Central Nervous System Tuberculosis

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Approximately one-third of the world’s population is currently infected with tuberculous bacillus, of which approximately 5% to 10% become sick or infectious at some time during their life. People with human immunodeficiency virus (HIV) are more likely to develop tuberculosis (TB). The World Health Organization (WHO) estimates that there were 9.4 million new cases in 2009, including 1.1 million cases among people with HIV. Approximately 1.7 million people died of TB, including 380,000 people with HIV. Most cases were in the south-east Asian, African, and western Pacific regions (35%, 30%, and 13%, respectively). In 2009, the estimated per capita TB incidence was stable or decreasing in all 6 WHO regions. However, the slow decline in incidence rates per capita is offset by population growth. Consequently, the number of new cases arising each year is still increasing globally in the WHO regions of Africa, the eastern Mediterranean, and south-east Asia.

Neurotuberculosis constitutes 1% of all tuberculosis and 10% to 15% of the extrapulmonary tuberculosis cases, most (>40%) of which are children. Central nervous system (CNS) tuberculosis also accounts for 1.5% to 3.2% of all tuberculosis-related deaths. CNS tuberculosis remains common and, despite the availability of effective antituberculous therapy, continues to cause significant morbidity and mortality. TBM constitutes 70% to 80% of all patients with neurotuberculosis. CNS tuberculosis is a prominent

Key Points: CNS Tuberculosis

- Central nervous system (CNS) tuberculosis is a major cause of sickness and death, especially in developing countries, and is increasing in developed countries because of the emergence of acquired immunodeficiency syndrome (AIDS).
- Isolation of Mycobacterium tuberculosis for the definitive diagnosis is possible only in a few patients. Culture has a low yield and needs 6 to 8 weeks.
- In tuberculous meningitis (TBM), precontrast magnetization transfer (MT) T1 imaging shows abnormal meninges with low MT ratio and is characteristic of the disease.
- Tuberculomas have solid and/or liquid caseation on noncontrast MT T1 images, a bright rim around T2 hypointensity is a characteristic feature of tuberculoma; the T2 hypointense rim appears bright in tuberculous abscess.
- When liquefaction of the caseation occurs within tuberculoma as well as abscess, it shows restriction on diffusion-weighted (DW) imaging with low apparent diffusion coefficient (ADC).
- Advanced imaging methods such as perfusion imaging and diffusion tensor imaging (DTI) may be of value in objective assessment of therapy in tuberculoma.
cause of sickness and death in developing countries. In developed countries, there has been an increase in the number of CNS TB cases, possibly related to the pandemic of AIDS. M tuberculosis is responsible for almost all cases of tubercular infection in CNS. Tubercular bacilli initiate a granulomatous inflammatory reaction involving different tissue types of the CNS such as meninges, brain, spinal cord, and covering bones. The CNS manifestation is in a variety of forms, such as TBM and its complications, focal cerebritis, tuberculoma, and tubercular abscess. Spinal cord infection is less common and causes either arachnoiditis and/or intramedullary tuberculomas.

Early diagnosis and treatment of CNS tuberculosis is necessary to reduce the morbidity and mortality. Noninvasive imaging modalities such as computed tomography (CT) and magnetic resonance (MR) imaging are routinely used in the diagnosis of CNS TB; however, MR imaging is preferred because it offers greater inherent sensitivity and specificity than CT. This article reviews the various forms of CNS tuberculosis, including its complications and imaging features.

PATHOPHYSIOLOGY

TBM

Tuberculosis is most often a primary infection in children and a postprimary infection in adults. CNS tuberculosis transpires hematogenously from a distant active site such as lung, bone, lymph nodes, or gastrointestinal or genitourinary tract. In the brain, the bacilli lodge in the cortical and subcortical regions and/or meninges, which are richly vascularized. Rarely, there is a direct spread from adjacent infected paranasal sinuses or mastoid air cells. Infection typically begins in a subpial or subependymal cortical location called the Rich focus. The site of this focus determines the type of CNS involvement. Initially, a nonspecific inflammatory reaction, tuberculous cerebritis, develops. Once sensitized, the inflammatory response results in a granuloma. This granuloma may erode into the subarachnoid space and cerebrospinal fluid (CSF), causing basal leptomenigitis. Subsequently, this leads to communicating hydrocephalus, and occasionally obstructive hydrocephalus caused by obstruction of the foramina of Luschka and Magendie. Vasculitis involving the lenticulostriate and thalamoperforating arteries may occur. The adventitial layer of these vessels develop changes similar to those of the adjacent tuberculous exudates followed by the intima, which may eventually be involved or be eroded by a fibrinoid-hyaline degeneration. In later stages, the lumen of the vessel may become completely occluded by reactive subendothelial cellular proliferation and cause small infarcts in the deep gray matter nuclei and deep white matter.

