

Clinical Findings & MR Features in CNS Tuberculosis. A Tertiary Care Hospital Study

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ABSTRACT

Objective: To know the clinical findings & MR features in CNS Tuberculosis. A tertiary care hospital study.

Study Design: cross-sectional study

Place and Duration of Study: This study was conducted at the Neurology department of Jinnah Postgraduate Medical Centre, Neurology Department DUHS and Medicine Department of Mohtarma Benazir Bhutto Medical College, Karachi from January 2018 to December 2019 for a period of 02 years.

Materials and Methods: The research was done on 89 serially registered patients of CNS tuberculosis selectively intracranial pathology in the said institutions. Enrolled subjects were between the age 15 to 52 years suggestive of cerebral tuberculosis with MRI evidence were involved and data was analyzed using the SPSS 25 software.

Results: The mean age of subjects was \pm SD 31.42 \pm 10.84 years while the mean presenting symptoms duration was found 11.46 with SD \pm 6.39. Percentage of male patients was 59.6 and Female patients were 40.4 Percent. 37.1% patients have positive family history of tuberculosis. 23.6% subjects have diabetes in their family. The most common presenting symptom was fever 82%, while headache was the second most common features that is 79.8%, neck stiffness was found in 76.4 percent, 68.5% had disturbed conscious level and hemiplegia was seen in 44.9%. Diverse MRI appearances for example enhancement of Basal cistern was found in 20.2 percent, enhancement of meninges in 66.3%, 29.2% have non obstructive hydrocephalus, tuberculomas were found in 67.4 percent patients and last but not the least 25.8 percent subjects have ischemic infarcts. About 14.6 percent patients have mixed MRI appearances a like tuberculomas with meningeal enhancement, basal cistern enhancement with tuberculoma in 9% patients. 12.4 percent patients have cerebral ischemia with tuberculomas. 5.6% patients have typical infarcts with enhanced meninges and ring enhanced tuberculomas.

Conclusion: In our study tuberculomas was on the top in MRI findings second most common was meningeal enhancement. Hydrocephalus was on third. So, it is concluded the patients should be referred promptly to tertiary care hospital for better diagnosis of difficult neurological case.

Key Words: CNS Tuberculosis; Cerebral TB; Tuberculoma, Meningitis

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INTRODUCTION

Cerebral tuberculosis is reflected as a serious community health issue.

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The main objective of our study was to document the CNS especially the cerebral TB manifestation and MRI findings.

Mycobacterium tuberculosis is a serious public health problem in under developed countries and still many peoples are affected by this disease. According to the recent WHO report tuberculosis was 10 million population till 2017 and about 1.6 million people died because of it¹. According to National TB Control Program (NTP) of Pakistan around 413,450 tuberculosis patients found in Pakistan per year. The incidence is 231/100,000 people, with the prevalence of 630,000 cases (at 364/100,000 people). The mortality rate is about 60,000 (34/100,000 people).² Pulmonary Tuberculosis is on the top, but the disease burden is additionally augmented by extra pulmonary TB, including CNS TB. The mortality rate is very high in extra pulmonary TB especially in the CNS disease.³

CNS tuberculosis is more common in immuno compromised patients including elderly population and patient with diabetes and HIV.⁴ Furthermore

Alcoholism, malignancy, prolonged use of steroids, and immunosuppressant medications are the other risk factors for tuberculosis.⁵

CNS manifestations of TB can be parenchymal or meningeal disease. Most common is meningeal involvement followed by enhancing Tuberculomas usually multiple. Cerebritis and Abscess formation can also occur. Contrast enhanced MRI is the investigation of choice for CNS TB along with CSF analysis.^{6,7} The prognosis of disease is mainly depending on prompt diagnosis and early treatment of CNS TB.⁸

MATERIALS AND METHODS

The research was done on 89 serially registered patients of CNS tuberculosis selectively intracranial pathology at the Departments of Neurology, Dow University of Health Sciences, Jinnah Postgraduate Medical Centre and SGLGH, Karachi, from January 2018 to December 2019. The patients were included in the study who satisfy the inclusion criteria for example age and Radiological findings¹⁸, clinical signs and symptoms of intracranial tuberculosis subacute to chronic in nature. Claustrophobic patients and patients with metal in body like prosthesis were excluded.

Criteria for the diagnosis of cerebral tuberculosis mostly based on a typical history of TB or past history, along with characteristic CNS symptoms and signs beside fever and headache, those include typical focal neurological deficits, sign of meningeal irritation, and/or seizures. GeneXpert and CSF culture and MRI findings of meningeal enhancement, ring enhanced lesions and hydrocephalus. CSF ADA level helps us in dubious cases.

