Neurological manifestations in tuberculosis

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Abstract: Central nervous system (CNS) tuberculosis (TB) is a potentially life threatening condition which is curable if the correct diagnosis is made in the early stages. Its clinical and radiologic manifestations may mimic other infectious and noninfectious neurological conditions. Hence, familiarity with the imaging presentations of various forms of CNS tuberculosis is essential in timely diagnosis, and thereby reducing the morbidity and mortality of this disease. Early diagnosis of CNS TB is necessary for appropriate treatment and subsequently decreases the morbidity and mortality associated with the disease. Routine diagnostic techniques involve culture and immunological tests of the tissue and biofluids, which are time-consuming and may delay definitive management. Noninvasive imaging modalities such as computed tomography (CT) scan and magnetic resonance imaging (MRI) are routinely used in the diagnosis of neurotuberculosis, with MRI offering greater inherent sensitivity and specificity than CT scan. The purpose of our study was to describe the imaging characteristics of the different forms of CNS tuberculosis, including meningitis, tuberculoma, miliary tuberculosis, abscess, cerebritis, and encephalopathy.

Index terms- TB: tuberculosis, CT: Computed Tomography, MRI: Magnetic Resonance Imaging, CNS: Central Nervous System.

AIMS :

To demonstrate the usefulness of cranial magnetic resonance imaging (MRI) and computed tomography **(**CT**)** in the evaluation of the tuberculosis infected patients presenting with the neurological symptoms.

Objective:

1.To describe the pattern of the cranial magnetic resonance and computed tomography imaging findings in tuberculosis infected patients presenting with neurological symptoms.

2.Correlation between neurological symptoms and cranial MRI and CT findings.

Material and Methods

The study was carried out on 50 patients who were TB positive and had Central nervous system complaints MRI and CT were performed on all the patients included in the study and the findings were compared. Relevant history of illness and significant clinical findings of all patients were recorded previous investigations were reviewed while performing MRI and CT, in selective patients sedative were used under the supervision of the anaesthetist. All patients were seen by appointments, except for emergency cases.

Inclusion criteria:

All patients diagnosed of TB with neurological symptoms were included in this study.

MRI was performed with 1.5 Tesla and 3 Tesla MR scanner using dedicated head coil. Conventional MR imaging was performed by taking T1W, T2W, T2WI TR and FLAIR sequences in axial, sagittal and coronal planes. Post gadolinium (dose 0.1 mmol/kg) enhanced MRI was performed in axial, coronal and sagittal planes in selected cases depending on findings on non contrast study or clinical suspicion. When required, DWI study and MR spectroscopy was performed by using point resolved spectroscopy.

Exclusion Criteria: Patients who were allergic to contrast media, those who had contra indications for MRI and those who were not willing were excluded from the study.

Risk involved: Adverse drug reaction due to contrast agent (gadolinium) used in MRI.

Introduction

Mycobacteria are small rod shaped acid fast bacilli with more than 125 species. Most TB is caused by mycobacterium tuberculosis. It causes more than 98 % of the CNS tuberculosis. Less common species that are also considered part of the M. tuberculosis complex include M. africanum, M. microti, M. canetti and M. bovis.

Tuberculosis has resurged and remained a major worldwide health problem. Although Mycobacterium tuberculosis can involve any organ, most commonly the lung, central nervous system (CNS) tuberculosis is the most devastating form of the disease. Approximately 5–10% of all patients with tuberculosis and up to 20% of patients with AIDS-related tuberculosis have CNS involvement.

CNS tuberculosis usually results from hematogenous spread, while direct spread from intra- or extracranial focus is rare [4]. The clinical and radiologic manifestations of CNS tuberculosis may mimic other infectious and noninfectious neurological conditions. Therefore, familiarity of infectious diseases specialists with the imaging presentations of CNS tuberculosis is essential for prompt and accurate diagnosis of this

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entity. Herein, we describe the different forms of CNS tuberculosis including meningitis, cerebritis, cerebral abscesses, tuberculomas, miliary tuberculosis, and spinal or calvarial involvement.