Tuberculoma

The initial lesion, a tubercle, consists of a central area of incipient or frank necrosis surrounded by inflammatory cells, lymphocytes, epithelioid and Langhans giant cells, with an encircling rich vascular zone. These lesions begin as a conglomerate of microgranulomata that join to form a noncaseating tuberculoma. Following the initial infection, most such lesions resolve and reactivation or further evolution of these lesions manifests as caseation within the center of this tuberculoma. Rarely, the lesion may continue to grow by successive addition of layers of granulation tissue and form growth rings.

Subsequently, central caseous necrosis develops in most cases, which is initially solid surrounded by a capsule comprising collagenous tissue, epithelioid cells, multinucleated giant cells, and mononuclear inflammatory cells. The central core of solid caseation consists of a cheesy material high in lipid contents, with macrophage infiltration, regional fibrosis/gliosis, macrophage by-products (free radicals), and perilesional cellular infiltrates. A few bacilli may be present in the center. The caseation then usually liquefies, beginning from the center. The capsule consists of granulation tissue and compressed glial tissue. If abscess formation occurs, this shows central caviation with chronic inflammatory reaction with fibrosis in the wall and the aspirate from the pus stains positive for acid-fast bacilli. All these lesions are usually accompanied by perilesional edema with some proliferation of astrocytes in the surrounding brain parenchyma.

Spine

M tuberculosis infection in the spine can involve any compartment in the spinal region: vertebrae, intervertebral disk, spinal cord, and its meninges. Meningeal involvement causes spinal meningitis and spinal arachnoiditis. The pathophysiology of spinal meningitis is the same as described earlier in TBM: during primary infection a submeningeal tubercle forms that ruptures into the subarachnoid space. It causes granulomatous inflammation, areas of caseation, and tubercles, with development of fibrous tissue in chronic or treated cases.

CLINICAL FEATURES

Children and older persons are more vulnerable to develop CNS tuberculosis because their immune
systems are less robust. TBM is also common in immune-suppressed patients (those with HIV or diabetes, and patients taking steroids or cytotoxic drugs). The onset of TBM is insidious and may be characterized by persistent low-grade fever, malaise, headache, and confusion. Typical clinical features of TBM include fever with nausea, vomiting, headache, neck stiffness, and photophobia. Cranial nerve palsies, especially of third, fourth, and sixth nerves, may also be present. The intracranial tuberculosis manifest with features of a space-occupying lesion of the brain and the patients can present with features of increased intracranial tension, focal or generalized seizures, and focal neurologic deficit. Isolation of M tuberculosis for the definitive diagnosis from the tissue on smear or culture is possible only in a few patients. Culture takes 6 to 8 weeks for the result and has a low yield. Thus the index of suspicion is mostly indirect; that is, concomitant tubercular involvement elsewhere (only 10% of cases may show disease elsewhere in the body), malaise, low-grade fever, loss of weight, positive tuberculin test, increased sedimentation rate, history of contact, and so forth.

CSF analysis in TBM normally shows a lymphocytic pleocytosis, increased CSF protein level, and decreased CSF sugar concentration. CSF culture for acid-fast bacilli and CSF polymerase chain reaction (PCR) examination are confirmatory tests for the diagnosis of TBM. The sensitivity of CSF culture for detection of acid-fast bacilli has been reported to be approximately 50%. CSF PCR examination is a new technique, and is more sensitive than the combination of microscopic examination and culture for M tuberculosis.

**IMAGING**

Imaging features of tubercular infections of the CNS, which may involve the meninges, brain, spinal cord, bones covering the brain and spinal cord, are as follows.

**Imaging Protocol**

The MR imaging protocol for CNS tuberculosis includes T2, T1, fluid-attenuating inversion recovery (FLAIR), magnetization transfer (MT) T1, susceptibility-weighted, DW imaging, and postcontrast T1-weighted images. In addition, inclusion of 1H MR spectroscopy for lesions more than 2 cm is helpful. The closest differential diagnosis of brain tuberculomas is neurocysticercosis (NCC) in the regions endemic for NCC. If lesions around 2 cm appear hyperintense on T2-weighted imaging and showing ring enhancement on postcontrast T1-weighted imaging, isotropic fast imaging excitation with steady state acquisition (FIESTA) should also be performed to show the scolex within a cyst, which is pathognomonic of NCC.

**Cranial Tuberculosis**

**TBM**

TBM is still a common problem in some parts of the world. The meninges are involved either by hematogenous seeding or by local spread from adjoining infected areas.