Data Collection Procedure: Admitted patients who met our inclusion criteria were registered. Informed consent was acquired from all the subjects. The respondents were curtain about the privacy of their data. Patients were referred to Department of Radiology of DUHS and JPMC for the MRI brain with Gadolinium contrast. MRI results were assessed by the Neuro-Radiologists having more than 12 years of experience. The radiologists were blinded from the purpose of the research.

Data Analysis: Data was analyzed by using 25th version of SPSS. Mean and standard deviation were used to assess Descriptive statistics of age and duration. Percentages and Frequency were mentioned for categorical variables for example hydrocephalus, meningeal enhancement, effect modifiers for example gender, age, Family history and duration of symptoms typical of tuberculosis were controlled via stratification. Fisher exact test and Chi-square were applied when needed and p-value of ≤ 0.05 was taken as noteworthy.

RESULTS

The mean standard deviation of age was 31.42 ± 10.84 years in patient from 15 to 52 years old. These patients

have typical symptoms of disease for 2 to 4 weeks and the mean duration was 11.46 days with 6.39 Standard Deviation (Table 1). When we looked at gender distribution it was found that the male patients were 59.6% (n=53) whereas females were 40.4% (n=36). Positive family history was found in 37.1% of patients whereas 23.6% patients have Diabetes Mellitus in family. When we look into the diverse MRI appearances of CNS tuberculosis it was found that meningeal enhancement seen in 66.3% (n=59), basal cistern enhancement was present in 20.2% (n=18), hydrocephalus was found 29.2% (n=26), 67.4% have tuberculomas (n=60) whereas ischemic infarction was noted in 25.8% (n=23) subjects (Figure 1).

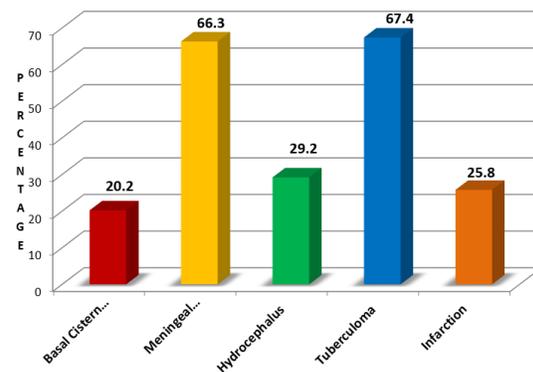


Fig ure No.1: MRI Manifestations in intracranial TB

Additionally, it was observed that only meningeal enhancement was seen in 15.7% patients. Ring enhancing tuberculomas with meningeal enhancement was seen in 14.6% cases, 12.4% have multiple tuberculomas. Meningeal with basal cistern enhanced MRI along with typical multiple Tuberculoma were seen in only 9% cases. Infarction was present in 12.4% cases, whereas tuberculoma, Ischemic infarction and meningeal enhancement in combination were found in 5.6% patients. Only 9 percent patient have infarction alone (Table 2).

About 33% of patients (n=30) registered through our outpatient clinics have history of only 1 week. Around 35 cases came between the duration of 8-14 days. History of 2 to 3 weeks was found in 18 patients. Six patients came in between 22-28 days whereas only 2 cases were brought in ER after a history of a month (30 days or later) (Figure 2).

Stratification of age, gender, symptoms duration and Tuberculosis in Family was done for assessment and adjustment of result related to MRI findings of CNS Tuberculosis (Table 3). Ring enhancing multiple Tuberculomas were spotted less in females (45%) than males (55%). Age was also an effect modifier for Basal meningeal enhancement, but it is more common in young age between 15-25 years. Only 11.1% have basal cistern enhancement in age group between 36-45 years. History of diabetes mellitus in family did not have an augmented effect on any of MRI appearances

(meningeal enhancement, basal cistern enhancement, Tuberculoma, hydrocephalus or cerebro-vascular lesions).

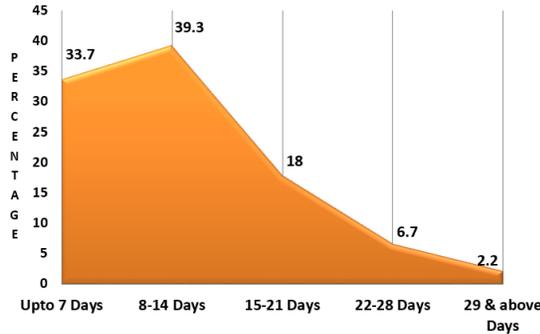


Figure No.2: Duration of presenting symptoms

Table No.1: Demographic data of the study population (n=89)

