic is common and is treated initially with frusemide 40 mg / 24 h and acetazolamide 10 to 20 mg/kg/d or repeated lumbar puncture[4]. Corticosteroids are recommended for all patients of TBM regardless of severity of disease. Dexamethasone should be started I/V at dosage of 0.4mg /kg per 24 h for one month then orally 4mg/day and reduce by 1mg/week for 4week. Non communicating

hydrocephalus requires rapid surgical intervention. Techniques used are venticuloperitoneal shunt and endoscopic third venticulostomy[5].

In addition to hydrocephalus other causes of raised Intracranial pressure (ICP) in TBM are cerebral edema, infarction and Tuberculoma. Hyponatremia, hyperthermia and hypercapnia may increase ICP. Management is directed at correction of these abnormalities and intervention to treat raised ICP including hyperosmolar agents as mannitol.

Hyponatremia (plasma sodium <135 mmol /l) occurs in 40 50 % of patients with TBM[6] one mechanism is cerebral salt wasting characterized by hyponatremia, natriuresis and hypovolemia in response to brain injury[7].

Second is syndrome of inappropriate antidiuretic hormone (SIADH) in which there is excessive release of antidiuretic hormone from posterior pituitary despite normal plasma volume resulting in Hyponatremia[8]. SIADH is managed with fluid restriction and cerebral salt wasting (CSW) with fluid administration. Tuberculoma can occur together with or without tuberculous meningitis. Clinical features depend on size and site of Tuberculoma and include focal weakness, seizure or symptoms of raised intracranial pressure. Dexamethasone has no effect neither on incidence nor on resolution of tuberculoma[9]. Tuberculoma is treated with 4 anti-tuberculous drugs for 18 month or until resolution of Tuberculoma. When optic chiasma is involved by Tuberculoma threatening vision and not responding to dexamethasone then alternative anti inflammatory drug thalidomide can be used[10]. When size and site of Tuberculoma is causing clinical deterioration surgical excision is required.

Stoke occurs in 15-57% of patient with TBM. Infarcts are usually bilateral, multiple and occur commonly in region of caudate nucleus, thalamus and internal capsule. Corticosteroids have no role in prevention of stroke[11]. Aspirin is most commonly used for treatment of stroke worldwide.

Seizure occurs in 20% of patients of TBM. In patients with CNS infection recurrent seizure are common after first seizure[12]. These patients should be given prophylactic anti antiepileptic drugs to prevent recurrence of seizure. After control of acute seizure with benzodiazepine, loading dosage of phenytoin should be followed by maintenance dosage for 3 to 6 month if there is high risk of recurrence. Leviteracetam is alternative. Valproicacid should be avoided.

Cranial Nerve Palsy is also the complications of Tuberculosis Meningitis affecting cranial nerves. Most frequently affected cranial nerves in TBM is VI followed by cranial nerve, III, IV and VII. Less commonly affected cranial nerve is II .VIII X XI and XII[13].

Purpose of study is to detect frequency of various complication of TBM and assess their severity. This will emphasize the importance of early diagnosis and treatment of TBM which is the only way to prevent complications.

METHODS:

This prospective descriptive study was conducted at PMC hospital Nawabshah from January 2016 to December 2016, on 122 cases who were admitted with complaints of headache, fever, neck stiffness or unconsciousness are studied. Detailed history was taken and examination was performed after taking consent. Baseline investigations were sent. Blood CP malarial parasite, blood glucose, blood urea, serum creatinine and serum electrolyte. X ray chest, and Contrast CT brain was also done where needed. After fundoscopy and imaging LP was done and CSF was sent for analysis, AFB, and TB culture. Once presumptive diagnosis of TB meningitis was made on CSF analysis then anti tuberculous drugs Rifampsin , INH ,PZA and Myambutol were started along with Dexamethasone. Patients with bacterial meningitis, cerebral malaria, encephalitis and metabolic encephalopathy were excluded from study. Diagnosis of TBM was made in 32 cases on following diagnostic criteria: presence of Mycobacteria in CSF by staining and / or culture or clinical meningitis with following features:

A- Headache, Fever, meningismus.
B- CSF showing increase protein, low glucose and pleocytosis with lymphocyte predominance
C- Response to anti tuberculous drugs.

Patients were examined daily for improvement. If patients developed any complication or condition deteriorated then CT or MRI brain was repeated.

RESULTS:

A total of 122 patients were enrolled in study from January to December 2016. Out of 122 patients 32 patients were having TB meningitis, 64 bacterial meningitis and 26 patients were having other diagnosis (Table No: I). 32 patients with TB meningitis were further studied for treatment

response and development of complications. Mean age of these patients was 40 ± 25 years. 60 % were male. Hydrocephalus was present in 6 patients (18.7 %), Seizure in 3 patients (9.3 %), Stroke in 5 patients (15.6 %), Cranial nerve palsy in 7 patients (21.8 %), Visual impairment in 5 patients (15.6 %). Tuberculoma in 3 patients (9.3 %). Hyponatremia in 9 patients (28 %). Death occurred in 6 patients (18.7 %).
Images of Tuberculoma are shown in Figure I.

