

Original Article

Evaluation of the Effectiveness of CT / MRI Brain in Detecting Central Nervous System Tuberculosis

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Abstract

Background : Central Nervous System Tuberculosis (CNS TB) is complex, atypical and associated with mortality as well as sequelae. Newer imaging techniques aid in improving the diagnosis of various forms of CNS TB.

Aims and Objectives : In this research, we aim to evaluate the role of neuro-imaging in detecting Central Nervous System Tuberculosis and describe the different forms of CNS Tuberculosis including Meningitis, Cerebritis, Cerebral Abscesses, Tuberculomas, Vasculitis and Spinal or Calvarial involvement.

Materials and Methods : A retrospective review of medical records of 101 patients with CSF positive TB were analysed for their findings in CT and or MRI scans. Prior administrative approval obtained.

Results : Majority were men and most common age group was 20 to 29 years. Fever, altered sensorium and seizures were the common presenting symptoms, while 25% were retrovirus positive. Baseline CT of 18.2% of patients had Hydrocephalus, 18.2% had Cerebral edema and 13.6% had Tuberculoma. More than half had evidence of Tuberculoma or signs of Meningitis in baseline MRI.

Conclusion : MRI appeared sensitive in detecting Tuberculomas, Edema and Meningeal enhancements.

Key words : Vasogenic Edema, Tuberculosis, Central Nervous System Tuberculosis, Tuberculoma, Tuberculous Meningitis.

Tuberculosis (TB) is a major public health problem even after almost three decades of its declaration as a global public health¹. Rightly named as the “captain of all men of death”², TB has been a scourge of the humankind from time immemorial. Historically, even though several other diseases like Smallpox and Plague have killed millions of people, their reign has been relatively short-lived; TB has been ever present. It tops the list of infectious diseases killing people globally. About a quarter of these deaths occur in India³.

Neurological Tuberculosis (TB) comprises 5-10% of the cases of extra-pulmonary TB⁴. The pandemic of Acquired Immunodeficiency Syndrome (AIDS) has resulted in an increased incidence of CNS TB worldwide with CNS involvement occurring in 2-5% patients with TB and in 10% of those with AIDS-related TB⁵. Involvement of the Central Nervous System (CNS) is one of the most serious forms of this infection and is responsible for a high mortality and morbidity.

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Editor's Comment :

■ MRI offers enhanced sensitivity for detecting subtle CNS tuberculosis changes compared to CT, which remains useful for identifying calcifications and acute complications. Both imaging techniques are most effective when combined with clinical and laboratory evaluations. Early and accurate neuroimaging is critical for guiding timely treatment and improving patient outcomes.

The spectrum of CNS-TB is wide. In the Brain, it can present as Tuberculous Meningitis (TBM), Tubercular abscess or Tuberculomas.

Granulomatous inflammatory reaction in CNS caused by *Mycobacterium Tuberculosis* may involve the Meninges, Brain, Spinal Cord, Vertebrae and Skull vault and may manifest clinically depending on the specific location of the disease process. The most common pathway for CNS entry of TB is by hematogenous spread of *Mycobacterium Tuberculosis* from a disease focus elsewhere in the body, such as Lung or Gastrointestinal Tract. Rarely, it can also spread directly from an intra- or extra-cranial focus.

Early and definitive diagnosis of TBM is difficult due to the subacute presentation with nonspecific clinical manifestations. The diagnosis of TBM cannot be

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confirmed or excluded on the basis of clinical findings. Microbiology is time consuming and has a low sensitivity in CNS TB whether it is acid-fast bacillus smear or culture⁶.

Imaging is the cornerstone of CNS TB diagnosis and its associated complications. Widespread availability and utilization of Computed Tomography (CT) and Magnetic Resonance Imaging (MRI), have facilitated an early diagnosis of complications⁴. It is also used in monitoring response to treatment. Contrast-enhanced MRI is generally considered the modality of choice. The CT or MRI of the brain may reveal thickening and enhancement of basal meninges, hydrocephalus, infarction, oedema (often periventricular) and mass lesions due to associated Tuberculoma or TB abscess⁴.