During the early stages of disease, conventional noncontrast MR imaging studies usually show little or no evidence of any meningeal abnormality. MT T1 imaging is considered superior to conventional spin-echo sequences for imaging the abnormal meninges, which are seen as hyperintense on pre-contrast T1-weighted MT images. As the disease progresses, mild shortening of T1 and T2 relaxation times may be seen compared with normal CSF. Postcontrast T1-weighted images show abnormal meningeal enhancement (Figs. 1–3). The common sites are interpeduncular fossa, pontine cistern, perimesencephalic cistern, suprasellar cistern, and sylvian fissures, with occasional involvement of sulci over the convexities (see Fig. 1).

MT ratio (MTR) quantification helps in identifying the cause of chronic meningitis; low MTR suggests TBM. Ex vivo MR spectroscopy of the CSF shows lactate, acetate, and sugar signals along with cyclopropyl rings (−0.5 to +0.5 ppm) and phenolic glycolipids (7.1 and 7.4 ppm), which are not seen in pyogenic meningitis. The combination of ex vivo MR spectroscopy with MT MR imaging may be helpful in diagnosing TBM.

The secondary complications of TBM may develop as the disease progresses or even while the patient is on treatment. The sequelae associated with TBM are as follows.

**Hydrocephalus** Hydrocephalus develops commonly as a result of blockage of the basal cisterns by the inflammatory exudates (communicating type) (see Fig. 2), or occasionally due to mass effect of a focal parenchymal lesion or entrapment of the ventricle by granulomatous ependymitis (obstructive type). Perventricular hyperintensity on T2-weighted or FLAIR images usually suggests seepage of the CSF fluid across the white matter. Atrophy of brain parenchyma may be a late sequela of chronic hydrocephalus. The choroid plexus may serve as an entry point for the pathogens into the CNS. Its involvement, choroid plexitis, presents as prominent contrast enhancement of the choroid plexus and is usually associated with ependymitis, ventriculitis, and meningitis.
Fig. 1. TBM without hydrocephalus in a young patient. T2 (A, E) and T1 (B) images at the level of the frontal horn and at the level of the quadrigeminal cistern are unremarkable. MT T1 images at the corresponding levels show bright meninges (C, F) that enhance diffusely on postcontrast T1 images (D) and (G).

Fig. 2. TBM with hydrocephalus. Axial T2-weighted (A) and T1-weighted (B) images show hydrocephalus. Note the hyperintense lesion in the left anterior temporal lobe (arrow), which is hypointense on the T1-weighted image. Precontrast MT T1 image (C) shows hyperintensity around the pons as well as tuberculomas (small arrow) that show enhancement on postcontrast T1-weighted images (D). ADC map shows low ADC in the left anterior temporal lobe tuberculoma (E). The CSF findings and CSF PCR were consistent with TBM.
Fig. 3. TBM with vasculitis. Axial T2-weighted (A–C) images show a large area of cortical and subcortical hyperintensity in the right frontal-parietal and occipital regions, left basal ganglia, and in the periventricular region with mild ventricular dilatation. DW images (D–F) show a large area of restricted diffusion in the right middle cerebral artery and posterior cerebral artery territory and left basal ganglia. Axial MT T1 (G) image shows basal exudates and abnormal meninges, which appear bright. Postcontrast T1 (H) image shows abnormal meningeal enhancement in the MT T1 bright regions (G). MR angiogram (I) of the circle of Willis shows segmental narrowing involving the supraclinoid portion of the right internal carotid artery, middle cerebral artery, and right posterior cerebral artery.
Vasculitis

Vasculitis is another common complication seen at autopsy in cranial TBM involving small and medium-sized vessels and causing ischemic cerebral infarction. Most of the infarcts are in the basal ganglia and internal capsule regions because of the involvement of the lenticulostriate arteries; however, involvement of the large vascular territory such as the middle cerebral artery may also be encountered. MR angiography may help in the detection of vascular involvement (see Fig. 3). Intracerebral inflammatory aneurysms may also be seen in CNS tuberculosis. MR angiography can reveal this rare vascular complication. DW imaging helps in early detection of infarcts. Vascular complications are usually seen following initiation of specific therapy, possibly due to the healing and fibrosis of meninges resulting in the occlusion of embedded vasculature.

Focal or diffuse pachymeningitis

CNS TB may involve the dura mater, causing pachymeningitis, which may occur either in isolation or with pial or parenchymal disease. Pachymeningitis may present as focal or diffuse involvement of the dura mater and occur secondary to hematogenous spread. Thickened dura mater may be evident on precontrast studies but is detected usually as abnormal enhancement on postcontrast images. However, the appearance of focal and diffuse pachymeningitis on MR imaging is nonspecific and may be seen in a large number of inflammatory and noninflammatory conditions.

Cranial nerve neuropathy

Clinical involvement of the cranial nerves is seen in 17.4% to 40% of patients with TBM caused by vascular compromise resulting in ischemia of the nerve or caused by entrapment of the nerves by the exudates.

