

## RADIOLOGIC AND CLINICAL FINDINGS IN TUBERCULOUS MENINGITIS

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We aimed to evaluate the radiologic and clinical findings of patients with tuberculous meningitis encountered during a 4-year period, retrospectively. Sixteen patients with tuberculous meningitis were admitted to our hospital. The diagnosis was based on abnormal neurologic symptoms and signs, cerebrospinal fluid findings, negative bacteria culture, and abnormalities on brain-imaging studies. CT and MR examinations were performed in 16 and 9 patients, respectively. A retrospective comparison was done between CT and MR findings. All patients had fever, lethargy, and some of them had cough. Neurologic presentations included increased intracranial pressure, vomiting, seizures, paresis, nuchal rigidity, and disturbance of consciousness. Acid-fast stain of cerebrospinal fluid for tuberculous bacilli was negative for all samples. All bacterial cultures of cerebrospinal fluid yielded no growth, with the exception of one that grew *Mycobacterium tuberculosis*. Radiologic findings compatible with tuberculous meningitis including hydrocephalus, basilar cistern enhancement and infarction was observed more clearly on MR than CT. Early diagnosis in tuberculous meningitis may prevent neurologic damage. Imaging studies is an important part of diagnosis and MR imaging should be performed as a first choice of imaging modalities in patients with tuberculous meningitis.

**Key words:** Tuberculosis, meningitis, computed tomography, magnetic resonance imaging

### INTRODUCTION

Tuberculous meningitis (TBM) is the most life-threatening form of extrapulmonary tuberculosis and the most common presentation of neurotuberculosis. Its presentation is often nonspecific, early recognition of this potentially treatable disease remains a challenge to clinicians; therefore the possible unique presentation could be overlooked. Early diagnosis followed by effective treatment may prevent neurologic damage or a fatal outcome (1,2). Therefore, the most important concern of the clinician is to diagnose and treat TBM as soon as possible.

Computed tomography (CT) has been a diagnostic aid by identifying exudate in the basal cisterns and basal meningeal inflammation on contrast enhanced scans. Its most significant contribution is in the detection and assessment of associated complications such as hydrocephalus, cerebral infarcts and tuberculomas.

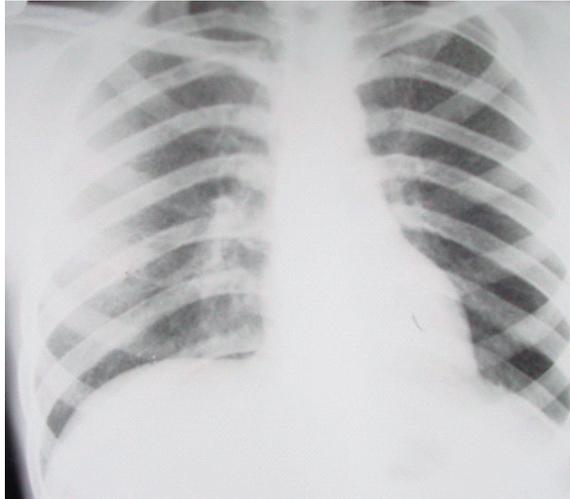
Contrast enhanced magnetic resonance imaging (MRI) is more sensitive than CT for the detection of ischemic changes, edema secondary to inflammation and basal meningeal inflammation (3-5).

In this report, we reviewed the radiologic and clinical findings of 16 patients with TBM encountered during a 4-year period.

### MATERIAL AND METHODS

From July 1999 to December 2003, 16 patients with TBM (median age 22, range 2-45, 8 male) were admitted to the our hospital. The diagnosis of TBM was based on abnormal neurologic symptoms and signs, cerebrospinal fluid abnormalities compatible with TBM, coexisting tuberculous infection in another organ, the response to antituberculous treatment, and negative bacteria culture and abnormalities on brain-imaging studies compatible with TBM either by cranial CT or MRI. Acid-fast stain of cerebrospinal fluid for tuberculous bacilli was negative for all samples. Bacterial cultures of cerebrospinal fluid yielded no growth of *Mycobacterium tuberculosis*. CT examinations were performed in all patients. CT scans before and after intravenously administered contrast medium were obtained with a Hitachi W-450.

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**Figure 1. Chest x-ray demonstrates bilateral miliary lesions**

Slice direction was parallel to the orbito-meatal line and the slice thickness varied between 5 to 10 mm. MR examinations were performed just after the CT examinations.