Table I. Final Diagnosis of 122 Patients

Diagnosis	Frequency
TB Meningitis	32
Bacterial Meningitis	64
Cerebral Malaria	10
Encephalitis	10
Metabolic Encephalopathy	6

Table II. Frequency of Complications in Tuberculous Meningitis (TBM) n=32

Diagnosis	N	%
Hydrocephalus	6	18.7
Seizure	3	9.3
Stroke	5	15.6
Cranial Nerve Palsy	7	21.8
Visual	5	15.6
Tuberculoma	3	9.3
Hyponatremia	9	28
Death	6	18.7

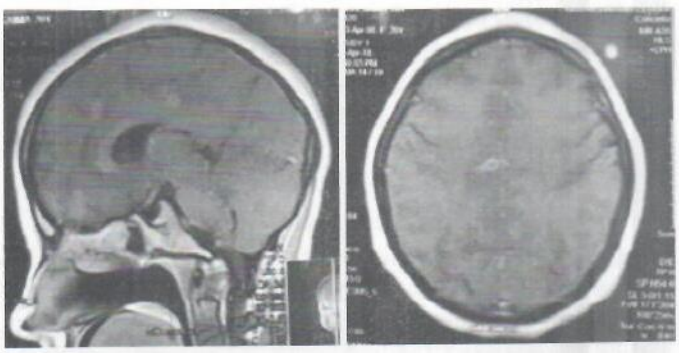

Figure-I: MRI Showing Tuberculoma

DISCUSSION:

In 32 Patients of TB Meningitis complication or death occurred in more than half of patients. These patients were having long duration of illness before hospitalization. Delay in diagnosis and treatment is main reason of complication or death in these patients.

Some of these complications like Hydrocephalus, cranial nerve palsy and visual impairment were present at time of admission while others like seizures, stroke and hyponatremia occurred during hospitalization. Hydrocephalus was present in 6 patients (18%). In five patients hydrocephalus was presents on admission while one patient developed hydrocephalus during hospitalization. One patient had mild hydrocephalus and was managed medically with frusemide and acetazolamide along with antituberculous drugs and corticosteroid while other patients were referred to neurosurgical ward for CSF diversion procedure. Two types of surgical procedure done are ventriculoperitonial shunt and endoscopic third ventriculostomy. These procedures are associated with significant mortility. Shunt surgry usually is done for obstructive hydrocephalus. Surgery is also indicated in advanced disease or when condition is deteriorating. Role of corticosteroid in treatment of hydrocephalus is uncertain.

All the patients who developed hydrocephalus were having history of illness for more than one month making duration of illness an important predisposing factor for hydrocephalus. This frequency of hydrocephalus in TBM of 18.7% is compareable to study of Ken et al[14] in which frequency of hydrocephalus was 12.1% and Merkler AE et al[15] with frequency of hydrocephalus of 8.4%. These finding differ with study done by T Raut, et al with frequency of hydrocephalus of 65%[16] and N.E. Anderson et al with frequency of 42%[17]. This high frequency of hydrocephalus may be due to long duration of illness before imaging was done

Stroke developed in 5 patients (15.6%). All these strokes were infarction. MRI can detect infarction which is missed by CT scanning brain. Corticosteroid can not prevent stroke. Aspirin is commonly used for treatment. This rate of stroke development in TBM 15.6% is within range of 15 to 57 % reported in other studies.

Hyponatremia was found in 9 patients (28%). Exact mechanism was not known. Symptomatic hyponatremia was treated with hypertonic 3% saline fluid.

Cranial nerve palsy occurred in 21.8 % of our patients and 20 to 52 % in others studies[19]. Sixth (VI) nerve and III nerve were commonly affected. Cause of cranial nerve palsy is ischemia or entrapment in exudates at base of brain. Tuberculoma can compress cranial nerves. Visual impairment was present in three patients (9.3%) Cause of visual impairment in TBM is hydrocephalus, optichochiasmatic arachnoiditis and occipital infarction[20]

Seizures were present in 18.6% of patients comparable to study by Merkler AE et al[15]. After Control of acute seizure with benzodiazepine, Phenytoin was started and continued for 6 month. Valproate should is avoided as it is Hepatotoxic. If it is given then liver function should be monitored.

Death occurred in 18.7% of our patients while in other studies mortality rate is from 7 to 65 %[21]. These patients were having long duration of illness before commencement of therapy and advanced stage of disease. High rate of mortality was in those who developed infarction and seizure. One limitation of study was that size of sample was small. Patients also did not come for follow up regularly after discharge to look for complication during treatment. MRI could not be obtained in all patients and this might have lead to underestimation of frequency of tuberculoma and stroke.

CONCLUSION:

Tuberculous meningitis is most severe form of tuberculosis associated with high mortality and many complications. Only early diagnosis and treatment can prevent complications and mortality.

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