Tuberculous Meningitis

Tuberculous meningitis (TBM) is the most common cause of chronic meningitis, especially in developing countries. Meningitis is the most common manifestation of CNS tuberculosis which is most frequently seen in the children and adolescents. Tuberculous meningitis is mostly due to the hematogenous spread of Mycobacterium tuberculosis. There can be spread secondary to the extension or rupture of subpial or subependymal focus (also known as Rich Focus). Tuberculous meningitis often has an insidious course with a nonspecific clinical presentation in early stages, especially in children. Therefore, the imaging plays a key role in the timely diagnosis and decreasing the morbidity and mortality.

TB meningitis has a striking predilection for the basal cisterns although exudates in the superficial convexity sulci do occur. Enhancing exudate in the basal cisterns is the most common and also a relatively specific manifestation of leptomeningeal tuberculosis on computed tomography (CT) and magnetic resonance (MR) images. Meningeal enhancement has been found in up to 90% of cases and is considered to be the most sensitive feature of tubercular meningitis. The subpial exudate is primarily located in the inferomedial surface of the frontal lobes, the anteromedial surface of the temporal lobes, the superior aspect of the cerebellum, and the floor of the third ventricle. Extension to suprasellar, interpeduncular, and pontomesencephalic cisterns may also occur from these primary sites. In most cases, some degree of meningeal involvement is seen within the sulci over the cerebral convexities, the sylvian fissures, and also the ependymal surfaces of the ventricles; the latter usually occurs in the later stages of the disease.

CT findings**:** CT can be normal in early stages. On CT images, the obliteration of the basal cisterns by isodense or mildly hyperdense exudates is the most common finding in tuberculous meningitis. “Blurred “ ventricular margins may be seen.

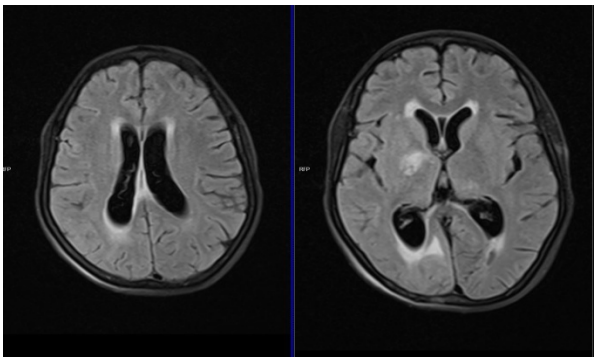
MR findings: The findings are better appreciated on MR imaging than on CT, especially on postcontrast MR images which show the enhancing cisternal exudates and leptomeningeal enhancement. Basilar exudates are isointense with brain on T1WI giving the appearance of “dirty” CSF. FLAIR scans show increased signal intensity in the sulci and cisterns. Marked linear or nodular meningeal enhancement is seen on T1 C + FS sequences. Focal or diffuse dura- arachnoid enhancement (pachymeningeal) with or without involvement of the underlying subarachnoid spaces may occur but is uncommon. Parmar et al. demonstrated that postcontrast fluid attenuation inversion recovery (FLAIR) images may have a higher specificity compared to contrast-enhanced T1-weighted images in detection of leptomeningeal enhancement. Magnetization transfer spin echo imaging following contrast injection is superior to the conventional postcontrast imaging in demonstrating meningeal inflammation. In later stages, there may be widening of subarachnoid spaces.

A similar pattern of meningeal enhancement may be seen in other infective meningitis, inflammatory diseases such as rheumatoid arthritis, sarcoidosis, or carcinomatous meningitis.

Carcinomatous meningitis is usually seen in older patients with a known systemic or primary CNS neoplasm. In neurosarcoidosis, infiltration of the pituitary gland, infundibulum and hypothalamus is common.

Other radiologic manifestations of tuberculous meningitis may be related to its possible complications, including progressive hydrocephalus, vasculitis, infarction, and cranial neuropathies.

