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# Tuberculosis of the central nervous system: overview of neuroradiological findings

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**Abstract** This article presents the range of manifestations of tuberculosis (TB) of the craniospinal axis. Central nervous system (CNS) infection with *Mycobacterium tuberculosis* occurs either in a diffuse form as basal exudative leptomeningitis or in a localized form as tuberculoma, abscess, or cerebritis. In addition to an extensive review of computed tomography and magnetic resonance features, the pathogenesis and the relevant clinical setting are discussed. Modern imaging is a cornerstone in the early diagnosis of CNS tuberculosis and may prevent unnecessary morbidity and mortality. Contrast-enhanced MR imaging is generally considered as the modality of choice in the detection and assessment of CNS tuberculosis.

**Keywords** Tuberculosis · Central nervous system · CT · MR imaging

## Introduction

The global increase in incidence of tuberculosis (TB) in both immunocompetent as well as in immunocompromised patients is a health issue of universal concern. Factors that have contributed to this increase are the acquired immunodeficiency syndrome (AIDS) and the problem of multi-drug-resistant TB (MDRTB) [1, 2, 3, 4].

Involvement of the central nervous system (CNS) by TB (CNS TB) is the most hazardous type of systemic TB because of its high mortality rate and possible serious neurological complications and sequelae [5]. A CNS infection with *Mycobacterium tuberculosis* can present either as a diffuse form (e.g., basal exudative leptomeningitis) or as a localized form (e.g., tuberculoma, abscess, or cerebritis). Central nervous system TB occurs in all age groups, but 60–70% of patients are below the age of

20 years [6]. Because of the increasing prevalence of CNS TB, especially in AIDS patients, and the more widespread use of cross-sectional imaging modalities, CNS TB will be more commonly seen by radiologists. Central nervous system TB occurs in 2–5% of all patients with TB and in 10% of those with AIDS-related TB [4, 7].

Unfortunately, the diagnosis of CNS TB remains difficult; therefore, one should be familiar with the various radiological features as neurotuberculosis can mimic numerous other disease entities. Co-existence of extra-neural tuberculosis is reported amongst 50% of cases of neurotuberculosis in the literature [6], which may be a clue to the diagnosis of CNS TB whenever observed. Contrast-enhanced MR imaging is generally considered to be superior to CT in the detection and assessment of CNS TB. Neuroimaging procedures should include both the brain and spine, as concomitant intracranial and intraspinal involvement is common [8].

## Meningeal tuberculosis

### Tuberculous leptomeningitis

Tuberculous meningitis (TBM) is undoubtedly the most common presentation of neurotuberculosis and occurs predominantly in young children and adolescents [9]. Pathologically, this granulomatous infection of the leptomeninges (arachnoid membrane and pia mater) is characterized by a thick exudate most notably affecting the basal portions of the brain [10, 11, 12]. The early meningeal exudate setting off the whole process is believed to arise from rupture into the subarachnoid space of a microscopic subependymal or subpial granuloma, frequently referred to as the "Rich focus" [13]. This initial tuberculous lesion in the brain arises from earlier hematogenous dissemination of a distant tuberculous focus elsewhere, often an affected lymph node eroding and discharging into a blood vessel. It can become active after a quiescent period, even years after initial infection. Alternatively, meningeal involvement may be secondary to rupture of a tuberculoma in a vessel related to the subarachnoid space, to rupture of one of the miliary tubercles in miliary TB of the brain, or, very rarely, via contiguous spread from tuberculous involvement of bone such as mastoiditis. Due to the paucity of polymorphonucleocytes, the cerebrospinal fluid (CSF) has poor defenses against the tubercle bacillus resulting in rapid spread along the meninges through the basal cisterns. Cell-mediated immunity leads to the development of a dense, glutinous exudate along the basal surface of the cerebrum. The interpeduncular fossa, the ambient cistern, and the chiasmatic region are particularly involved. Severe or late-stage TBM also demonstrates the advance of leptomeningeal changes over the cerebral convexities and ependymitis in the ventricular walls. The exudate is composed of neutrophils, mononuclear cells, erythrocytes, and variable numbers of bacilli within a loose fibrin network in which lymphocytes and monocytes reorganize into countless, microscopic tubercles [2, 3, 4, 10, 13, 14, 15].

Clinically, TBM most often presents with fever, headache, decreased level of consciousness, and meningeal signs such as neck stiffness, photophobia, and vomiting. In addition, symptoms related to cranial nerve involvement and focal ischemic syndromes may occur [16].