Intracranial tuberculoma

Brain tuberculosis is a space-occupying mass of granulomatous tissue that is encountered more frequently in developing countries and is responsible for high morbidity and mortality. The incidence of tuberculoma is higher in the developing world (15%-50% of all intracranial lesions), compared with developed countries where the incidence is about 0.2% of all biopsied brain lesions. Early recognition and treatment of this condition on imaging plays an important role in patient management. Intracranial tuberculomas may be solitary or multiple and variable in size. These tuberculomas are found across all age groups; however, a predilection for children has been reported. The common sites include cerebral hemispheres, basal ganglia, cerebellum, and brainstem. Rarely, ventricular system and meninges are also involved.

Extra-axial tuberculomas may also occur, which may cause widening of the basal foramen or adjacent bone destruction. Tuberculoma in the hypophyseal region is rare and it is frequently associated with thickening of the pituitary stalk.

MR features

From the appearance on T2-weighted imaging, the intra-axial tuberculomas may be classified as:

1. T2 hyperintense lesion
2. T2 hypointense lesion
3. T2 hyperintense center with peripheral hypointense rim
4. Lesion with mixed/heterogeneous signal intensity.

T2 hyperintense lesion

Noncaseating tuberculomas, typically less than 1.5 cm in diameter, appear hyperintense on T2-weighted images, isointense to hypointense on T1, hyperintense on MT T1, and FLAIR, and show nodular or ring enhancement on postcontrast studies. On DW imaging, these lesions may show hyperintensity with low ADC. These tuberculomas may be part of miliary tuberculosis or TBM (Fig. 4). This appearance may resemble metastases, lymphomas, demyelinating plaques, and other infective granulomas. The presence of a bright rim on noncontrast MT T1 along with low MTR may help in its differentiation from other lesions.

T2 hypointense lesion

Tuberculomas with solid caseation are usually isointense to hypointense on both T2-weighted and T1-weighted images. These lesions are surrounded by a rim of variable thickness that may appear hyperintense on T1-weighted and T2-weighted images. On DW images, there is no restriction seen in the solid caseation of the tuberculoma with a high ADC. On noncontrast MT T1 images, this rim shows hyperintensity, a characteristic feature seen in tuberculomas, and the solid caseation remains hypointense (Figs. 5–7). The rim comprises inflammatory cells, some of which may contain fragmented portions of the lipid-rich cell wall of M tuberculosis. Lipids are known to have no MT effect; the rim has a lower MT ratio than the core and appears bright on MT. Biochemically, the core contains necrotic tissue and macromolecules that are responsible for the higher MT ratio compared with the rim. The rim shows enhancement on postcontrast T1 images, whereas solid caseation does not enhance. The solid caseation contains cheesy material high in lipid contents, with macrophage infiltration, regional fibrosis/gliosis,
and macrophage by-products (free radicals), components that are possibly responsible for the hypointensity seen on T2-weighted images.\textsuperscript{25} These are seen as slight hypointensities on a T1-weighted image (B). DW image (C) does not reveal any abnormality. MT T1 (D) shows multiple small lesions with bright rims in the regions of hypointensity noted on T2 (A). Susceptibility-weighted imaging (E) does not show any blooming that would indicate calcification or bleeding. Contrast-enhanced T1-weighted image (F) confirms the presence of multiple small lesions with rim enhancement in the areas of MT T1 (D) and T2 hyperintensities (A). Chest skigram of the patient showed miliary tuberculosis.

\textbf{Fig. 4.} Miliary tuberculomas. Multiple areas of focal hyperintensity are seen on T2-weighted axial image (A). These areas are seen as slight hypointensities on a T1-weighted image (B). DW image (C) does not reveal any abnormality. MT T1 (D) shows multiple small lesions with bright rims in the regions of hypointensity noted on T2 (A). Susceptibility-weighted imaging (E) does not show any blooming that would indicate calcification or bleeding. Contrast-enhanced T1-weighted image (F) confirms the presence of multiple small lesions with rim enhancement in the areas of MT T1 (D) and T2 hyperintensities (A). Chest skigram of the patient showed miliary tuberculosis.

T2 hypointense lesions. Susceptibility-weighted sequences such as SWAN may differentiate hemorrhage and calcification from other T2 hypointense lesions.