Hydrocephalus: Hydrocephalus is the most common complication encountered in TBM and can be broadly divided into two types: (1) communicating type, which is common, secondary to an obstruction of the basal cisterns by inflammatory exudates and (2) obstructive type, which is less common and either secondary to a focal parenchymal lesion (tuberculoma or a brain abscess) causing mass effect or due to the entrapment of a part of the ventricle by granulomatous ependymitis.



T2W FLAIR axial images in the same patient showing hydrocephalus.

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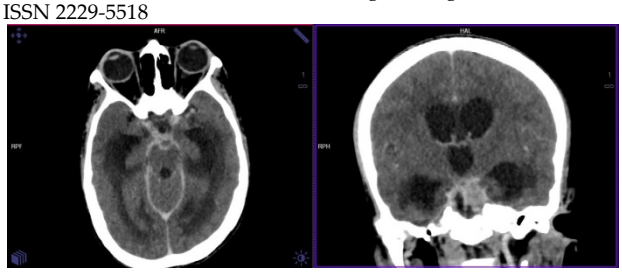

CT brain axial and coronal plain and delayed c + images showing tuberculomas in the left cerebellar hemisphere and in the midbrain with enhancing basilar exudates and communicating hydrocephalus.

Vasculitis: It is a complication that is commonly seen at autopsy in cranial TBM. The adventitial layer of small and medium-sized vessels develops changes similar to those of the adjacent tuberculous exudates. The intima of the vessels may eventually be affected or eroded by fibrinoid–hyaline degeneration. In later stages, the lumen of the vessel may get completely occluded by reactive subendothelial cellular proliferation. Ischemic cerebral infarction resulting from the vascular occlusion is a common sequelae of tuberculous arteritis. Ischemic infarct is also a common complication, being detected in 20–41**%** of patients on CT, mostly within the basal ganglia or internal capsule regions and resulting from vascular compression and occlusion of small perforating vessels **(**necrotizing arteritis**),** particularly the lenticulostriate and thalamoperforating arteries, vessels which perfuse the so-called medial tuberculosis zone**.**

Tuberculous meningitis may also cause dural venous sinus thrombosis with resultant hemorrhagic infarct. Rarely, tuberculosis may present as isolated dural venous sinus thrombosis without any evidence of meningitis or its complications.

Cranial nerve involvement is associated with high morbidity and disability in meningitis patients. Cranial nerve involvement occurs due to vascular compromise, ischemia, or nerve entrapment in the basal exudates in 17–40% of cases, most commonly affecting the second, third, fourth, and seventh cranial nerves. The affected cranial nerves are best evaluated by MRI, where they may appear thickened, especially in their proximal segments, with high signal intensity on T2-weighted images and marked enhancement on postcontrast images.

Parenchymal Tuberculosis

Parenchymal disease may be isolated or associated with tuberculous meningitis. Parenchymal involvement usually presents as tuberculoma. It can also manifest as cerebritis, cerebral abscess, miliary tuberculosis, or tuberculosis encephalopathy.

Cerebritis and Cerebral Abscess

Parenchymal tuberculosis may occur with or without accompanying meningitis. Tuberculosis cerebritis or abscess may have an appearance similar to that of pyogenic bacterial infection on neuroimaging studies.

Focal tuberculous cerebritis is very rare,cerebritis is a term that represents inflammation of the brain in the setting of infection before the development od abscess.

CT : Hypoattenuation due to edema is seen. Small areas of hemorrhage can sometimes be seen. Faint heterogenous contrast enhancement can be seen.

MRI: T1 iso to hypointensity , T2 hyperintensity, and minimal post contrast enhancement on T1 C + images is seen. Patchy restricted diffusion is seen.

Tuberculous pseudo-abscess is rare and is characterized by a central area of liquefaction with pus. It may be solitary or multiple and is frequently multiloculated. Tuberculous abscess is different from tuberculomas which contain central caseation and liquefaction mimicking pus.