MR examinations were performed in 9 patients with a 0.3 Tesla Hitachi AIRIS 1. MRI was performed using spin echo sequences with T1-(TR 650/ TE 20) and T2-weighted (TR 4800/TE 117) images in axial, sagittal and coronal planes with a slice thickness varying between 5 and 10 mm. After the intravenous administration of contrast medium (0.1 mmol/kg) T1-weighted images were obtained in the axial and coronal planes.

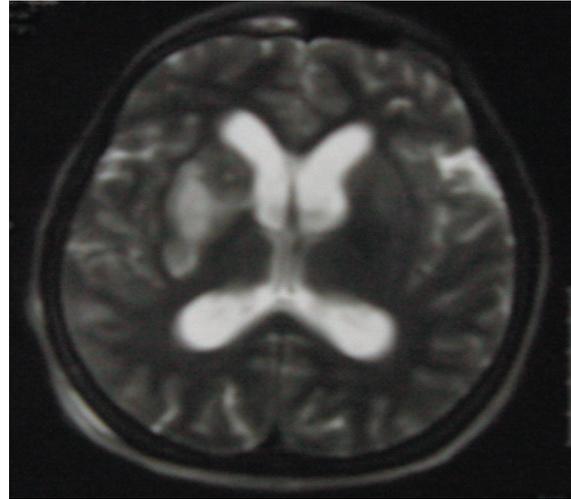
We administered the treatment protocol including isoniazid (12 months), rifampicin (12 months), pyrazinamide (2 months), Streptomycin (2 months) in all our patient.

A retrospective comparison was done between CT and MR findings with attention to identification of parenchymal signal abnormalities including ischemia/infarct, granuloma, abscess, hemorrhage, periventricular edema, abnormal meningeal enhancement, and other associated findings.

## RESULTS

Based on clinical severity at admission the patients were categorized according to previous reports (1,6); stage 1 (n:4), without definite neurologic symptoms; stage 2 (n: 8), with signs of meningeal irritation and focal neurologic signs, although without change of consciousness; stage 3 (n:4), severe impairment of consciousness or delirium, seizures, and serious neurologic signs.

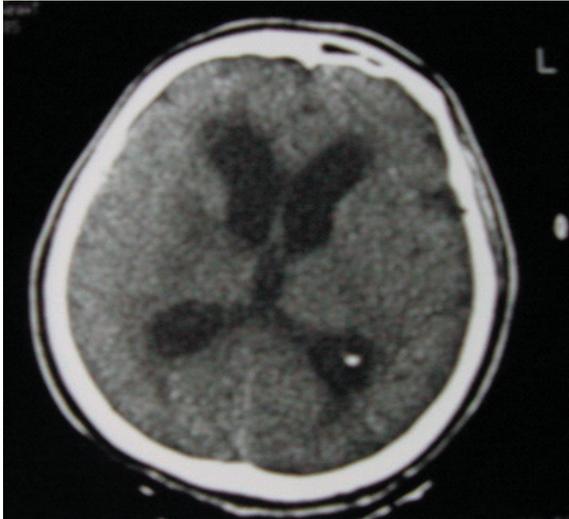
All patients had fever, lethargy, and 4 of them had cough. Only two patients (12.5%) had definite history of tuberculosis contact



**Figure 2. T2-W image demonstrates marked hyperintensity regions suggesting ischemia/infarct are evident in the bilateral basal ganglion regions**

and one patient had miliary pulmonary tuberculosis (Figure 1). Neurologic presentations on admission included increased intracranial pressure, vomiting (70%), seizures (65%), paresis (14%), 3<sup>rd</sup> cranial nerves paralyzes (24%), nuchal rigidity (65%), and disturbance of consciousness (35%). The seizure pattern in 2 patients was generalized tonic-clonic in nature. The ten of sixteen patients (62%) had pleocytosis in cerebrospinal fluid, and the mean white blood cell (leukocyte) count was 222/mm<sup>3</sup>. Only one patient had cell counts greater than 500 cells/mm<sup>3</sup>. Elevated cerebrospinal fluid protein, ranging from 47.5 mg/dL to 990 mg/dL, and low glucose level, ranging from 17 to 49 mg/dL, were revealed in all patients. Acid-fast stain of cerebrospinal fluid for tuberculous bacilli was negative for all samples. All bacterial cultures of cerebrospinal fluid yielded no growth, with the exception of one that grew *Mycobacterium tuberculosis*.

