

A Retrospective Analysis of 38 Cases of Intracranial Tuberculosis Using Mr Imaging and Its Management In A Tertiary Care Hospital

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ABSTRACT:

Introduction: It is estimated that approximately one-third of the world's population are infected with Mycobacterium tuberculosis, the agent that causes tuberculosis (TB).¹ Central nervous system TB is a major health concern in developing countries, and is increasing in developed countries because of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) and multidrug-resistance.^{1,2} Intracranial inflammatory granulomas are a diagnostic challenge both to clinicians and radiologists.

Materials and Methods: Our department's records were reviewed from May 2017 to May 2018, and MRI scans of patients diagnosed with intracranial tuberculosis at our hospital were retrospectively studied. The study population comprised of 38 cases (08 children and 30 adults) with ages ranging from 11 to 60 yrs. (mean age 26.58 yrs.), suspected of suffering from intracranial tuberculosis based on clinical history and CSF analysis either before or after a diagnosis of intracranial tuberculosis was given on MRI scan. The known cases of treated intracranial tuberculosis/any brain space occupying lesions/previous history of stroke due to known vascular risk factors such as hypertension, diabetes and heart disease were excluded from the study.

Results: Thirty eight cases of intracranial tuberculosis were included in the study, out of which 30 (78.94%) were adults (≥ 18 yrs.) and 08 (21.05%) cases were children (< 18 yrs.). Majority of cases were in the age group of 11 - 20 yrs. (44.2%). The most frequent tuberculous lesions encountered in our study were tuberculomas (79.1%) followed by tubercular meningitis (72.1%), cerebritis (6.9%) and abscesses (4.6%). The most frequent tubercular Meningitis-induced complications encountered were infarcts seen in 15 cases (34.9%) and obstructive hydrocephalus in 15 cases (34.9%).

Conclusion: MRI plays an important role in the diagnosis of intracranial tuberculosis and its associated complications. It helps in identifying the extent of involvement and differentiating tuberculous lesions from other pathologies.

Key Words: cerebellar hemisphere, MRI, Tuberculosis.

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I. Introduction

It is estimated that approximately one-third of the world's population are infected with *Mycobacterium tuberculosis*, the agent that causes tuberculosis (TB).¹ Central nervous system TB is a major health concern in developing countries, and is increasing in developed countries because of human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS) and multidrug-resistance.^{1,2} Intracranial inflammatory granulomas are a diagnostic challenge both to clinicians and radiologists. Magnetic resonance imaging (MRI) findings are usually non-specific and differentiation from malignant lesions is very difficult, particularly in the absence of TB in other parts of the body such as the lungs or lymph nodes. Magnetic resonance spectroscopy (MRS) provides additional biochemical information that can be useful. Our purpose is to describe the most common MRS findings in brain tuberculomas with emphasis on potential specific markers.

II. Materials And Methods

Our department's records were reviewed from May 2017 to May 2018, and MRI scans of patients diagnosed with intracranial tuberculosis at our hospital were retrospectively studied. The study population comprised of 38 cases (08 children and 30 adults) with ages ranging from 11 to 60 yrs. (mean age 26.58 yrs.), suspected of suffering from intracranial tuberculosis based on clinical history and CSF analysis either before or

after a diagnosis of intracranial tuberculosis was given on MRI scan. The known cases of treated intracranial tuberculosis/any brain space occupying lesions/previous history of stroke due to known vascular risk factors such as hypertension, diabetes and heart disease were excluded from the study.

The patients enrolled to the study were subjected to MRI using Siemens Magnetom AVANTO 1.5 TESLA machine. Head coil was used in all the patients in supine position. Conventional spin echo sequences, axial T1, T2 and FLAIR; Coronal T2; Sagittal T1; axial GRE (Gradient Recalled Echo); followed by post-contrast axial, coronal and sagittal images were obtained. Additional sequences like MR spectroscopy and DWI were acquired for tuberculous lesions whenever required. Multi-voxel spectroscopy data was acquired after contrast administration using a CSI sequence with TE 135 msec. Spectroscopy was avoided in small lesions which were in close proximity to the bone. Spectral heights of metabolites like choline, creatine, N-acetyl aspartate, lactate, lipid and amino acids were studied. Metabolite ratios like Cho/Cr and NAA/Cr were also studied. As reference standards values of Cho/Cr >1.5 and NAA/Cr <1.6 were taken as abnormal which was similar to the study conducted by N Meena et al (2015).[4]

It is a descriptive type of study and patients' characteristics were presented using numbers and percentages. All the statistical calculations were done using SPSS (Statistical Package for the Social Sciences) 16.0.