**T2 hyperintense center with peripheral hypointense rim** When liquefaction of the caseation occurs within a tuberculoma, it appears as a T2 hyperintense lesion with peripheral hypointense rim. On T1-weighted and MT T1-weighted images, the centers of these lesions are hypointense. Tuberculomas with liquid caseation show restriction on DW images (see Figs. 2, 5, and 8). There is rim enhancement on postcontrast studies. The MTR remains significantly lower in tuberculoma compared with other conditions such as NCC. This appearance of a T2 hyperintense center with peripheral hypointense rim may also be seen in other conditions such as pyogenic or tubercular
abscesses, degenerating NCC, toxoplasmosis, and metastases. In NCC, the scolex appears as an eccentrically placed hypointense nodule on T2-weighted imaging that differentiates it from tuberculoma. The susceptibility-weighted and isotropic T2-weighted imaging techniques are helpful in differentiating these lesions from neurocysticercosis. MR spectroscopy may differentiate this stage of tuberculomas from pyogenic abscesses by showing cytosolic amino acids resonances in the latter.

Lesion with mixed/heterogeneous signal intensity At times, tubercular lesions show mixed intensity on spin-echo imaging with a rim of variable thickness that may appear minimally hyperintense on T1 and show variegated enhancement (Fig. 9). Similar-appearing lesions include lymphomas, glioblastoma, metastases, fungal granulomas, and toxoplasmosis. $^1$H MR spectroscopy may be nonspecific in its differentiation. This type of tubercular lesions show large choline and lipid resonances with variable creatine resonance and correlate with predominantly cellular infiltrate along with small areas of solid caseation on histopathology. It is suggested that the presence of choline is caused by the contribution from the cellular component in this type of tuberculosis. On MT images, the rim shows hyperintensity, whereas the caseous regions are heterogeneously hypointense.

Miliary tuberculosis Miliary brain tuberculosis is a result of hematogenous spread of infection in which multiple, small miliary tubercles of less than 2 mm are seen. It is usually associated with TBM. These lesions may not be visible on conventional spin-echo MR images or show only tiny foci of hyperintensity on T2-weighted images. The spin-echo invisible lesions are clearly visible on MT T1-weighted imaging. T1-weighted images after gadolinium administration show numerous small, homogeneous enhancing lesions.
Role of advanced imaging

In a recent study, Gupta and colleagues performed dynamic contrast enhancement MR (DCE-MR) imaging in 13 patients with brain tuberculoma and showed that the regional cerebral blood volume (rCBV) of the cellular portion significantly correlated with the cellular fraction volume, microvascular density (MVD), and vascular endothelial growth factor (VEGF) of the excised tuberculomas. MVD also correlated significantly with VEGF. Correlation between rCBV, MVD, and VEGF confirms that rCBV is a measure of angiogenesis in the cellular fraction of the brain tuberculosis. In another recent DCE-MR imaging study in brain tuberculosis, the investigators reported a significant positive correlation between physiologic indices ($K^{\text{trans}}$ and $v_a$) and matrix metalloproteinase-9 (MMP-9) expression (a marker of blood-brain barrier disruption) in excised tuberculoma. However, a weak correlation between physiologic indices and VEGF expression in excised tuberculoma suggests a limited role of VEGF in opening of the blood-brain barrier. Correlation between $K^{\text{trans}}$ and MMP-9 suggests that $K^{\text{trans}}$ can be used as a surrogate marker of blood-brain barrier disruption. These parameters may be useful in assessment of therapeutic response in tuberculoma.

Diffusion tensor MR imaging (DTI) has been widely used for the detection of white matter abnormality in various clinical conditions. A recent serial DTI study showed strong negative correlation of MMP-9 expression in excised tuberculoma with fractional anisotropy (FA), linear anisotropy (CL), and planar anisotropy (CP), and significant direct correlation with spherical anisotropy (CS). The investigators also reported significant increase in FA, CL, and CP along with significantly decreased CS with time in patients who were serially followed up with antitubercular therapy (ATT). These methods may be of value in objective assessment of therapy in tuberculoma and guide the clinician in modulation of treatment.

Fig. 6. Vermian tuberculoma in a 17-year-old boy. T2-weighted axial image (A) shows a hypointense mass with small central hyperintensity in the vermis that appears isointense with central hypointensity on the T1-weighted image (B) with obstructive hydrocephalus. The rim of the lesion is hyperintense on the MT T1 image (C). No diffusion restriction is noted on the DW image (D). Postcontrast BRAVO axial (E), and sagittal (F) images show rim enhancement. $^1$H MR spectroscopy (G) shows prominent lipid peaks. Histology confirmed it as tuberculoma.
Tuberculous brain abscess

Tuberculous brain abscesses constitute approximately 4% to 7% of the total CNS TB in developing countries. These abscesses are diagnosed from macroscopic evidence of abscess formation along with histologic demonstration of vascular granulation tissue in the wall containing both acute and chronic inflammatory cells, and isolation of *M tuberculosis*. On MR imaging, these appear as large, solitary, and frequently multiloculated ring-enhancing lesions with surrounding edema and mass effect. DW imaging in tuberculous abscesses shows restricted diffusion with low ADC values. High lipid-containing *M tuberculosis* bacilli are probably responsible for significantly lower MTR values from the rim of tuberculous abscesses (19.89 ± 1.55) compared with pyogenic abscesses (24.81 ± 0.03).