Bhargava, *et al* demonstrated the presence of Hydrocephalus (83%), Cerebral Infarction (28%) and Tuberculoma (10%) on CT in patients with TB meningitis⁷. Rajashekar, *et al* concluded in their research that based on clinical findings (evidence of raised intracranial tension and a progressive neurological deficit) and CT appearance (size, shape and association with a midline shift) it is possible to distinguish Tuberculomas and granulomas in a majority of patients presenting with seizures and single small enhancing lesions⁸.

Serial CT imaging is very helpful in assessing the course of Tuberculomas and Hydrocephalus. Gadolinium enhanced MRI is superior to the CT in detection of basal meningeal enhancement and small Tuberculomas⁴. Contrast enhanced MRI has been found to be superior to contrast enhanced CT in the detection of diffuse and focal meningeal granulomatous lesions. The MRI is also superior to CT in delineating focal infarcts of the basal ganglia and diencephalon. Furthermore, MRI is superior to CT in defining the presence, location and extent of associated brainstem lesions⁴.

The clinical and radiologic manifestations of CNS TB may mimic other infectious and non-infectious neurological conditions, such as Brain Tumors and non-TB related granuloma such as Sarcoidosis. A better understanding and familiarity with CT and MRI features of CNS TB will aid prompt and accurate diagnosis of CNS Tuberculosis. If undiagnosed and untreated, severe complications can occur like obliterative Vasculitis, Cerebral Infarction, Cerebral Edema, Obstructive Hydrocephalus and Multiple

Cranial Nerve Palsies, resulting in increased morbidity and mortality. Therefore, familiarity with the imaging presentations of CNS Tuberculosis is essential for prompt and accurate diagnosis of this entity. The objective of this research was to describe the neuro-imaging findings of patients with Central Nervous System Tuberculosis diagnosed based on CBNAAT analysis of their CSF.

MATERIALS AND METHODS

A cross sectional study was conducted in a Tertiary Care Hospital in Mangalore, Western Karnataka in India on patients diagnosed as positive for CNS Tuberculosis based on CSF analysis by CBNAAT. Among them, those who underwent radiological imaging such as CT and or MRI brain were included for the study. Those patients who were suspected for CNS TB but had a negative CSF analysis on CBNAAT were excluded.

Sample size was estimated to be 101 based on previous research⁹ on radio-imaging in CNS Tuberculosis, taking p as 82%, with an absolute precision of 10% at 95% confidence levels and 10% non-response rate. A random sample of patients fitting the eligibility criteria was selected from the hospital information management system till the desired sample size was achieved.

Study variables included for the analysis were age, gender, time since onset of illness, status of retrovirus positivity, presence of Pulmonary Tuberculosis, baseline and follow up radiological findings. Imaging parameters included in the study were Computerised Tomogram (contrast enhanced) and Magnetic Resonance Imaging. The sequences of MRI performed include T1-weighted, T2-weighted, diffusion, perfusion, MRS and post gadolinium (0.2 mg/kg). The radiological findings were obtained from PACS software for evaluation. CT and MRI scans were reviewed by two Radiologists. The scans were assessed using a predesigned questionnaire with defined categories. The number of lesions, their localizations, dimensions, signal characteristics and contrast enhancement patterns were recorded.

Permission from Medical Superintendent of the hospital was obtained to access MRD files and CT/MRI Brain findings of Tuberculosis patients prior to start of the study. Permission from the Ethics Committee was requested for waiver of informed patient consent.

The collected data was entered in Microsoft excel software and analysed using SPSS version 22.0. Categorical data was summarised in frequencies and percentages, while continuous data was summarised in mean and Standard Deviation.

RESULTS

Totally 101 patients with CNS Tuberculosis were included in the research during our study period. Of them, 64 (63.4%) were Men. The mean ($\pm$ SD) age of the patients was 36.8 ($\pm$ 14.1) years. The most common presenting symptom was Fever (94.1%) followed by Altered sensorium (74.3%), Seizures (72.3%) and headache (21.8%). Neck stiffness was observed in two patients (2.0%) while one patient had Bell's palsy (0.9%). About 25 patients (24.8%) were retrovirus positive as well. Of the 101 patients, 15 (14.9%) also had Pulmonary Tuberculosis as evidenced by CBNAAT (Table 1).

