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Study of Clinical Profiles of Tubercular Meningitis Patients with Seizures

Pradeep Prajapati
Associate Professor, Department of Medicine, Gajra Raja Medical College, Gwalior, MP, India

Krishnapriya M R
PG Student, Department of Medicine, Gajra Raja Medical College, Gwalior, MP, India

Ajay Pal Singh
Professor, Department of Medicine, Gajra Raja Medical College, Gwalior, MP, India

Rajkishori Prajapati
Consultant Gynecologist, ParivarSuperspeciality Hospital, Gwalior, MP, India

***Abstract*---**Background: Tuberculosis remains a serious global health problem, with an estimated 10 million new cases occurring globally during 2019. CNS involvement one of the most devastating clinical manifestations of tuberculosis (TB) is noted in 5-10% of extrapulmonary TB cases, and accounts for approximately 1% of all TB cases and it also carries significant higher mortality and neurological disability among infected individuals especially in low income countries. Materials & Methods: It's a hospital based prospective study which will include 80 patients admitted in department of Medicine and Neurology diagnosed as tubercular meningitis with a duration of 3 years. All Subjects were subjected to anthropometric measurements and routine biochemical tests – Hemogram, Urea, Serum Creatinine, LFT, Lipid Profile. Results: In patients who developed seizures before hospital admission, most common finding in neuroimaging is hydrocephalus, inflammatory edema and ventriculomegaly in patient who developed seizure within first week of hospital admission, majority had normal CT finding (27.27%) followed by metabolic cause like hyponatremia and hepatitis(18.18).In patients who developed seizure after 1st week of hospital admission, commonest cause found is Hydrocephalus(25.69%) and tuberculoma (17.64%) followed by calcified granuloma (15.68%).

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***Corresponding author**: Prajapati, R.; Email: drpradeepp2512@gmail.com*
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Keywords---health problem, meningitis patients, neuroimaging, seizures, tuberculosis.

Introduction

Tuberculosis remains a serious global health problem,with an estimated 10 million new cases occurring globally during 2019[1]. CNS involvement one of the most devastating clinical manifestations of tuberculosis (TB) is noted in 5-10% of extrapulmonary TB cases, and accounts for approximately 1% of all TB cases and it also carries significant higher mortality and neurological disability among infected individuals especially in low income countries.[(1)]the clinical characteristics of TBM include fever, headache, vomiting, impaired consciousness, focal neurological signs and seizures[2].

The current data is showing that seizures is more common in children than adults this may be attributed to the immaturity of the brain[3]. Over half of children with TBM may experience seizures at any time point ,but more often during the later stage.There is accumulating data suggested that brain inflammation and the subsequent neuronal injury and reactivation of glial cells play an essential role in seizure induction following CNS infection[4]. The underlying etiology of seizures in TBM is multifactorial, therefore the type and duration of treatment may vary between individual cases depending on the possible underlying cause of convulsion. In patients with CNS infections recurrent seizures are common observation after the first seizure therefore these patients are probably in need of prophylactic antiepileptic drugs to prevent further seizure recurrence. In this study we are studying the clinical profile of Tubercular Meningitis with pathogenesis and mechanisms of seizures as well as clinical and electrophysiological characteristics of these seizures.

Table 1
Staging of TBM[5]

Contemporary criterion for staging TBM
I Alert and oriented without focal neurological deficit
II Glasgow coma score of 14 -11 0r 15 with focal neurological deficit
III Glasgow coma score of 10 or less with or without focal neurological deficit

Two rare forms of TBM are serous TB meningitis and TB encephalopathy. Serous TB meningitis is characterized by signs and symptoms of a mild meningitis with spontaneous recovery.TB encephalopathy usually occurs in a young child with progressive primary TB; the presentation is that of reduced levels of consciousness with few focal signs and minimal meningism. The pathogenesis is uncertain but is presumed to be immune mediated. Diagnosis is important because anecdotal reports suggest agood response to corticosteroid.