All the cases were put on first line Antitubercular drugs and followed up clinically wherever possible. Isoniazid (300 mg/d), Rifampicin (10 mg/kg/d), Pyrazinamide (30 mg/kg/d in divided doses), ethambutol (15-25 mg/kg/d in divided doses) and pyridoxine (50 mg/d). In cases showing good response to Antitubercular drugs, ethambutol and pyrazinamide were discontinued and only isoniazid and Rifampicin were continued for 6 months. In cases with inadequate resolution of symptoms of meningitis, isoniazid and Rifampicin were prolonged for 9 - 12 months. In cases diagnosed with tubercular meningitis, Ceftriaxone (2 g IV twice daily), ampicillin (2 g IV four times daily and dexamethasone (8 mg IV twice daily) were administered. Dexamethasone was administered for 3 weeks and tapered over 3 weeks. In cases having infarcts, antiplatelet (aspirin 75 mg once daily) were administered. Majority of the patients showed improvement of symptoms after starting antitubercular treatment. 4 cases of TBM complicated by infarctions had poor prognosis despite adjunctive dexamethasone treatment.

III. Results

Thirty eight cases of intracranial tuberculosis were included in the study, out of which 30 (78.94%) were adults (≥18 yrs.) and 08 (21.05%) cases were children (<18 yrs.). Majority of cases were in the age group of 11 - 20 yrs. (44.2%). The most frequent tuberculous lesions encountered in our study were tuberculomas (79.1%) followed by tubercular meningitis (72.1%), cerebritis (6.9%) and abscesses (4.6%). The most frequent tubercular Meningitis-induced complications encountered were infarcts seen in 15 cases (34.9%) and obstructive hydrocephalus in 15 cases (34.9%). Tuberculomas were frequently located in cerebral hemispheres (88.2%) followed by cerebellar hemispheres (61.7%), brainstem (26.5%) and basal ganglia (8.8%) (Table/Fig. 1). Out of 34 cases which showed tuberculomas, caseating tuberculomas were seen in 27 cases (79.4%) and non-caseating tuberculoma in 19 cases (55.8%). Tubercular abscess diagnosis was made in 2 (4.6%) cases and in both cases the lesion was located in the parietal lobe. Both cases of tubercular abscess showed elevated lipid/lactate peak and mildly elevated choline peak with no evidence of amino acid peak, thus excluding pyogenic abscess (Fig. 3). Tubercular Meningitis-induced infarcts were most commonly located in basal ganglia (73.3%) followed by thalamus (33.3%), brainstem (33.3%), frontal lobe (33.3%), internal capsule (26.7%), cerebellar hemisphere (26.7%), corpus callosum

Location	Number (N=30)	Percentage
Cerebral hemispheres	28	86.3
Cerebellar hemispheres	19	60.2
Brain Stem	8	25.3
Basal Ganglia	3	8.8

Table 1: Location of Tuberculomas

Lesion	Number (N=31)	Percentage
Tuberculoma	25	81
Tubercular Meningitis	26	79
Tubercular Abscess	1	5
	9	31

Infarcts		
Obstructive Hydrocephalus	6	23
Cerebritis	3	9
Ependymitis	2	6
Choroid Plexitis	1	3

Table 2. Types of Tuberculous Lesions and Associated Complications in Adults

Lesion	Number (N: 11)	Percentage
Tuberculoma	7	72
Tubercular Meningitis	5	53
Infarcts	4	44
Obstructive Hydrocephalus	7	63
Ependymitis	1	9