The most of the patients who were examined with MR had abnormal radiologic findings compatible with TBM including hydrocephalus (25%), basillar cistern enhancement (18%), and infarction in the bilateral basal ganglia (43%) (Figures 2). In contrast, the most of the patients who were examined with CT had no abnormal radiologic finding except hydrocephalus (Figure 3). Of 16 patients with TBM, cisternal obliteration and abnormal enhancement were identified in 3 patients on MR and in only one on CT (Figures 4 A,B). In one patient in whom a disparity was seen between CT and MR, CT could not differentiate cisternal enhancement. The most common site of enhancement was



**Figure 3. Enlarged lateral ventricles corresponding hydrocephalus are seen on CT image**

the suprasellar cistern; next were the ambient cistern and sylvian fissure. Curvilinear meningeal enhancement along the convexity surface of brain was noticed in one patient on MR only. Associated granulomas ranging from 2 to 10 mm were readily identified in three patients on MR but in only one on CT (Figures 5 A,B).

The granulomas usually were multiple, nodular shaped and located at the basal cisterns and cortical areas of brain. Some tiny nodules were seen only on MR. These enhancing lesions were demonstrated only on postcontrast T1-W images, and not on precontrast T1-W and T2-W images. Focal parenchymal signal abnormalities suggesting ischemia/infarct were identified in 8 patients on MR and in 2 on CT. These abnormalities

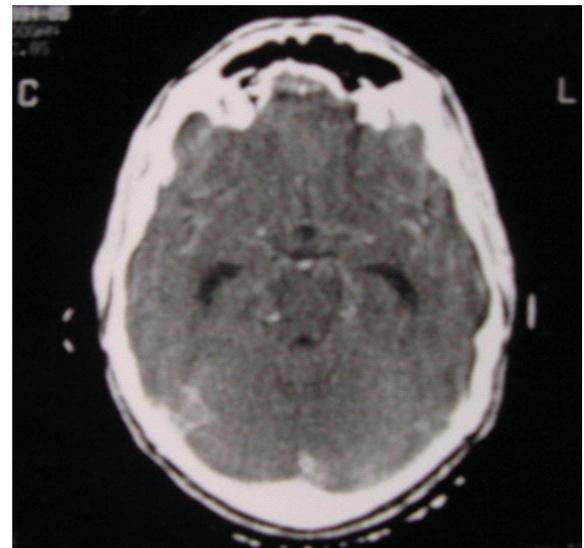
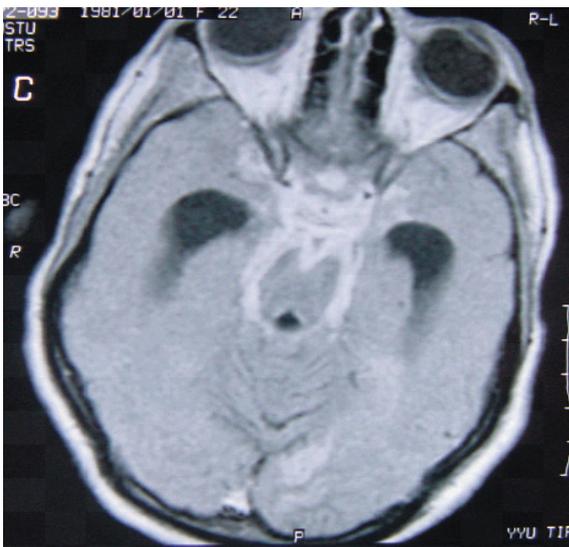
were seen most often in the basal ganglia, and, less often, at the thalamus, midbrain and periventricular white matter. The T2-W and FLAIR (fluid attenuated inversion recovery sequences) sequences were the most sensitive in detecting these lesions (Figure 6).

The hemorrhagic focuses were demonstrated at the subarachnoid spaces in one patient on CT images, but missed on MR (Figure 7). Hydrocephalus of varying degrees was identified in 4 patients on both CT and MR. Periventricular and basal ganglia edema was demonstrated clearly in 8 of the 16 patients on T2-W images but in only five on T1-W images and one on CT.