Table 2
Modified Ahuja criteria for diagnosis in TBM[6]

Mandatory Finding
1) Fever lasting more than 14 days
2) Abnormal CSF finding
Pleocytosis with more than 20 cells
More than 60% are lymphocytes
Proteins >100 mg/dl
Sugar <60% of blood sugar
PLUS ANY TWO OF FOLLOWING CRITERIA
1) Evidence of extraneural TB
2) Positive family history of exposure to case
3) Positive Mantoux test
4) Abnormal CT scan findings (2 or more)
Exudates in basal cistern
Hydrocephalus
Infarcts
Gyral enhancements

Material and Methods

It's a hospital based prospective study which will include 80 patients admitted in department of Medicine and Neurology diagnosed as tubercular meningitis with a duration of 3 years with following inclusion and exclusion criteria

- Inclusion Criteia
  - Age >18 yrs
  - Patients who fulfilling the criteria of TB Meningitis by clinical radiological and CSF criteria and presented with seizures.
  - CSF cell count (>.02×109/L or more with lymphcytic predominance.

- Exclusion Criteria
  - Patient known case of seizure disorder, braintumour, hydrocephalus, CVA, dementia, alzheimersdisease, psychiatric disorder.
  - Patient <18 yrs.
  - Patient not giving written consent.

Observation and Results

Table 3
Age distribution

Age in years	No : of patients	Percentage (%)
15-25	32	40.0
26-35	14	17.5
36-45	8	10.0
46-55	8	10.0
56-65	15	18.75

>66	3	3.75
Range :15-72		
Mean:35.03±15.742		

In the Present study patients of age >15 ys are included. The youngest age observed is 15 years and oldest is 67 years. The majority of patient belong to the age group 15 -25 years (40%) and 26-35 years (14%).in the present study 88 % belong to 2nd to 6th decade of life and approximately 10 % above 6th decade.

Table 4
Sex distribution

Sex	No: of patients	Percentage
Female	32	40
Male	48	60

In the present study out of 80 patients, 48 patients are male and 32 patients are female.

Table 5
Clinical type of seizures

Type of seizures	No of patients	Percentage (%)
Generalized	51	63.75
Focal	29	36.25
Total	80	100

Table 6
Clinical type of seizures

Type Of Seizure		No. Of Patients	Percentage
Generalized	GTCS	47	58.75
	Atonic seizures	3	3.75
Focal seizures	With secondary generalization	17	21.25
	Without dyscognitive feature	9	11.25
	With dyscognitive feature	4	5.00
Total		80	100

In present study most common type of seizure is generalized in this GTCS is the most common which accounts for 62.5 % of the total study, focal seizures found in 37.5% of the patients , in this common type is focal seizures with secondary generalization (21.25%)

Table 7
Correlation between timing of seziure and neuroimaging finding and probabale etiologies

	Timing Of Seizure						TOTAL
	Pre hospital	(%)	<1 WEEK	(%)	>1 WEEK	(%)	
Hydrocephalus	2	25	1	9.09	13	25.49	17
Tuberculoma	0	00	1	9.09	9	17.64	11
Tuberculoma with hydrocephalus	0	0	1	9.09	2	3.9	4
Calcified granuloma	0	0	0	0	8	15.68	9
Infarct	0	0	0	0	4	7.8	5
Ventriculomegaly	2	25	2	18.18	2	3.9	7
Inflammatory edema	2	25	0	0	1	0	4
Demyelination	0	0	0	0	0	0	2
Metabolic	0	0	2	18.18	3	5.88	6
Idiopathic	1	12.5	3	27.27	5	7.84	10
Encephalitis	1	12.5	0	0	1	1.96	2
Rare causes	0	0	0	0	3	5.88	3
Total	8	100	11	100	51	100	80

In patients who developed seizures before hospital admission,most common finding in neuroimaging is Hydrocephalus,inflammatory edema and ventriculomegaly, in patient who developed seizure within first week of hospital admission, majority had normal CT finding(27.27%) followed by metabolic cause like hyponatremia and hepatitis(18.18).In patients who developed seizure after 1stweek of hospital admission ,commonest cause found is Hydrocephalus(25.69%) and tuberculoma(17.64%) followed by calcified granuloma(15.68%).