Table 3: Types of Tuberculous Lesions and Associated Complications in Children

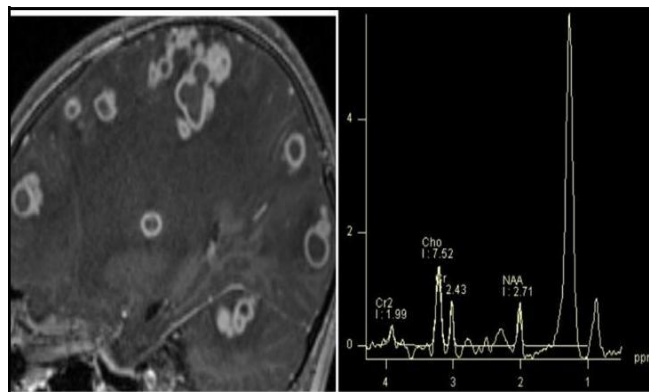


Figure 1: Sagittal Post-contrast T1 Fat Saturated Image shows Multiple Peripherally Enhancing Discrete and Conglomerated Lesions.

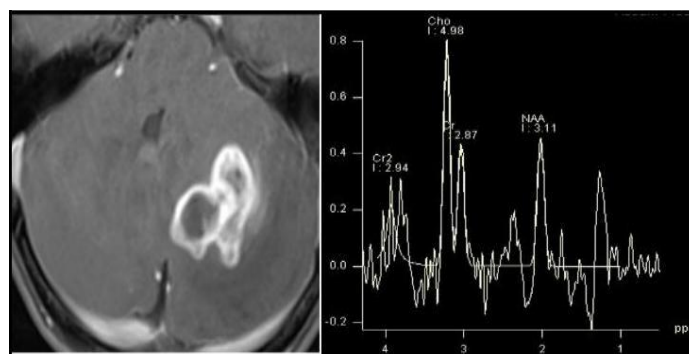


Figure 2: Necrotic Caseating Tuberculoma

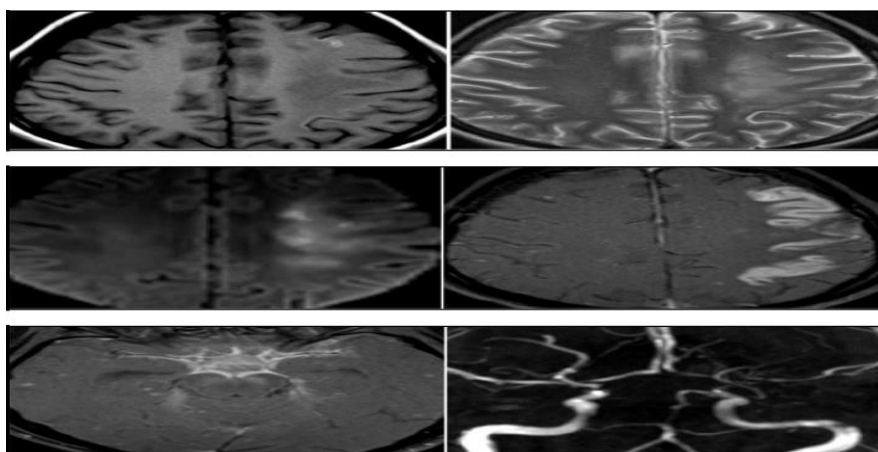


Figure 3: Meningitis-induced Vasculitis and Infarcts

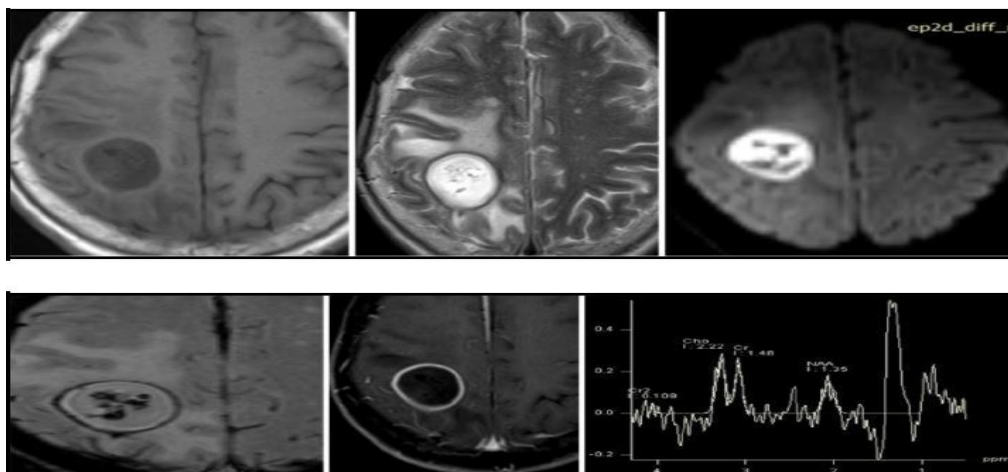


Figure 4: Tubercular Abscess

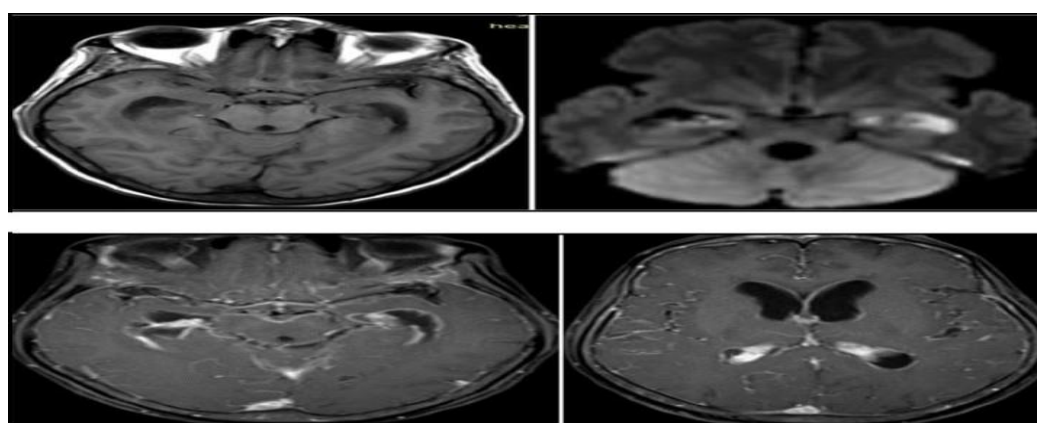


Figure 5: Meningitis with Ependymitis, Choroid Plexitis & Communicating Hydrocephalus

IV. Management Of Tuberculosis

Tuberculosis management refers to the medical treatment of the infectious disease tuberculosis (TB). The standard "short" course treatment for TB is isoniazid (along with pyridoxal phosphate to obviate peripheral neuropathy caused by isoniazid), rifampicin (also known as rifampin in the United States), pyrazinamide, and ethambutol for two months, then isoniazid and rifampicin alone for a further four months. The patient is considered to be free of living bacteria after six months. For latent tuberculosis, the standard treatment is six to nine months of daily isoniazid alone or three months of weekly (12 doses total) of isoniazid/rifampentine combination.^{[1][2]} If the organism is known to be fully sensitive, then treatment is with isoniazid, rifampicin, and pyrazinamide for two months, followed by isoniazid and rifampicin for four months. Ethambutol need not be used.

First line

All first-line anti-tuberculous drug names have semistandardized three-letter and single-letter abbreviations:

- ethambutol is EMB or E,
- isoniazid is INH or H,
- pyrazinamide is PZA or Z,
- rifampicin is RMP or R,
- streptomycin is SM or S.

First-line anti-tuberculous drug names are often remembered with the mnemonic "RIPE," referring to the use of a rifamycin (like rifampin), isoniazid, pyrazinamide, and ethambutol. US practice uses abbreviations and names that are not internationally convened: rifampicin is called rifampin and abbreviated RIF; streptomycin is abbreviated STM. Other abbreviations have been widely used (for example, the notations RIF, RFP, and RMP have all been widely used for rifampicin, and the combination regimens have notations such as IRPE, HRZE, RIPE, and IREP that are variously synonyms or near-synonyms, depending on dosage schedules), but for clarity, the semistandardized abbreviations used above are used in the rest of this article. In this system, which the WHO supports, "RIPE" is "RHZE". (Both have mnemonic potential, as tuberculosis is named after tubercles (small tubers), and a tuber can be ripe and can be a rhizome.)