Characteristics	Frequency	
Age (Years)	31.42 ± 10.84 (Range: 15-52 years)	
Duration of Symptoms (Days)	11.46 ± 6.39 (Range: 15-30 days)	
Gender	Males: 53 (59.6%)	Females: 36 (40.4%)
Family history	Tuberculosis: 33 (37.1%)	Diabetes: 21 (23.6%)
Age category (Years)	15-25	33 (37.1%)
	26-35	21 (23.6%)
	36-45	21 (23.6%)
	46 & Above	14 (15.7%)
Clinical features	Fever	73 (82.0%)
	Headache	71 (79.8%)
	Neck Stiffness	68 (76.4%)
	Altered Consciousness	61 (68.5%)
	Paresis	40 (44.9%)

Table No.2: Combinations of MRI manifestations in patients of Intracranial TB

MRI manifestations	Frequency (n)	Percentage (%)
Meningeal Enhancement alone	14	15.7
Meningeal Enhancement & Tuberculoma	13	14.6
Tuberculoma alone	11	12.4
Tuberculoma, Meningeal, Basal Cistern Enhancement & Hydrocephalus	8	9
Infarction alone	7	7.9
Meningeal Enhancement with Tuberculoma & Infarction	5	5.6
Meningeal Enhancement with Hydrocephalus	4	4.5
Tuberculoma with Hydrocephalus	4	4.5
Tuberculoma, Meningeal & Basal Cistern Enhancement	4	4.5
Basal Cistern Enhancement & Tuberculoma with Infarction	2	2.2
Meningeal & Basal Cistern Enhancement	2	2.2
Tuberculoma, Infarction, Basal Cistern Enhancement & Hydrocephalus	1	1.1

Table No.3: Effect of gender, age, duration of disease and family history of T.B and diabetes on frequency of different patterns of MRI manifestations

Patterns	Basal cistern Enhancement (n=18)	Meningeal Enhancement (n=59)	Hydrocephalus (n=26)	Infarction (n=23)	Tuberculoma (n=60)
Gender					
Males (n=53)	3 (16.7%)	34 (57.6%)	14 (53.8%)	12 (52.2%)	33 (55.0%)
Females (n= 36)	15 (83.33%)	25 (42.4%)	12 (46.2%)	11 (47.8%)	27 (45.0%)
p-value	<0.001**	0.388	0.319	0.276	0.152
Age categories (in years)					
15-25 (n=33)	10 (55.6%)	21 (35.6%)	10 (38.5%)	3 (13.0%)	26 (43.3%)
26-35 (n=21)	2 (11.1%)	12 (20.3%)	4 (15.4%)	7 (30.4%)	11 (18.3%)
36-45 (n=21)	2 (11.1%)	14 (23.7%)	7 (26.9%)	10 (43.5%)	14 (23.3%)
46 above (n=14)	4 (22.2%)	12 (20.3%)	5 (19.2%)	3 (13.0%)	9 (15.0%)
p-value	0.129	0.309	0.676	0.010*	0.241
Duration of disease (in days)					
≤7 (n=30)	5 (27.8%)	14 (23.7%)	8 (30.8%)	8 (34.8%)	21 (35.0%)

8-14 (n=35)	8 (44.4%)	28 (47.5%)	7 (26.9%)	8 (34.8%)	21 (35.0%)
15-21 (n=16)	4 (22.2%)	10 (16.9%)	6 (23.1%)	3 (13.0%)	12 (20.0%)
22-28 (n=6)	1 (5.6%)	5 (8.5%)	4 (15.4%)	3 (13.0%)	4 (6.7%)
≥29 (n=2)	0 (0.0%)	2 (3.4%)	1 (3.8%)	1 (4.3%)	2 (3.3%)
p-value	0.816	0.030*	0.048*	0.600	0.973
Family history of Tuberculosis (T.B) and Diabetes Mellitus (DM)					
T.B present (n=33)	12 (66.7%)	21 (35.6%)	14 (53.8%)	8 (34.8%)	24 (40.0%)
T.B absent (n=56)	6 (33.3%)	38 (64.4%)	12 (46.2%)	15 (65.2%)	36 (60.0%)
p-value	0.005*	0.428	0.032*	0.499	0.281
DM present (n=21)	3 (16.7%)	14 (23.7%)	8 (30.8%)	5 (21.7%)	14 (23.3%)
DM absent (n=68)	15 (83.3%)	45 (76.3%)	18 (69.2%)	18 (78.3%)	46 (76.7%)
p-value	0.438	0.594	0.224	0.527	0.566

All p-values are computed through chi-square test and Fisher's Exact test as indicated, with ≤ 0.05 is considered significant (represented by *) & ≤ 0.001 is considered highly significant (represented by **).