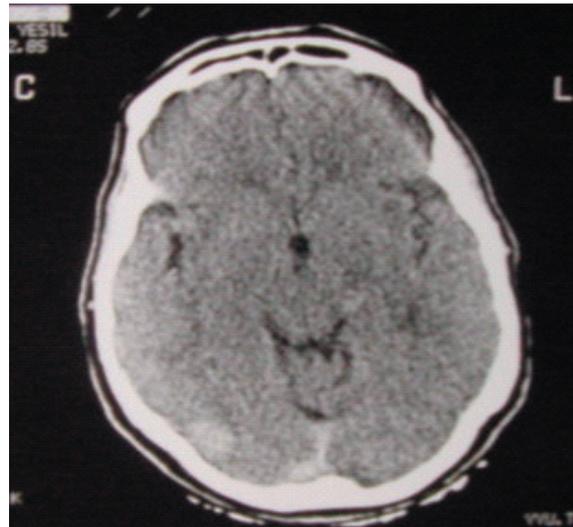
**DISCUSSION**

Tuberculous involvement of the central nervous system continues to be significant health problem in many underdeveloped countries. Infection with *Mycobacterium tuberculosis* begins with inhalation of *M.tuberculosis* bacilli, which then spreads through the lymphohematogenous system to the brain and meninges. The tuberculous bacilli are then discharged from these foci directly into the subarachnoid space to cause meningitis. The mycobacteria are deposited in the cerebral tissue where they incite a granulomatous reaction. The granulomas may remain asymptomatic or rupture into the subarachnoid space and leading to the formation of gelatinous exudate at predominantly the basal cisterns (1,2), as seen in our three patients.

Cough and fever are common symptoms in patients (4). All patients in this study had fever and cough.



**Figure 4 A-B. Basal cistern enhancement is seen more prominent on contrast enhanced T1-W image (A) than Contrast enhanced CT (B)**



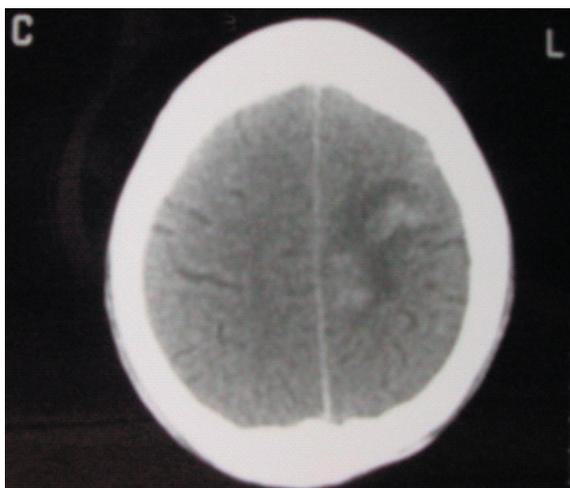
**Figure 5 A-B. Contrast enhanced MR (A) and CT (B) image shows smooth and round lesion at the right occipital lobe. Note strong contrast enhancement.**

However, chest radiography revealed abnormal findings in only two patients (12.5%), including miliary tuberculosis, hilar lymphadenopathy, and right-sided pulmonary consolidation.

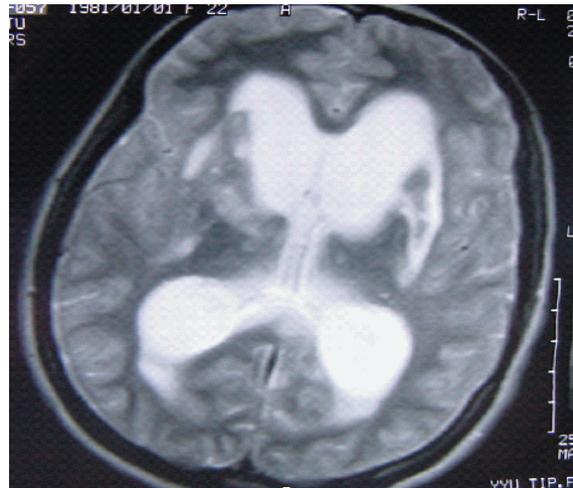
The neurologic symptoms and signs in patients with TBM included drowsiness, meningeal irritation, cranial nerve paresis, seizures, hemiparesis, consciousness alternation, and coma (7). In our patients the most prominent sign was meningeal irritation signs in older patients and bulging anterior fontanel because of increased intracranial pressure in younger patients. Vomiting was also evident in all patients. Seizures are less often observed in adults than children and elderly people. The purified protein derivative test still plays a role in the early diagnosis of TBM, even in infant patients.