On CT : Tb pseudoabscesses are hypodense on NECT with significant mass effect and surrounding edema. Ring enhancement is seen on CECT.

On MRI: Unlike tuberculomas, Tb pseudoabscesses are usually hyperintense to brain on T2/FLAIR images and restrict on DWI. A ring enhancing multi-loculated lesion or multiple separate lesions is the typical finding on T1 C + images. MRS shows lipid and lactate peaks without evidence of cytosolic amino-acids.

TB pseudoabscesses appear identical to pyogenic abscesses on standard imaging studies. Both show restricted diffusion. On MR spectroscopy, the peak of amino acids, which is the spectral hallmark in pyogenic abscess, is not usually seen in tuberculous pseudoabscess.

Magnetization transfer (MT) images improve the conspicuity of all CNS tuberculosis lesions.

Tuberculoma

Tuberculoma is the most common parenchymal lesion in CNS tuberculosis which could be found in any portion of the intracranial space. The lesion may be solitary or multiple and may be seen with or without meningitis. Histologically, the mature tuberculoma is composed of a necrotic caseous center surrounded by a capsule that contains fibroblasts, epithelioid cells, Langhans giant cells, and lymphocytes.

On CT : NECT scans show one or more iso to slightly hyperdense round, lobulated or crenated masses with variable perilesional edema. Calcification can be seen in

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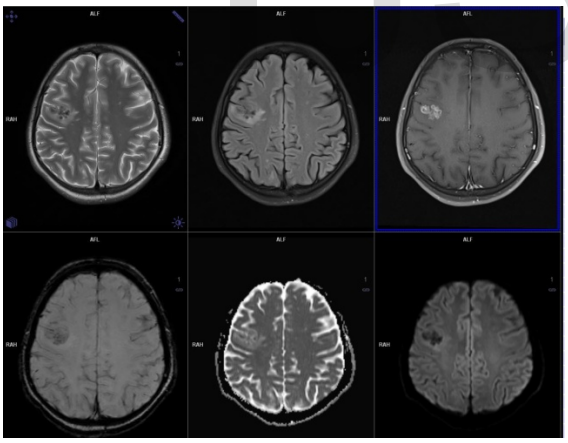
healed granulomas. CECT scans demonstrate punctate, solid or ring like enhancement.

MRI: Most TB granulomas are solid caseating lesions that appear hypo or isointense with brain on T1WI and hypointense on T2WI. Liquefied areas may be T2 hyperintense with a hypointense rim. Enhancement is variable ranging from small punctate foci to multiple rim enhancing lesions. Mild to moderate round or lobulated ring like enhancement around a non enhancing center is the most typical pattern. pMR shows elevated rCBV in the cellular, hypervascular enhancing rim. Solid caseating tuberculomas do not restrict on DWI although liquefied foci may restrict. MRS is helpful in characterizing tuberculomas and distinguishing them from neoplasm or pyogenic abscess. A prominent decrease in the NAA : Cr with a modest decrease in the NAA : Cho is typical. A large lipid peak with absence of other metabolites such as amino acids and succinate is seen in 85-90 % of the cases.

The major differential for multiple parenchymal tuberculomas is seen is neurocysticercosis (NCC). NCC usually shows multiple lesions in different stages of evolution. Tuberculomas can also resemble pyogenic abscesses or neoplasms. Abscesses restrict on DWI. Tuberculomas have a large lipid peak on MRS and lack the elevated Cho typical of neoplasm.



T2W axial, T2W FLAIR axial, T1W C +,SWI, ADC and DWI images showing tuberculomas in the right frontal lobe.

Follow-up CT or MR studies are useful in monitoring the response to medical treatment. Paradoxical enlargement of a preexisting tuberculoma or evolution of a new intracranial and spinal tuberculoma in patients receiving adequate treatment may be occasionally seen. However, with continuation of antituberculous therapy, eventual resolution of the tuberculoma usually occurs.