Table 8
Distribution of imaging abnormality and other associated etiologies

Etiology	No Of Patients	Percentage
Hydrocephalus	17	21.25
Tuberculoma	11	13.75
Tuberculoma with hydrocephalus	4	5.00
Calcified Granuloma	9	11.25
Infarct	5	6.25
Ventriculomegaly	7	8.75
Inflammatory edema	4	5.00
Demyelination	2	2.50
Metabolic	6	7.50
Idiopathic	10	12.50
Encephalitis	2	2.50
Rare causes	3	3.75
Total	70	100

Most common finding in neuroimaging is Hydrocephalus (21.25%) followed by Tuberculoma (13.75%),followed by Calcified Granuloma (11.25%). Or less common pathologies found are ventriculomegaly,inflammatory edema and demyelination. Metabolic cause found in7.5% patients, 3 patients have hyponatremia. One patient has hypoglycemia and 1patient had hepatitis.Other rare findings on imaging are encephalitis andencephalomalacia

Table 9
Distribution of eeg pattern

EEG PATTERN	No OF PATIENTS	PERCENTAGE
ABNORMAL	20	25
NORMAL	60	75

EEG is done in 80 patients, out of which 20(25%) patients show abnormal EEG pattern rest 60 patients show patients show normal EEG recording .most of the EEG are taken during interictal period. Among abnormal EEG generalized continuous diffuse slowing and abnormal generalized epileptiform discharges present.

Discussion

In this study 80 patients with TB meningitis presented with seizures are included as per inclusion and exclusion criteria, and observation is compared with similar study. In present study, total numberof patient is 80,out of which 48 are males and 32 are females.Age of the patients is between 15 and 67.In a study done by Xiasong song in 2020 in Dept of neurology Chongqing china,out of 223 patients with TBM 99 were female and 124 were males. The age of the patients was between 16 and 82.Mean age of the population is 40 years.

In the present study majority of patients developed generalized seizures contributing to a total of 62.5%, in this out of 50 patients with generalized seizures 47(58.75%) developed GTCS and 3 developed Atonic seizures, focal seizures developed in rest 30 patients out of which 17(21.25%) developed focal seizures with secondary generalization,9 (11.25%)patients developed focal seizures without dyscognitive feature and 4(5.00%)developed focal seizures with dyscognitive feature. In N J Farinha in Great Ormond street hospital trust London out of 38 patients with TBM 20 (50%) had seizures. Focal seizures was noted in 15 (39.5%) and GTCS were observed in 5 (13.2%) patients (N J Farinha)[7].

In the study done by UshaKMisra about seizures in TBM .Focal seizures were observed in11 patients(13.9%), focal to bilateral in 9 (11.4%),generalized tonic clonic in 7 (8.9%) and status epilepticus in 6(7.6%).In the study done by Xiaosong song focal seizures occurred in 11 out of 46 patients (23.9%) and generalized seizures occurred in 38 out of 46 patients (82.6%). In a study done by patwari in 136 TBM patients,GTCS were reported in 59 patients (43.4%), followed by focal seizures (28%) and tonic spasm (3%)[8].

In present study most common finding in neuroimaging is Hydrocephalus (21.25%) found in 17 out of 80 TBM patients, followed by Tuberculoma (13.75%).

Calcified granuloma (11.25%), combination of Tuberculoma with Hydrocephalus found in 5%, ventriculomegaly (8.75%), encephalitis (2.50%) whereas in 18.5 % there is no imaging abnormality.In study done by Xiasong song meningeal enhancement found in 95 patients (50.8%), tuberculoma (70 patients,33.8%),Hydrocephalus (52 patients 25.1%)and infarction (32 patients 15.5%).In a study done by Usha K Misra it was shown meningeal irritation in 3 (11.1%), Tuberculoma in 9(33.3%), Infarction in 4(14.8%) and multiple associations in 9(33.3%)[9].