The inverse relation between the delay in the start of adequate treatment and the clinical outcome makes early diagnosis of TBM essential. Diagnosing TBM at an early stage may be very difficult owing to the unfamiliarity of doctors with this almost forgotten disease, the often nonspecific presenting symptoms, and inconclusive laboratory results. Once the immune system has been triggered, CSF analysis usually demonstrates lymphocytic pleocytosis, increased protein, and decreased glucose levels. Elevated levels of adenosine deaminase in CSF and visualization of acid-fast bacilli in CSF smears may be early clues; however, until recently the definitive diagnosis could only be established after growth and identification of *M. tuberculosis* in culture which could take 4–8 weeks and could be false negative in 15–75% of cases [4, 7, 8, 15]. Currently, polymerase chain reaction in CSF can diagnose TBM with a higher sensitivity than microscopic examination and cultures; however, its full use for the diagnosis of TBM is limited by the lack of standardization and availability [4]. Even though there are no specific radiological characteristics of TBM, neuroimaging can be helpful in the early diagnosis [9].

The common triad of neuroradiological findings in TBM are:

1. Basal meningeal enhancement
2. Hydrocephalus
3. Infarctions in the supratentorial brain parenchyma and brain stem

Basal meningeal enhancement (Fig. 1) is the most consistent feature, caused by the "leaky" inflammatory neovessels [1]. On non-contrast CT scans, obliteration of the basal cisterns is observed. After contrast administration, there is typically diffuse enhancement of the basal subarachnoid cisterns and occasionally meningeal enhancement is seen over the cerebral convexities, the sylvian fissures (Fig. 2b), and the tentorium [1, 12, 15]. In the early stages, MR imaging without the use of a paramagnetic contrast agent may show little or no abnormalities. In a later stage, distension of the affected subarachnoid spaces occurs with associated mild shortening of T1 and T2 relaxation times compared with normal CSF. Gadolinium-enhanced T1-weighted imaging demonstrates abnormal meningeal enhancement and is generally consid-

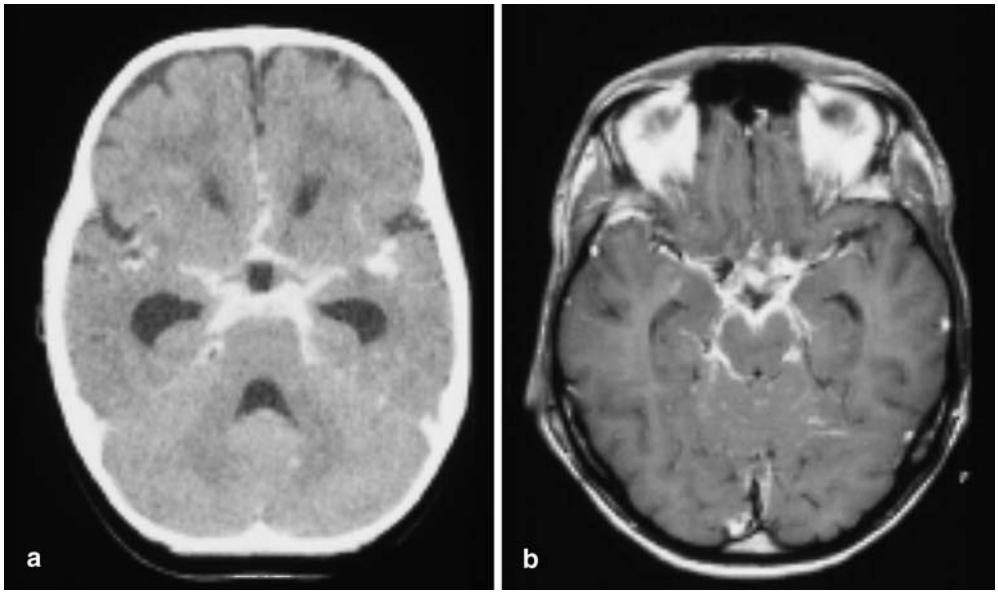


**Fig. 1a, b** Basal exudative tuberculous meningitis. **a** Contrast-enhanced CT scan demonstrates an intense enhancement of the basal meninges. Note the widening of the temporal horns, due to communicating hydrocephalus. **b** Axial gadolinium-enhanced T1-weighted MR image demonstrates marked enhancement in the basal subarachnoidal cisterns