A baseline CT was done for 22 (21.8%) patients. Among them, four (18.2%) had hydrocephalus, four (18.2%) had Cerebral Edema, three (13.6%) had tuberculoma. About 14 (13.9%) patients had CT done in the follow up period, of which four (28.6%) were normal. Follow-up period from three months to 15 months. The follow-up CT had evidence of hydrocephalus in seven (50.0%) patients, while one each had Cerebral Edema (7.1%) and Tuberculoma (7.1%) respectively (Table 2).

A baseline MRI was available for 89 (88.1%) patients. Of them, 77 (86.5%) had meningeal enhancing

lesions, 48 (53.9%) had evidence of Tuberculoma, 47 (52.8%) showed signs of Meningitis and 31 (34.8%) had Cerebral Edema. About 21 (20.8%) patients had MRI done in the follow up period of which only one (4.8%) was normal. Follow-up period ranged from 1-14 months. Meningeal enhancing lesion (71.4%) was the commonest finding in the follow up MRI, followed by Cerebral Edema (42.9%) and Meningitis (33.3%) and Tuberculoma (28.6%) (Table 3).

The baseline CT as well as MRI was normal for only two (1.9%) patients. Eleven (10.9%) patients had completed both baseline CT and MRI investigation. MRI was more sensitive in picking up a larger number of Tuberculoma lesions, infarcts, vasogenic edema and meningeal enhancement as compared to CT (Fig 1).

Core hypo-intensity on T2-weighted and FLAIR images was related to extensive necrosis and the large number of cells in the lesion. The rims of Tuberculomas were composed of fibrous tissue and gliosis. The signal characteristics of the rims had no reliable correlation with fibrosis or gliosis. The pattern of enhancement was the same as in CT scans, showing marked variability, including homogenous, ringlike, and lobular patterns.

DISCUSSION

TB Meningitis is one of the common causes of chronic Meningitis in the developing countries and is a major public health problem due to its permanent neurological sequelae as well as mortality¹⁰. The diagnosis of CNS TB is elusive and high index of suspicion is necessary for early diagnosis. It involves demonstrating *M Tuberculosis* on smear as acid fast bacilli or culture of the CSF. CSF acid fast bacillus has a low sensitivity of 20-40%¹¹ and CSF culture is a time-consuming procedure. Moreover, CSF culture can be negative in 15-75% of cases¹². A delay in

Table 1 — Clinical profile of study subjects (n=101)

Symptom	Frequency	Percentage
Fever	95	94.1
Altered sensorium	75	74.3
Seizures	73	72.3
Headache	22	21.8
Mono / hemiplegia	3	3.0
Neck pain	2	2.0
Others	3	3.0

Table 2 — CECT Brain findings of study subjects

CT finding	Baseline (n=22)		Follow-up (n=14)	
	Frequency	Percentage	Frequency	Percentage
Hydrocephalus	4	18.2	7	50.0
Cerebral edema	4	18.2	1	7.1
Tuberculoma	3	13.6	1	7.1
Infarct	3	13.6	2	14.3
Periventricular CSF seepage	0	0.0	3	21.4

Table 3 — MRI Brain findings of study subjects

MRI finding	Baseline (n=89)		Follow-up (n=21)	
	Frequency	Percentage	Frequency	Percentage
Hydrocephalus	14	15.7	5	23.8
Cerebral edema	31	34.8	9	42.9
Tuberculoma	48	53.9	6	28.6
Infarct	24	27.0	4	19.0
Enhancing lesions	77	86.5	15	71.4
Exudates	26	29.2	2	9.5
Meningitis	47	52.8	7	33.3
Ventriculitis	3	3.4	0	0.0