In present study probable cause of convulsion could be attributed to Hydrocephalus (22.85%) followed by Tuberculoma (14.28%),followed by Calcified Granuloma (11.4%). Or less common pathologies found are ventriculomegaly, inflammatory edema and demyelination. Metabolic cause found in 8.57%. Among metabolic cause,3 patients have hyponatremia .one patient has hypoglycemia and 2 patients has hepatitis.Other rare findings on imaging are encephalitis and encephalomalacia. In study done by Patwari A K probable causes of convulsions can be correlated to cerebral edema (57%), syndrome of inappropriate secretion of ADH (35%), Hydrocephalus (32 %), Tuberculoma (27%), and abnormal electric focus (25%) and cerebral infarction(13%)[10].

In the present study patients with early seizures are associated with Hydrocephalus (25.5%) followed by Tuberculoma (14.5%), metabolic (9.5%) where as in patients who presented with late seizures were associated with Calcified granuloma (50%) followed by Tuberculoma, infarct and Demyelination.In a study done by Usha K Misra early onset were associated with meningeal irritation in 37.5%, Tuberculoma in 25%, and multiple associations in 37.5%. While Tuberculoma, Infarction and Hyponatremia were more common in patients with late onset seizures compared to early onset. Multiple associations were equally responsible for both rarely and late onset seizures[11].

EEG done in 80 patients, out of which 20(25%) patients show abnormal EEG pattern rest 60 patients show patients show normal EEG recording .most of the EEG are taken during interictal period. Among abnormal EEG generalized continuous diffuse slowing present in 60% and abnormal generalized epileptiform discharges present in 40%.In a study done by Usha K Misra out of 2 were normal and 17 were normal. Among abnormal EEG 11 showed generalized slowing(theta slowing), Delta slowing in 4,Frontal intermittent rhythmic delta activity in 2and lateralized discharges (spike and wave with secondary generalization in 2 patients in study done by Xiasong song out of 207 patients with TBM,123 showed abnormal EEG .in this slow background activity in 108 patients (54.8%) and epileptiform discharges were observed in 41 patients (20.8%)[12].

In patients with generalized diffuse slowing out of 11, 7 presented with generalized seizures among patients whose EEG showed generalized epileptiform discharges presented exclusively with generalized seizures. In 46 patients with generalised seizures most patients were associated with Hydrocephalus (followed by metabolic causes and no cause can be localised in 6 patients .where as in patients with focal seizures Tuberculoma is the most probable cause associated followed by calcified granuloma in patients with Hydrocephalus, clinical type of seizure found mainly is GTCS followed by Focal seizures. In patients with

Tuberculoma,the focal seizures is commonly seen. In patients with Tuberculoma with hydrocephalus GTCS is more common than focal seizures.In patients with calcified granuloma Focal seizures is more common than GTCS. In patients with associated infarct both generalised and focal seizures is seen. In patients with associated metabolic abnormalities,GTCS is solely seen. In patients with normal neuroimaging and no other etiologies associated GTCS is commoner than focal seizures.In study done by Kalita J among 60%of TBM patients with Hydrocephalus, among the 11 (34.4%) patients presented with clinical seizures,9 had generalised seizures and 2 had focal seizures .in a study done by El Sayed 20 patients with CNS tuberculomas found that 60% of the cases have developed focal seizures with secondary generalisation and only 30% of patients presented with primary generalised seizures[13-15].

Conclusion

Seizures are a common finding in patients with TBM .and can occur at any point of the disease course. Neuro-inflammation,diffuse brain injury,reactive gliosis and mass effect.The early onset seizures most commonly associated with Hydrocephalus and Tuberculoma whereas late seizures are associated with calcified granuloma. In patients with generalised seizures most common associated etiology is Hydrocephalus where as in patients with focal seizures most commonly association found is Tuberculoma.Adequate treatment of TB infection along with early identification and management of seizures and other complications may reduce the risk of developing chronic epilepsy and improve the overall outcome in TBM patients.

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