Sometimes, healed tuberculomas appear as calcified foci on nonenhanced CT. Similarly, calcification in the basal cisterns has been demonstrated a few years after meningeal tuberculosis.

Miliary Tuberculosis

Miliary tuberculosis is seen mostly in severely immunocompromised patients and is usually associated with meningeal involvement or extracranial primary sites. Since the dissemination is hematogenous, the lesions are usually located at the corticomedullary junctions. The lesions are tiny (2-3 mm in diameter) scattered lesions that may be invisible on non contrast MR sequences In visible lesions, MRI shows small lesions that are hypointense on T2-weighted sequences. These lesions occasionally can be seen as small hypodensities on CT scan.

Postcontrst T1-weighted MR images show numerous, round, small, homogeneous, enhancing (usually ring enhancement) lesions. Invisible lesions that may or may not enhance after intravenous injection of gadolinium can be clearly visible on magnetization transfer spin echo T1-weighted imaging with or without contrast.

Tuberculous Encephalopathy

Tuberculous encephalopathy typically occurs in young children who may present with convulsion, stupor, and coma with no signs of meningeal irritation or focal neurological deficit. Neuroimaging studies show severe cerebral edema, which may be unilateral or bilateral. Myelin loss in the white matter may result in hypodensity on CT images and hyperintensity on T2-weighted MR images.

Miscellaneous Forms of CNS Tuberculosis

Osseous and nonosseous spinal/spinal cord tuberculosis, subdural/epidural abscess, and calvarial tuberculosis are other forms of tuberculosis that may involve CNS with direct or indirect pathways.

Tuberculous spinal meningitis presents on MR imaging as a CSF loculation and obliteration of the spinal subarachnoid space, with loss of the outline of the spinal cord in the cervicothoracic spine and matting of the nerve roots in the lumbar region. Contrast-enhanced imaging reveals nodular, thick, linear intradural enhancement, which may completely fill the subarachnoid spaces.

Longstanding arachnoiditis may result in the development of syringomyelia (spinal cord cavitation) that typically demonstrates CSF signal intensity on all MR sequences.

Tuberculous spondylitis results from hematogenous spread of infection to the vertebral body via paravertebral venous plexus of Batson. Typical presentation is involvement of multiple vertebral bodies

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with sparing of intervertebral disc in early stage and disc involvement in later stages. Paraspinal extension and resultant paravertebral abscess (Pott's abscess) as well as subdural/epidural abscess formation with associated spinal cord compression are other common findings.

Intracranial subdural or epidural abscess formation may or may not be associated with a primary CNS tuberculous focus and have imaging findings identical to that of other pyogenic abscesses, that is, iso- to hypointensity on T1-weighted images, hyper- or mixed signal intensity on T2-weighted images, and rim enhancement on postcontrast images.

Statistical Analysis

The final diagnosis was made after considering clinical features, and radiological findings.

Presenting symptoms in cases of TB with neurological complications

Fever	30
Altered sensorium	44
Headache	15
Convulsion	40
Stroke	9
Vomiting	5

Comparative evaluation of radiological diagnosis in TB infection

	% in our study
Meningitis	30
Tuberculomas	21
Hydrocephalous	14
Vasculitis	12
Cerebritis and cerebral asbcess	10
Military tuberculosis	8
Tuberculous encephalopathy	5

Conclusion:

CNS tuberculosis has various imaging appearances, including meningitis, tuberculoma, miliary tuberculosis, abscess, cerebritis, and encephalopathy. In addition, the radiologic manifestations of this disease are not always typical and sometimes may be mistaken with other lesions. CT and MRI are both excellent means of detection of cerebral lesion in AIDS patients useful in initial diagnosis and in therapeutic follow up evaluation. MRI has a higher sensitivity. Familiarity with the various imaging presentations of CNS tuberculosis is of key importance for the radiologists and infectious diseases specialists in timely diagnosis, thereby reducing the morbidity and mortality of this potentially life threatening disease.

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