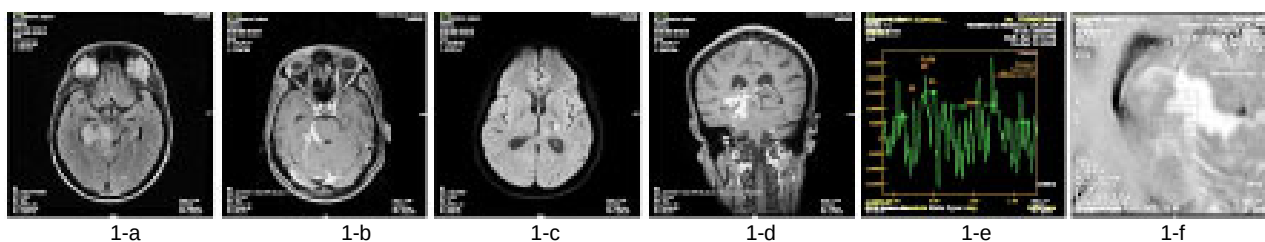


Fig 1 — MRI - a, b, c, d, e, f: Axial FLAIR, Axial T1 Contrast enhanced, Axial DWI, Coronal T1 Contrast enhanced Wt and MR Spectroscopy images. Multiple ring enhancing altered signal intensity lesions in bilateral cerebral and cerebellar hemispheres with mild perilesional edema, displaying hypo intense signal intensity on T1 and hyper intense signal intensity on FLAIR sequences. Enhancing lesion with conglomeration in the ambient and quadrigeminal cisterns with thick enhancing exudates. Diffuse restriction focus in left thalamus - TUBERCULOMAS WITH TUBERCULOUS MENINGITIS AND VASCULITIS.

treatment is often associated with high mortality, thus ensuring early recognition is of paramount importance as the clinical outcome depends upon the stage at which therapy is initiated^{13,14}. Current antitubercular drugs are highly effective when the chemotherapy is provided prior to the onset of complications.

Cranial imaging is useful in diagnosing CNS TB, predicting its complications and also has a prognostic value¹⁵. Typical neuroradiological findings of CNS TB can aid in the diagnosis of this illness¹⁶. Despite of this, the diagnostic value of neuroimaging in CNS TB has not been fully validated in studies. Moreover, data on the utility of neuroradiology in predicting the outcome is even more limited. Researchers elsewhere have done studies comparing CT to MRI and have documented MRI as a superior diagnostic imaging modality for neuro-Tuberculosis¹⁷⁻¹⁹.

Present study was conducted with 101 CSF positive CNS TB patients in Radiology Department of a Tertiary Care Centre, wherein their CT and or MRI findings were assessed for the various presenting features of CNS Tuberculosis.

Most common age group observed was between 20 to 29 years in the present study. Dinesh M, *et al* observed that 60% of their subjects were aged between 20 to 40 years⁵. The mean age of study subjects in present study was similar to that of Nabi S, *et al*⁶ and Aher, *et al*²⁰. A male preponderance was observed in our research, similar to the study done in Nagpur²⁰, though it was in contrast to that done on similar CNS TB patients in Chengalpattu⁵. It is even evident from the data of the national TB program that Tuberculosis had a male preponderance²¹.

The triad of presenting symptoms in our research were Fever, Altered sensorium and Seizures. Etlik O, *et al* observed that all subjects in their study had presented with Fever and Lethargy, while four had cough²². Neurologic presentations included raised

intracranial pressure, vomiting, seizures, paresis, third cranial nerves palsy, nuchal rigidity and disturbance of consciousness. Meanwhile, Idris, *et al* documented that headache, convulsions and hemiparesis with or without hemisensory symptoms were commonest neurological symptoms in their study¹⁷. Increased intracranial pressure leading to papilledema was encountered in more than half of their patients.

The clinical presentation of TB Meningitis appears vague sometimes with nonspecific symptoms that are tough to distinguish it from other causes of bacterial meningitis. The typical sign of meningeal stiffness was present in very minimal proportion in our study. A longer duration of illness (more than a week) has previously been shown to be a clinical variable highly predictive of TB meningitis^{9,10}, we have similar findings.