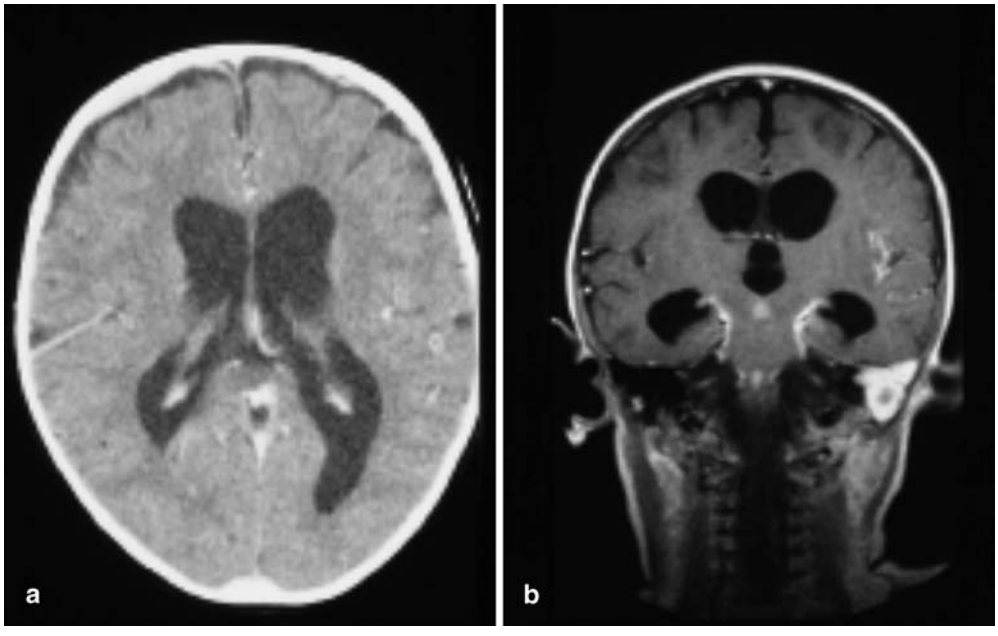


**Fig. 2a, b** Hydrocephalus. **a** Axial contrast-enhanced CT scan demonstrates enlargement of the lateral ventricles. **b** Coronal T1-weighted MR image after gadolinium contrast administration shows enlargement of third and lateral ventricles. Note associated enhancement of the leptomeninges along the left sylvian fissure and the basal cisterns. There is also contrast enhancement of the left mastoid, due to tuberculous otomastoiditis

ered to be more sensitive than CT [1, 17]. Some authors have reported minimal or absent meningeal enhancement on CT or MR images in patients with AIDS-related neurotuberculosis, supposedly due to an impaired immunological response resulting in the absence of basal meningeal exudates [18]; however, other reports have not shown major imaging differences as compared with non-immunosuppressed patients [19]. Extension of the inflammatory response to the ventricular system through the CSF pathways resulting in ependymitis or choroid plexitis can cause ependymal or choroid plexus enhancement [15, 20].

Hydrocephalus (Fig. 2) is the most frequent complication of TBM and is usually more prominent in children. Hydrocephalus is generally of the communicating type and is secondary to blockage of CSF resorption by inflammatory exudates in the basal subarachnoidal cisterns. Occasionally, the hydrocephalus is of the obstructive type, secondary to narrowing of the aqueduct or a ventricle by a focal parenchymal lesion with mass effect otherwise due to entrapment of a ventricle by granulomatous ependymitis [7, 13]. A new view for the understanding of pathogenesis and hemodynamics of hydrocephalus has recently been proposed by Özates et al.

[21]. It may result from disturbed hemodynamics caused by any process that restricts the pulsation of the intracranial arteries. Late obstruction of CSF absorption pathways by fibrous tissue is a frequent cause of late development of hydrocephalus [3, 14]. Plain radiography may show suture diastasis in small infants due to increased intracranial pressure. In babies, and if the diastasis is sufficient, ultrasonography can be used to demonstrate the basal meningeal changes and the ventricular dilatation [11]. In addition to the dilatation of lateral ventricles, an increased periventricular signal may be seen on T2-weighted images as a sign of interstitial edema due to increased intraventricular pressure with transependymal migration of CSF [10, 22]. Hydrocephalus may also occur in bacterial meningitis but is often transient compared with TBM associated hydrocephalus, where it is progressive. The persistence of hydrocephalus should alert the radiologist to the possibility of TB etiology [23].