DISCUSSION

Extrapulmonary tuberculosis can damage and major vital organ of the body but tuberculosis of central nervous system is the most devastating among the others because of significantly high mortality or the patient can developed permanent neurological deficit.⁹ About 6-12% cases of extrapulmonary tuberculosis are related to central nervous system, which are about 2-3 % of entire cases of Mycobacterium Tuberculosis.⁹ Tuberculosis of the central nervous system, is secondary to granulomatous inflammation of meninges, brain parenchyma or vertebral column and spinal cord secondary to Mycobacterium species.

Gene Xpert testing, Culture of mycobacterium and ADA are some specific tests done on the sample taken from Cerebrospinal fluid, but result of all these tests took quite a lot of time so management might be delayed. Alternatively, MRI imaging of the brain are spinal cord provide time saving are faster result with better image resolution of brain parenchyma and soft tissues than CT scans, therefore smoothing the process of speedy diagnosis and early treatment. MRI imaging is superior to CT scan as better soft tissues exposure and for lesions of posterior fossa. Through MRI brain we can easily judge the stage of disease either early disease or late with complications. In our study the mean age of patients was 33.5 ± 18.5 SD years the subjects were in between 15 to 52 years age group. The majority of the case are in their twenties as we found in the study of Wasay M. et-al.¹⁰ Gender seemed to be major modifier in our research as male to female ratio was 6:4. The stratified analysis showed female subjects have more basal cistern enhancement than males. Tuberculomas were on the top in MRI findings noticed in male patients (55%) which is about 10% more when compare with female cases (P-value of 0.151). Fever was the topmost clinical feature in 82%, followed by neck stiffness seen in 76.4% of cases indicative of meningeal inflammation. Headache, impaired consciousness and limb weakness were found in 79.8%, 68.5%, and 44.9% cases correspondingly. In our study

none of the patient presented with seizures. A variety of MRI features were noted, which varied from a single lesion to multiple lesions. Tuberculomas with meningeal enhancement were found in 67.4% and 66.3% cases respectively, whereas hydrocephalous seen in 29% cases. Infarction was found in 25.8% of patients followed by basal cistern enhancement in 20.2% patients. The one of the major complication of hydrocephalus in CNS TB is secondary to inflammation and obstruction of the basal subarachnoid cisterns granulomatous infection, or by blockade of third ventricle by tuberculomas.¹¹ Even a small tuberculoma varies from 0.5 to 2.0 mm in size is sufficient to block the aqueduct of third verticle.¹² In our study it was found that the size of largest tuberculoma was 4.0mm. In our study 26 patients (29.2%), have hydrocephalus and from those, 19 patients went into neurosurgery procedure for VP shunt. We found that frequency of hydrocephalus directly corresponded to stage of illness as stated by Bhargava S, et al.¹³ So it is essential for the physician from rural areas or primary health care to recognize the alarming clinical features of CNS TB and promptly refer them to tertiary care unit for imaging and better management.

Some patients have multiple lesions that is meningeal enhancement with multiple tuberculomas were seen in 14.6% cases, basal cistern and meningeal inflammations were seen in only 2.2% cases. Whereas basal cistern and meningeal inflammation with tuberculoma, were noticed in 4.5% patients and tuberculoma with hydrocephalus, and inflammation of meninges were diagnosed in 9% patients. These findings are indicative of predominance of tuberculoma and meningeal inflammation were the frequent MRI manifestations. In various previous researches, these findings slightly differ from our result.^{10,14,15,16,17} The additional MRI appearances in second or third stage of the disease were meningeal inflammation as noted by (P-value = 0.030 & 0.048 respectively). In addition to the obstructive hydrocephalus secondary to tuberculoma or inflammation, additional alarming complication was ischemic infarction mostly in "TB

zone” the area of the brain especially the thalamus and the area supplied by the medial lenticulostriate arteries. The infarcts are mostly ischemic and usually in stage 3 of illness. In many studies 21% to 38% patients with CNS TB have infarcts, similar findings were found in our study.¹⁸ In our study it was found that about 25% patients have MRI proof of ischemic infarction and signs of acute infarct were seen in about 44.9% patients.

CONCLUSION

In our study tuberculomas was on the top in MRI findings, the second most common was meningeal enhancement. Hydrocephalus was on third. So, it is concluded the patients should be referred promptly to tertiary care hospital for better diagnosis of difficult neurological case.

Unfortunately, patients were referred to us from the peripheral areas after they developed neurological complications. The morbidity and mortality can be straightforwardly controlled by correct early diagnosis and management.

Author’s Contribution:

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Revisiting Critically: Naeemullah Bullo,
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Final Approval of version: Naeemullah Bullo

Conflict of Interest: The study has no conflict of interest to declare by any author.

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