In vivo $^1$H MR spectroscopy in tuberculous abscesses shows only lactate and lipid signals (at 0.9 and 1.3 ppm), without any evidence of cytosolic amino acids. This pattern may be useful but is not characteristic because a similar pattern may also be seen in staphylococcal abscess. Quantitative MT T1 imaging may be needed to help in its differentiation (Fig. 10).

Spinal Tuberculosis

Intraspinal TB

The MR features of spinal meningitis are usually visible on contrast-enhanced images in which at times a thin, diffuse meningeal enhancement may be noted. In arachnoiditis, imaging features include CSF loculation and obliteration of the spinal subarachnoid space with loss of outline of the spinal cord and clumping of the nerve roots.
Fig. 8. A large tuberculoma in the left temporal region. T2-weighted axial image (A) shows central hyperintensity with a peripheral hypointense rim and perifocal edema. The lesion appears hypointense in the center with peripheral isointensity on the T1-weighted (B) image. MT T1 image (C) shows a hyperintense rim beyond the T2 hypointensity, suggesting a cellular rim of the tuberculoma that enhances on the postcontrast T1-weighted image (D). The lesion does not show restriction of diffusion on the DW image (E) with high ADC (F). $^1$H MR spectroscopy (G) shows prominent lipid resonance at 1.3 ppm with small resonance of choline. Histology confirmed it as tuberculoma.

Fig. 9. Tuberculoma presenting as a heterogeneous mass in the left temporal lobe in a 40-year-old man. A mass lesion with mixed signal intensity appears with surrounding edema on T2-weighted (A), T1-weighted (B), and FLAIR (C) images. Small areas of hyperintensity are seen within this mass on DW images (D), which have low signal on the ADC map (E). MT T1 image shows multiple small hyperintense rings around these hyperintense DW imaging lesions (F), which enhance on the postcontrast T1-weighted image (G). $^1$H MR spectroscopy (H) of this lesion reveals a large lipid with increase in choline. Histology confirmed it as tuberculoma.
in the lumbar region. Contrast studies may show nodular, thick, linear dural enhancement, often completely filling the subarachnoid space on postcontrast MR images.\(^{50-52}\) In chronic stages of disease, there may not be any enhancement even though unenhanced images show signs of arachnoiditis.\(^{50,51}\) The spinal cord may be involved secondarily and show infarction, syringomyelia, myelitis, and tuberculoma formation. Syringomyelia is seen as cord cavitation with CSF-like intensity that does not show any enhancement on postcontrast images.\(^{50,51}\)

**Myelitis**

Tuberculous myelitis is usually associated with tuberculous intracranial involvement of the meninges or brain parenchyma, or with tuberculous arachnoiditis of the spine (Fig. 11). Intramedullary tuberculomas are uncommon and have similar imaging features to brain tuberculomas.\(^{53,54}\) MR imaging features of spinal tubercular abscess, another rare condition, are similar to cerebral tubercular abscess. As the treatment begins, there is reduction in the T2 hyperintensity in the spinal cord and enhancement becomes more clearly defined on postcontrast T1-weighted images.\(^{55}\) The surrounding edema continues to be extensive. These findings suggest the beginning of intramedullary abscess formation with imaging features seen in brain abscesses.\(^{55}\) The abnormalities visible on T2-weighted images subside in weeks, whereas contrast enhancement may persist for months.\(^{55}\)

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**Fig. 10.** Tubercular abscess in the left cerebellar hemisphere. Axial T2-weighted image (A) shows a well-defined, round, heterogeneously hyperintense lesion with peripheral hypointense rim. On the T1-weighted image (B), the lesion is heterogeneously hypointense centrally with a peripheral isointense rim. Axial FLAIR (C) image shows minimal perilesional edema. On the MT T1 images, with MT pulse off (D) and pulse on (E), the T2 hypointense rim appears hyperintense. Axial postcontrast T1-weighted (F) image shows thick nodular rim enhancement. The DW image (G) shows restriction in the dependent part of the cavity with corresponding low ADC (H) suggesting cellular debris. FA map (I) and color-coded FA map (J) show high FA in the wall as well as in parts of the cavity of the lesion. \(^{1}H\) MR spectroscopy (K) shows dominant lipid resonances. Histology from the wall was consistent with tuberculous abscess. Pus culture was positive for \textit{M tuberculosis}.
Dural and subdural disorders
Tuberculous pus formation may occur between the dura and the leptomeninges and appear as a loculation. This appears hyperintense on T2-weighted images and isointense to hypointense on T1-weighted images. However, the dural granulomas appear hypointense to isointense on T2-weighted images and isointense on T1-weighted images. Peripheral enhancement can be seen on postcontrast images.51