Cerebral infarction (Fig. 3) is another common complication of basal meningitis which adds to morbidity and mortality [24]. The aforementioned inflammatory exudate involves the adventitia and progresses to affect the entire vessel wall, leading to panarteritis with secondary thrombosis and occlusion [4, 10, 11]. Dastur et al. found infarcts in 41% of the specimens in an autopsy series of 100 patients [25]. The majority of the infarcts are seen in the basal ganglia and internal capsule related to the encasement of the basal perforating arteries, particularly the origin of the lenticulostriate arteries, by the extensive basal meningeal exudates that characterize TBM. The large vascular distribution territories of the anterior and middle cerebral arteries are less commonly involved [10, 24]. A high proportion of these infarctions are hemorrhagic and this may lead to cavitation [10]. In addition to focal ischemic neurological syndromes, changes in consciousness are more commonly observed in patients with TBM who develop infarctions [5]. The conventional angiographic features of TBM consist of a triad of a hydrocephalic pattern, narrowing of arteries at the base of the brain, and narrowed or occluded small- or medium-sized arteries with early draining veins [26]. Following infarction, CT shows ill-defined hypodense areas with mass effect and variable peripheral, sometimes diffuse, IV contrast enhancement. These lesions progress to circumscribed hypodensities. Magnetic resonance imaging is more accurate than CT in depicting basal ganglia infarctions. A hyperintense lesion on T2-weighted images with mass effect and variable enhancement pattern after intravenous administration of gadolinium of a recent infarct will progress to a cavitated infarct which is typically hypointense on T1-weighted images and hyperintense on T2-weighted images [11, 14]. Furthermore, fluid-attenuated inversion-recovery (FLAIR) imaging may even be more useful to define the exact extent of the lesion and to differentiate old cerebral infarctions with cystic appearance from the surrounding tuberculous border zone encephalitis. On FLAIR imaging the old infarcts are characterized by a central area of low signal intensity (cavity due to tissue loss), surrounded by a hyperintense rim (presumably reflecting gliotic scar tissue). Conversely, T2-weighted images demonstrate both areas as equally hyperintense [27]. Magnetic resonance angiography has also been reported to be a useful and non-invasive technique for assessment of vascular involvement in TBM [24].

In addition to the triad of basal meningeal enhancement, hydrocephalus, and infarction, other manifestations of TBM are common. Clinically, involvement of cranial nerves is seen in 17.4–70% of patients with TBM. Cranial nerves II, III, IV, VI, and VII are most frequently affected. Cranial nerve impairment can be due to vascular compromise resulting in ischemia of the nerve or entrapment of the nerve in the basal exudates [1, 3, 23, 24]. Cranial nerve involvement may also be due to direct mass effect of a tuberculoma within the subarachnoid course on the cranial nerves or by direct involvement of the cranial nerve nuclei in the brain [1]. Late-stage fibrotic changes can cause permanent loss of function in these nerves [10]. The proximal portion of the nerve at the root entry zone is most vulnerable, and on contrast-enhanced MRI this portion of the nerve may be thickened and enhancing [1].

The brain tissue immediately underlying the tuberculous exudate shows various degrees of edema, perivascular infiltration, and microglial reaction, a process that is called “border zone encephalitis” [3]. Recognition of border zone encephalitis is difficult, as the bright signal on MR T2-weighted images in these border zones merge with the high signal of the leptomeningeal exudate [10, 27].

Meningeal, parenchymal, and ependymal tuberculoma formation is common during the course of TBM [10, 14, 28]. The specific imaging features of tuberculoma are discussed further in the section on parenchymal tuberculosis.

The differential diagnosis of TBM includes other infectious diseases (e.g., nontuberculous bacterial, viral or parasitic meningitis, as well as fungi such as coccidioidomycosis and cryptococcosis), non-infectious inflammatory disease affecting the leptomeninges (e.g., rheumatoid disease, sarcoidosis, idiopathic pachymeningitis), and meningeal carcinomatosis (e.g., meningeal spread of a medulloblastoma in children or breast carcinoma in adults) [1, 14, 17]. The suspicion of fungal meningitis is always increased in immunocompromised patients [14].

Radiologically, healing may be recognized by absence of basal meningo-vascular enhancement, but the end stage is difficult to judge [11]. Some patients may develop an initial increase in the degree of basal meningeal enhancement despite adequate antituberculous therapy [28]. After treatment, meningeal enhancement may even persist in some cases of TBM [29].