George, *et al* noted that age above years, a GCS score <8, absence of Headache, CSF protein below 60 mg% and Medical Research Council (MRC) Stage III at presentation were significant predictors of in-hospital mortality in both HIV sero-positive as well as sero-negative patients²³. Also, transtentorial herniation was observed in neuro imaging of a patient, who eventually expired.

The prevalence of HIV seropositivity in our study was 24.8%. Out of the 25 PLHIV, 21 had an abnormal baseline MRI. Among the PLHIV, 20 had enhancing lesions, 12 had features of Meningitis and nine had Tuberculoma in MRI. Research by Aher, *et al* in Nagpur²⁰ on 50 CNS TB patients observed a higher prevalence of HIV (36.0%). Mortality was more in HIV positive patients (25%) with stage III disease. Of the 18 HIV patients in their study, 16 had Meningitis and two patients had Tuberculomas. Two patients had CD4 count below 50, eight patients had count between 51 to 100, six had counts between 101 to 150 while two patients had counts between 151 to 200²⁰. It is

reported that HIV-infected patients have fewer Tuberculomas compared to non-HIV-infected patients²⁴. These findings add to the hypothesis that Tuberculomas are formed because of a robust immunological response to Tuberculous infection.

About 15% of the patients in our study also had TB infection coexisting in their Lung parenchyma, evident in sputum analysis. Etlik, *et al* observed a similar prevalence of PTB in their research (12.5%), although it was by Chest radiography²². But studies done elsewhere observed a higher PTB prevalence of 44%²⁰ to 46%²⁵. The reason for low prevalence in present study could be attributed to absence of sputum analysis for some of our patients. This reiterates the importance of Chest X-rays and microbiological analyses on respiratory specimens in the diagnostic process of extra pulmonary Tuberculosis.

Hydrocephalus was the commonest CT imaging finding in the present study. In three out of four patients who had Hydrocephalus at baseline, it had resolved during the follow up period. A study by Botha *et al* in Cape Town on evaluating the sensitivity, specificity and reliability of CT imaging in diagnosing TB Meningitis observed that CT scan criteria for basal meningeal enhancement had good intra-rater agreement (k range 0.35-0.78) and fair to moderate inter-rater agreement (k range 0.20-0.52). The criteria for basal meningeal enhancement had better specificity (61.5% - 100%) but poorer sensitivity (5.9% - 29.4%)²⁶.

Apart from enhancing lesions, more than half of our patients had MRI evidence of Tuberculoma and Meningitis, while a third of our patients had cerebral edema. Similar finding was observed by other authors as well^{20,22,25}. Nabi, *et al* in their study on 100 TB Meningitis patients documented that Hydrocephalus (61%), Tuberculomas (54%), Leptomeningeal involvement (46%) and infarcts (13%) were the most frequent radiological signs on MRI of their patients⁶. Presence of infarct was significantly associated with mortality. Possible reason could be that majority of patients in that study had presented in MRC Stage II. MR scans especially DWI sequences were superior in detecting infarcts.

Christensen, *et al* observed that MRI scans proved more sensitive for identifying meningeal enhancement than CT scans (86% *versus* 0%) and Cranial CT scans seem to be just as sensitive as MRI scans in

identifying Hydrocephalus, Infarcts and Tuberculomas²⁵.

Our study is not without any limitations. It was not possible to have both the imaging scans for all patients, because the decision to perform the imaging in each patient was not according to predefined criteria, but at the discretion of the Physician. Also, follow up scans could not be performed in many patients due to attrition, which is unavoidable. Hence, status of neuroimaging after initiation of treatment could not be ascertained in them.

The treating Physician should interpret the CT imaging findings with caution and rely on other parameters as well for diagnosing CNS TB, with the understanding that a normal CT Brain imaging is not uncommon in initial phases of the disease particularly in adult patients.

CONCLUSION

CNS TB remains a serious disease of concern irrespective of the incidence of TB in our setting. The disease has a high mortality rate as well as sequelae among the survivors. Given the fact that diagnosis of this disease is difficult due to lack of specific tools, the clinician should remain vigilant to treat empirically if there is suspicion of CNS Tuberculosis.

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