Epidural tuberculous abscesses may be seen in isolation or in association with arachnoiditis, myelitis, spondylitis, and intramedullary and dural tuberculomas.51,55 These lesions appear to be isointense to the spinal cord on T1-weighted images and show mixed intensity on T2-weighted images (Fig. 12). Uniform enhancement is seen if the TB inflammatory process is phlegmonous in nature on postcontrast images, which converts to peripheral enhancement if epidural abscess formation or caseation develops.51,55

Tuberculous spondylitis
Tuberculous spondylitis is a frequent occurrence in developing countries and is an important cause of spine-related morbidity. Early diagnosis and prompt treatment are required to avoid permanent damage or deformity in the spine.

Tuberculous spondylitis commonly involves vertebral bodies; however, disease in other structures, such as posterior osseous elements, epidural space, paraspinal soft tissue, and intervertebral disks, is also seen.56 The most commonly involved sites in tuberculous spondylitis are dorsal and lumbar spine, especially the thoracolumbar junction. Usually more than 1 vertebral body is affected, but solitary vertebral lesions can also occur.

MR has the unique ability to detect marrow abnormalities before any bony destruction; hence it has assumed the role of primary imaging modality. The involved vertebrae are hyperintense on T2-weighted images and hypointense on T1-weighted images.56,57 As the disease progresses, diskovertebral involvement may be visible. Features such as vertebral intraosseous abscesses (Figs. 13–15), paraspinal abscesses, diskitis, skip lesions, and spinal canal encroachment can all be seen. Reduction in disk height and morphologic alteration of the paraspinal soft tissue is a late occurrence. Enhanced MR studies are valuable for characterizing tuberculous spondylitis by
showing rim enhancement around intraosseous and paraspinal soft tissue abscesses (see Figs. 13–15) and, rarely, in lesions with solid caseation.\(^5^7\) Therapeutic response is assessed by showing progressive increase in signal intensity on T1-weighted images (Fig. 16) in the affected vertebrae caused by fatty marrow deposition that indicates healing.\(^5^6\)

Demonstration of bone fragments in the intraspinal and/or extraspinal soft tissue is considered characteristic of tuberculous spondylitis.\(^5^6\) This is caused by the lack of proteolytic enzymes that lyse the bone in the tuberculous inflammatory exudate. These fragments are best shown on CT; however, T2*-weighted images can also show these by accentuating the diamagnetic susceptibility properties of the calcium salt present in the bone fragments. The presence of bone fragment is characteristic of tuberculous spondylitis even in the absence of abscess formation.\(^5^7\)

As in brain, diffusion imaging is useful for demonstrating restriction of diffusion in spinal

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**Fig. 12.** Posterior epidural tuberculous abscess in an HIV-positive patient. Sagittal T2-weighted image (A) shows a curvilinear area of increased signal intensity in the posterior subarachnoid space of the mid-dorsal spinal canal. The corresponding area is hypointense on the T1-weighted image (B). The underlying spinal cord is compressed and shows increased signal intensity with almost complete obliteration of the subarachnoid space (A–C) caused by mass effect. Sagittal (D) and axial (E) postcontrast T1-weighted images show thick peripheral wall enhancement with a central nonenhancing area of liquefaction suggesting epidural abscess. No abnormal enhancement is noted in the adjacent vertebral bodies and intervertebral disks.
infections. Tubercular abscesses in soft tissues as well as within the vertebrae also behave in a similar manner and show restriction of diffusion (see Fig. 15) with low ADC.

TUBERCULOSIS IN HIV/AIDS

Tuberculosis has seen a resurgence in the past 2 decades because of the increasing numbers of patients with AIDS. A total of 5% to 9% of patients with AIDS develop tuberculosis, and, of these, 2% to 18% have CNS involvement. CNS tuberculosis may be the initial clinical manifestation of AIDS and may result from reactivation of a previous infection or from a primary, newly acquired infection. The predominant mechanism of disease spread is hematogenous.

Pathologic Features

The most common intracranial manifestation of tuberculosis is basal meningitis; however, tuberculomas, tuberculous abscess, and cerebral infarction are also seen. HIV infection may alter the pathologic features of TBM. Fewer basal exudates and greater numbers of acid-fast bacilli occur in the brain parenchyma and meninges in patients with HIV infection.