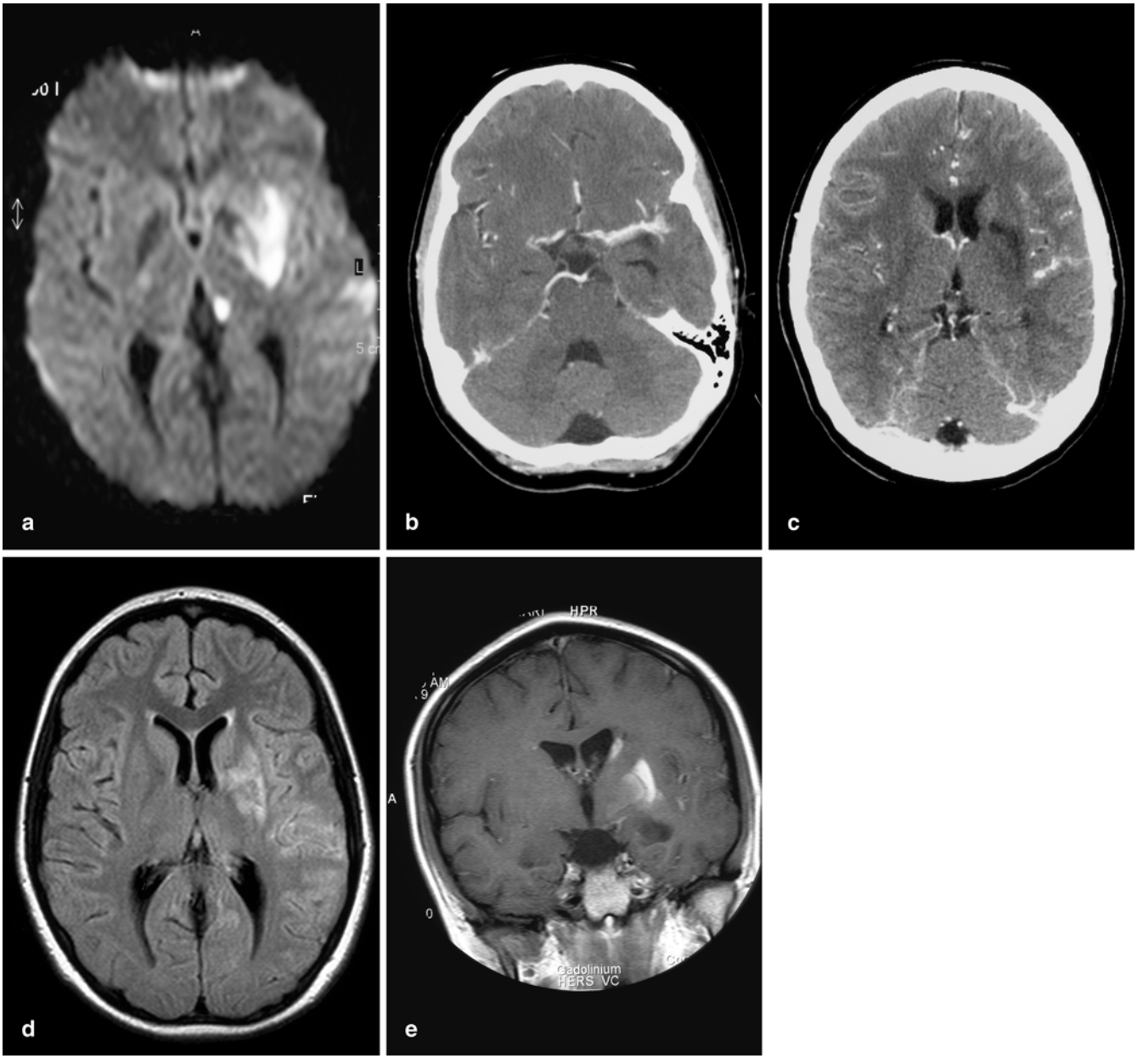


**Fig. 3a–e** Cerebral infarction complicating tuberculous meningitis in a 14-year-old girl. **a** Diffusion-weighted MR image (b=1000) reveals a focal area of decreased diffusion involving the left lentiform nucleus, and a smaller hyperintense focus in the posterior medial aspect of the left thalamus. These findings are indicative of acute infarction with cytotoxic edema. **b**, **c** Contrast-enhanced axial CT scans, obtained 6 weeks later, demonstrate irregular perivascular enhancement along the course of the left middle cerebral artery (**b**), as well as a hypodense lesion involving the anterior limb of the internal capsule and the lentiform nucleus on the left (**c**). **d** Axial turbo fluid-attenuated inversion recovery (FLAIR) MR image through the basal ganglia shows areas of increased signal intensity in the left lentiform nucleus. **e** Gadolinium-enhanced coronal T1-weighted MR image through the basal ganglia reveals enhancement in the head of the left caudate nucleus as well as in the left lentiform nucleus, indicating residual breakdown of the blood-brain barrier. This finding is consistent with late subacute infarction

Potential sequelae of TBM include meningeal or ependymal calcifications, focal areas of atrophy secondary to infarcts and hydrocephaly, encephalomalacia in the areas of cerebral infarction, and occasionally syringomyelia or syringobulbia [1, 3, 17]. The presence of ventriculomegaly and/or infarction is a precursor of severe sequelae [23].