Drug regimens are similarly abbreviated in a semistandardised manner. The drugs are listed using their single letter abbreviations (in the order given above, which is roughly the order of introduction into clinical practice). A prefix denotes the number of months the treatment should be given for; a subscript denotes intermittent dosing (so₃ means three times a week) and no subscript means daily dosing. Most regimens have an initial *high-intensity phase*, followed by a *continuation phase* (also called a consolidation phase or eradication phase): the high-intensity phase is given first, then the continuation phase, the two phases divided by a slash. So 2HREZ/4HR₃

means isoniazid, rifampicin, ethambutol, pyrazinamide daily for two months, followed by four months of isoniazid and rifampicin given three times a week.

In the US only, streptomycin is no longer considered a first line drug by ATS/IDSA/CDC because of high rates of resistance.^[3] The WHO have made no such recommendation.

Second line

The second line drugs (WHO groups 2, 3 and 4) are only used to treat disease that is resistant to first line therapy (i.e., for extensively drug-resistant tuberculosis (XDR-TB) or multidrug-resistant tuberculosis (MDR-TB)).^[4] A drug may be classed as second-line instead of first-line for one of three possible reasons: it may be less effective than the first-line drugs (e.g., *p*-aminosalicylic acid); or, it may have toxic side-effects (e.g., cycloserine); or it may be effective, but unavailable in many developing countries (e.g., fluoroquinolones):

- aminoglycosides (WHO group 2): e.g., amikacin (AMK), kanamycin (KM);
- polypeptides (WHO group 2): e.g., capreomycin, viomycin, enviomycin;
- fluoroquinolones (WHO group 3): e.g., ciprofloxacin (CIP), levofloxacin, moxifloxacin (MXF);
- thioamides (WHO group 4): e.g. ethionamide, prothionamide
- cycloserine (WHO group 4)
- terizidone (WHO group 5)

Third line[edit]

Third-line drugs (WHO group 5) include drugs that may be useful, but have doubtful or unproven efficacy:

- rifabutin
- macrolides: e.g., clarithromycin (CLR);
- linezolid (LZD);
- thioacetazone (T);
- thioridazine;
- arginine;
- vitamin D;
- bedaquiline.

These drugs are listed here either because they are not very effective (e.g., clarithromycin) or because their efficacy has not been proven (e.g., linezolid, R207910). Rifabutin is effective, but is not included on the WHO list because for most developing countries, it is impractically expensive.

V. Discussion

Magnetic resonance imaging is highly sensitive in demonstrating intracranial tuberculous lesions accurately. Conventional MRI with additional techniques like MR spectroscopy and DWI provide an accurate assessment of various intracranial tuberculous lesions and associated complications. Overall tuberculous lesions of brain can be categorised into tuberculomas, tuberculous abscess and meningitis.

Sonmez G et al[5] retrospectively reviewed the data of 17 women and 10 men with age ranging from 14 – 51 years (mean age of 26 years) with intracranial tuberculomas. In our study, most of the cases were between the ages of 11 - 20 yrs. (mean age of 26.6 yrs.) which closely coincides with the study conducted by Sonmez G et al.[5]

Kadriye Yasar et al[6] evaluated the radiological findings of 160 adult patients with tuberculous meningitis (TBM). Tuberculoma (37%), basal meningitis (27%), and hydrocephalus (21%) were the most frequent signs found in the cranial CT or MRI scans. In our study, the most frequent tuberculous lesions encountered in adults in decreasing order of frequency were tuberculomas (81.25%), tubercular meningitis (78.1%) and abscess (6.3%) which closely coincide with the findings given by Kadriye Yasar et al[6] (Fig. 4). In our study, hydrocephalus was included in one of the complications which resulted from tuberculous lesions such as basal meningitis or tuberculomas. The most common complications encountered in adults in decreasing order

of frequency were infarcts (31.25%), obstructive hydrocephalus (25%), cerebritis (9.37%) and ependymitis (6.25%).

VI. Conclusion

MRI plays an important role in the diagnosis of intracranial tuberculosis and its associated complications. It helps in early diagnosis and management of meningitis thereby minimising potential life-threatening complications such as hydrocephalus and meningitis-induced infarcts. MRI also helps in identifying the extent of involvement and differentiating tuberculous lesions from other pathologies. Therefore, MRI should be the investigation of choice in a suspected case of intracranial tuberculosis whenever possible.

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