Imaging Features

Imaging features depend on the site of infection. In TBM, hydrocephalus and meningeal enhancement are seen. The hydrocephalus results primarily from obstruction of the basal

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Fig. 13. Tuberculous spondylitis involving the craniovertebral junction. Axial T2-weighted (A) image shows area of heterogeneous signal intensity in the occipital condyle and lateral mass of atlas on the left side. Axial (B) and midsagittal (E) fat-suppressed postcontrast T1-weighted image shows moderate heterogeneous contrast enhancement of the altered area. (C–D) Extension of the enhancing soft tissue between the anterior arch of atlas and dens on T2 images resulting in atlantoaxial dislocation (AAD) of 4.3 mm with mild basilar invagination causing mild narrowing of the foramen magnum. No abnormal cord signal intensity or enhancement is seen.
cistern by inflammatory exudates. In addition, cerebral abscesses and tuberculomas may be seen.60

Tuberculomas occurred in 24% of patients in a study by Whiteman and colleagues.23 The appearance of tuberculomas in AIDS is similar to those seen in patients who do not have HIV and was described earlier. On postcontrast images, noncaseating tuberculomas show nodular homogeneous enhancement. Caseating tuberculomas have ring enhancement. Tuberculous abscesses are more common in HIV-infected patients. Among patients with CNS tuberculosis, 4% to 8% of those without HIV infection developed abscesses, compared with 20% in the group of patients with HIV.23 Abscesses tend to be larger than tuberculomas, frequently greater than 3 cm. Abscesses are also more frequently solitary unlike tuberculomas. The imaging features of tubercular abscesses are described in an earlier section.9

Cerebral infarction complicates CNS tuberculosis and was seen in 36% of the patients in the study by Whiteman and colleagues.23 Imaging features are similar to those described in patients without HIV.

Fig. 14. Tuberculous spondylitis of the dorsal spine. Midsagittal T2-weighted (A) and fat-saturated T1-weighted (B) images show contiguous involvement with an area of altered signal intensity in D2 and D3 vertebral bodies and the intervening disk, resulting in wedge collapse and kyphotic deformity. Hyperintense signal intensity that indicates edema is noted in the underlying cord caused by mass effect. Fat-suppressed postcontrast T1-weighted (C) image shows moderate heterogeneous enhancement of the altered signal area within the vertebral bodies. Axial postcontrast T1-weighted (D, E) images show a thick-walled abscess in the prevertebral and paravertebral region. Bilateral minimal pleural effusion is also noted.
ASSESSMENT OF THERAPEUTIC RESPONSE

Once the diagnosis is made on imaging and other laboratory investigations, the patients are given antitubercular treatment (ATT). MR imaging is the modality of choice for following these patients. Serial imaging in responding patients usually shows a decrease in lesion size after 3 to 4 months and its disappearance by 12 months. Rarely, a paradoxic progression of intracranial tuberculomas or development of new lesions during the treatment of CNS tuberculosis has also been recognized. Advanced imaging techniques such as perfusion imaging and DTI may be useful in the assessment of response in these patients (see Fig. 7). It has been shown that changes in $K_{\text{trans}}$ and $v_0$ closely match the therapeutic response in brain tuberculoma even in the presence of a paradoxic increase in the lesion volume.

A reduction in the intensity of the meningeal enhancement is considered a positive response to treatment in patients with TBM. In a recent serial DTI study in TBM, it was shown that the cortical FA values decreased on treatment ($0.13 \pm 0.02$) compared with baseline values ($0.15 \pm 0.03$). The investigators also reported a significant positive correlation between FA and proinflammatory molecules (PMs), thereby suggesting that the DTI metrics may be used as noninvasive surrogate marker of PMs in assessing therapeutic response in patients with TBM.

Calcification of the meninges and parenchymal tuberculoma is seen as sequelae of TBM, and usually appear markedly hypointense on all spin-echo sequences. An isointense or hypointense core with a hyperintense rim on T2-weighted and FLAIR images is the most common imaging appearance.

SUMMARY

CNS tuberculosis is a major cause of sickness and death in developing countries and is being increasingly seen in the developed world because...
of the emergence of AIDS. It spreads hematogenously and involves meninges, brain parenchyma, spinal cord, and covering bones. The presenting clinical features vary according to the site of infection, and are usually nonspecific. Isolation of \textit{M tuberculosis} for the definitive diagnosis is possible only in a few patients. MR imaging plays an important role in its early recognition. MT-T1 imaging is considered superior to conventional spin-echo sequences for imaging the abnormal meninges and tuberculomas. The MT ratio of tuberculomas remains significantly lower compared with other conditions such as cysticercosis. Use of $^1$H MR spectroscopy in combination with other MR imaging techniques may also help in its differentiation from similar diseases. Imaging characteristics of tuberculomas in HIV remain the same as in patients without HIV. Advanced imaging methods such as perfusion imaging and DTI may be of value in objective assessment of therapy in tuberculoma and guide the clinician in modulation of treatment.

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