## Pachymeningeal tuberculosis

Pachymeningeal tuberculosis consists of either isolated dural involvement or a predominantly dural-based lesion with secondary pial or parenchymal involvement. Focal

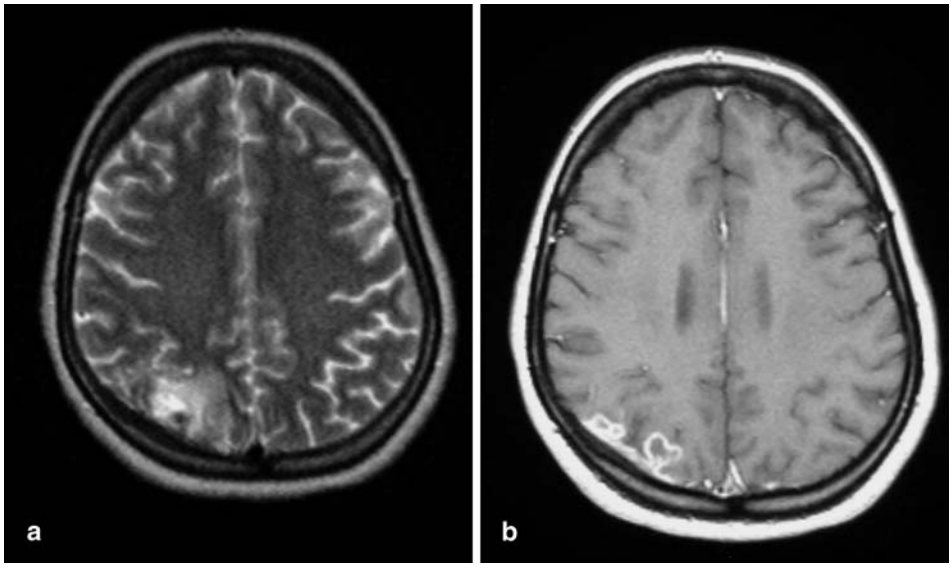


**Fig. 4a, b** Cerebral tuberculoma associated with meningitis. **a** Axial T2-weighted MR image demonstrates a hypointense subcortical lesion within the right parietal lobe, with surrounding edema. **b** Axial contrast-enhanced T1-weighted MR image at a slightly lower level reveals associated gyriform and meningeal enhancement

and diffuse patterns of tubercular pachymeningitis exist. In the literature, the term "en plaque tuberculoma" has been used to describe the focal involvement of the pachymeninges. This term, however, refers to all types of tuberculoma with en plaque morphology, including those that are primarily intraparenchymal [30].

Most focal lesions of pachymeningeal tuberculosis are seen as en plaque, homogenous, uniformly enhancing, dural-based masses (see Fig. 7d). Lesions appear hyperdense on plain CT scans, isointense to brain parenchyma on T1-weighted MR images and isointense to hypointense on T2-weighted MR images. Differential diagnosis includes meningioma, in which there is associated hyperostosis in the adjacent bone [30].

## Parenchymal tuberculosis

Parenchymal tuberculosis is more common in HIV-infected patients and can occur with (Fig. 4) or without meningitis [4]. The most common parenchymal form of CNS TB is tuberculous granuloma (tuberculoma). Other presentations of parenchymal diseases are tuberculous abscesses, focal cerebritis, and "allergic" tuberculous encephalopathy.

### Parenchymal tuberculomas

Parenchymal TB granulomata can occur at any age. They are commonly found in patients with miliary pulmonary TB who are neurologically asymptomatic [31]. Tuberculomas can involve the brain, spinal cord, subarachnoid, subdural or epidural space, and may be solitary or multiple [4, 11]. In children, tuberculomas predominate infratentorially, whereas in adults lesions are predominantly found in the supratentorial compartment [3, 15]. The frontal and parietal lobes are the most commonly affected regions [2, 3]. Occasionally, tuberculomas have been described in the intrasellar region, brain stem, thalami, basal ganglia, cerebellopontine angle, optic pathways, pineal region, and the ventricles [6, 32].

Most tuberculomas occur at the corticomedullary junction. This supports the hypothesis of hematogenous spread in their pathogenesis, for there is a dramatic narrowing of the arterioles supplying the cortex as they enter the white matter [10, 31]. A small number of tuberculomas develop from extension of CSF infection into the adjacent parenchyma via cortical veins or perivascular Virchow-Robin spaces around small penetrating arteries [7, 10]. These lesions originate as a conglomerate of microgranulomata in an area of TB cerebritis that join to form a mature noncaseating tuberculoma. In most cases subsequent solid central caseous necrosis will develop which may eventually liquefy [1]. Pathologically, the caseating granuloma is composed of a central zone of solid caseation necrosis containing only rare TB bacilli, surrounded by a capsule of collagenous tissue, epithelioid cells, multinucleated giant cells, and mononuclear inflammatory cells. Outside the capsule, there is parenchymal edema and astrocytic proliferation [3, 7, 33].