The purified protein derivative test is routinely used as one of the criteria for the diagnosis of tuberculosis (8). Six of our patients (37.5%) had positive purified protein derivative tests to 1 tuberculin unit.

Although there has been a warning of herniation precipitated by lumbar puncture, lumbar puncture carries no risk of herniation in the absence of hemiparesis or papilledema whether cerebrospinal fluid pressure is raised or not (8). Therefore we suggest that if brain imaging reveals no evidence of abscess, subdural empyema, or brain infarct, lumbar puncture can be performed safely in clinically suspected TBM patients. We observed no any complications related with lumbar puncture in all patients. The cerebrospinal fluid findings in TBM often demonstrate reduced glucose concentration, increased protein level,



**Figure 6. Acute subarachnoid hemorrhage is seen as a high density areas in the left hemispheric sulcus. Note hypodensity areas just near the hemorrhage corresponding edema.**



**Figure 7. T2-W axial image demonstrates prominent hyperintensity signals suggesting ischemia/infarct at the bilateral basal ganglia.**

and elevated leukocyte counts. However, cerebrospinal fluid seldom contains more than 500 cells/mm<sup>3</sup>, and most cells are lymphocytes (9). In this study, 8 patients had cell counts of less than 500/mm<sup>3</sup> with lymphocytic predominance. However, it should be borne in mind that initial negative results or atypical cerebrospinal fluid findings have also been reported (10).

The culture of *Mycobacterium tuberculosis* from the cerebrospinal fluid is the gold standard of diagnosis. The search for acid-fast bacilli is the most crucial part of the diagnosis. The reported probability of acid-fast bacilli observed in cerebrospinal fluid smears ranged between 10% and 87% (11). Unfortunately, none of our patients had positive finding.

The findings of brain imaging in TBM include hydrocephalus, basilar enhancement, and infarcts, among which the most common abnormality is hydrocephalus (3-5). Waecker et al. (12) reported that all of the 30 TBM patients in their study had hydrocephalus detected by CT. Hydrocephalus has been detected in 12% of adults with TBM. In 4 of 16 patients (25%), hydrocephalus was detected by CT or MR. The basal meningeal enhancement is the second most common finding in CT, which is usually associated with a poor prognosis. In our study patients, basal meningeal enhancement was detected in three patients on MR and only one patient on CT.

Cerebral infarction occurs in 38% of patients with TBM. The meningeal inflammatory exudate involves the adventitia, progressively spreads to the entire vessel wall, and leads to necrotizing panarteritis with secondary thrombosis and occlusion (10). The perforating vessels at the base of the brain, particularly at the origin of the lenticulostriate arteries, are predominantly involved.

Most of the exudate is usually produced within the subarachnoid cisterns, thus accounting for the basal ganglia infarction (3). The infarcted areas were demonstrated as hyperintensity regions on T2-W images and hypointensity on T1-W images. These findings were more evident on T2-W images than T1-W images. In addition MR images are more sensitive than CT in the detection of inflammatory and infarcted areas. In our patients, we detected hyperintensity signal regions compatible with ischemia/infarct on MR in 7 patients which were missed on CT. In addition, focal parenchymal signal

abnormalities suggesting ischemia/infarct in 8 patients were identified on MR but six of them were missed on CT.

In conclusion, our results indicate that although precontrast T2-W images were most sensitive in delineating ischemia/infarct and edema, there were not as specific as Gd-DTPA-enhanced T1-W images in defining the diffuse active inflammatory process of the meninges and basal cistern. T1-W images showed the ischemia/infarct and edema as a subtle low-intensity signal. However, precontrast T1-W imaging is necessary because it helps in detection of subacute hemorrhage. Therefore both precontrast T1 and T2-W imaging and post-contrast T1-W imaging are considered necessary in the evaluation of the patient with suspected meningitis. All the possible abnormalities including pericranial lesions (paranasal sinusitis and otitis media), meningeal inflammation, hydrocephalus, ischemia/infarct, tuberculoma, abscess and surrounding edema can be identified more clearly on MR than CT. We concluded that MR imaging should be performed as a first choice of imaging modality in patients with suspected TBM.

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