The clinical presentation is more subtle than that of TBM. The common presenting symptoms and signs are headache, intracranial hypertension, seizures, focal neurological signs, and papilledema [4, 10, 31]. Fever may be present [3, 10, 34]. The CSF findings are unremarkable or show a mild non-specific increased protein content. The CSF culture is usually negative. The diagnosis is therefore made on the basis of neuroimaging findings,

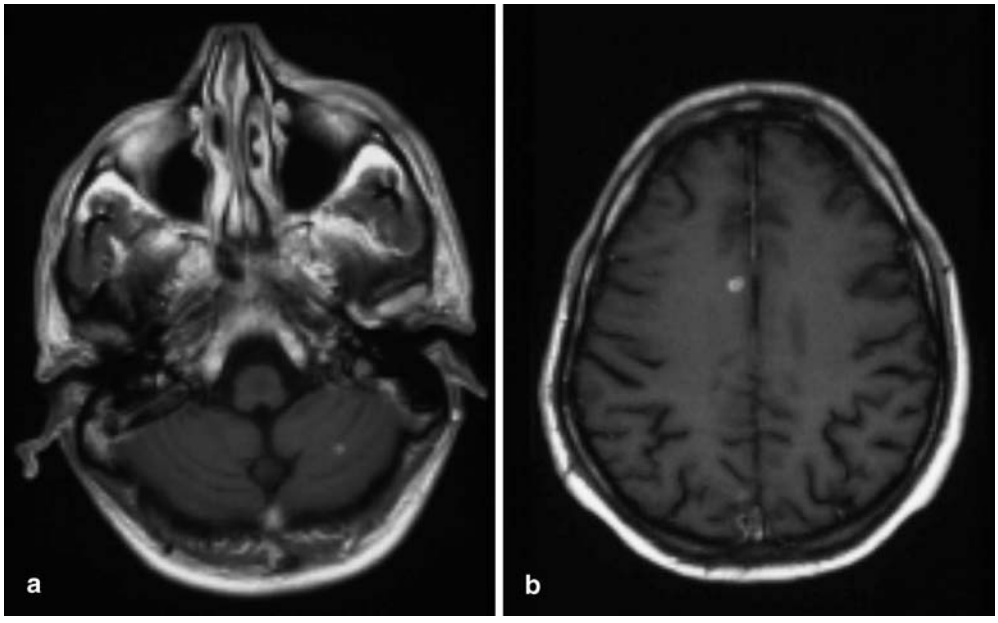


**Fig. 5a, b** Non-caseating granulomas. Axial gadolinium-enhanced T1-weighted MR imaging. Enhancing nodular lesions are seen at the gray–white matter interface within **a** the left cerebellar hemisphere and **b** the right frontal parafalcine area

**Table 1** The CT and MRI features of parenchymal tuberculomas. *NECT* nonenhanced CT; *CECT* contrast-enhanced CT; *T1WI* T1-weighted image; *T2WI* T2-weighted image; *T1WI Gd* T1-weighted image after gadolinium contrast administration; *SI* signal intensity

| | CT | MRI |
|---|---|---|
| Noncaseating granuloma | NECT: hypo-/isodense<br>CECT: homogenous enhancement | T1WI: low SI<br>T2WI: high SI<br>T1WI Gd: homogenous enhancement |
| Caseating granuloma with a solid center | CECT: heterogenous enhancement centrally<br>Ring enhancement of the capsule | T1WI: low/intermediate SI<br>T2WI: intermediate/low SI<br>T1WI Gd: rim enhancement |
| Caseating granuloma with a liquid center | NECT: hypodense<br>CECT: rim enhancement | T1WI: hypointense SI<br>T2WI: hyperintense SI<br>T1WI Gd: rim enhancement |

protein-purified derivative reactivity, and response to antituberculous therapy [3, 4].

The radiological presentation depends on whether the granuloma is noncaseating, caseating with a solid center, or caseating with a liquid center (Table 1) [1, 10]. The degree of surrounding edema is variable and is thought to be inversely proportional to the maturity of the lesion.

The non-caseating granuloma (Fig. 5) is usually slightly hypodense or isodense to the surrounding brain tissue on CT studies. On contrast-enhanced CT (CECT), these solid lesions are characteristically round, oval, or lobular, and they enhance homogenously. On MR imaging, these lesions are hypointense relative to brain tissue on T1-weighted images and hyperintense on T2-weighted acquisitions. On contrast-enhanced MR studies, homogenous enhancement is seen. In the early stage of these lesions, they are frequently surrounded by a halo of contiguous vasogenic white matter edema, which can be demonstrated by CT and MRI [1, 10].

In the solid, caseating granuloma (Figs. 6, 7) the central portion enhances heterogenously, whereas the capsule presents a ring-enhancing pattern. This ring enhancement tends to be unbroken and is usually of uniform thickness [21]. This type of lesion appears relatively hypointense or isointense on T1-weighted images and isointense to hypointense on T2-weighted images. The rim of a caseating TB granuloma is often strikingly hypointense on T2-weighted images and enhances on T1-weighted gadolinium-enhanced MR imaging. The reason for shortening of the T2 signal in some tuberculomas is not clear but may be the result of the presence of paramagnetic free radicals in the enclosed macrophages [1, 10].

In the next stage, central liquefaction of the tuberculoma develops. This granuloma with central liquefaction of caseous material (Fig. 8) is seen as a hypodense core surrounded by a dense ring of enhancement on CECT. The central signal is hypointense on T1-weighted images and hyperintense on T2-weighted images. T1-weighted gadolinium demonstrates intense rim enhancement of the lesion. In this stage, lesions may be indistinguishable on MR imaging from true tuberculous or pyogenic abscess formation [1, 10].

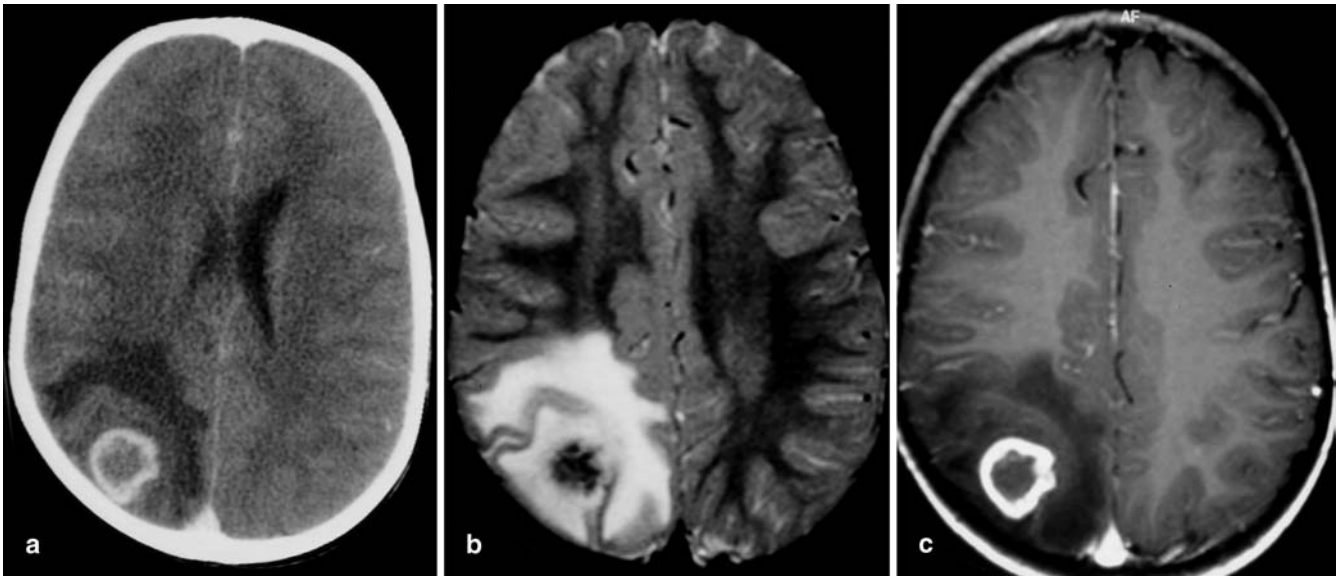


**Fig. 6a–c** Solid caseating granuloma. **a** Contrast-enhanced CT scan displays a ring-enhancing granuloma in the right occipital region with surrounding vasogenic edema. **b** Axial T2-weighted MR image shows that the center of the lesion is markedly hypointense, corresponding to caseous necrosis. The wall of the lesion is slightly hyperintense and is therefore not distinguishable from the perilesional edema. **c** Gadolinium-enhanced axial T1-weighted MR image shows strong ring-like enhancement of the thick wall. The center of the lesion does not enhance, nor does the surrounding edema

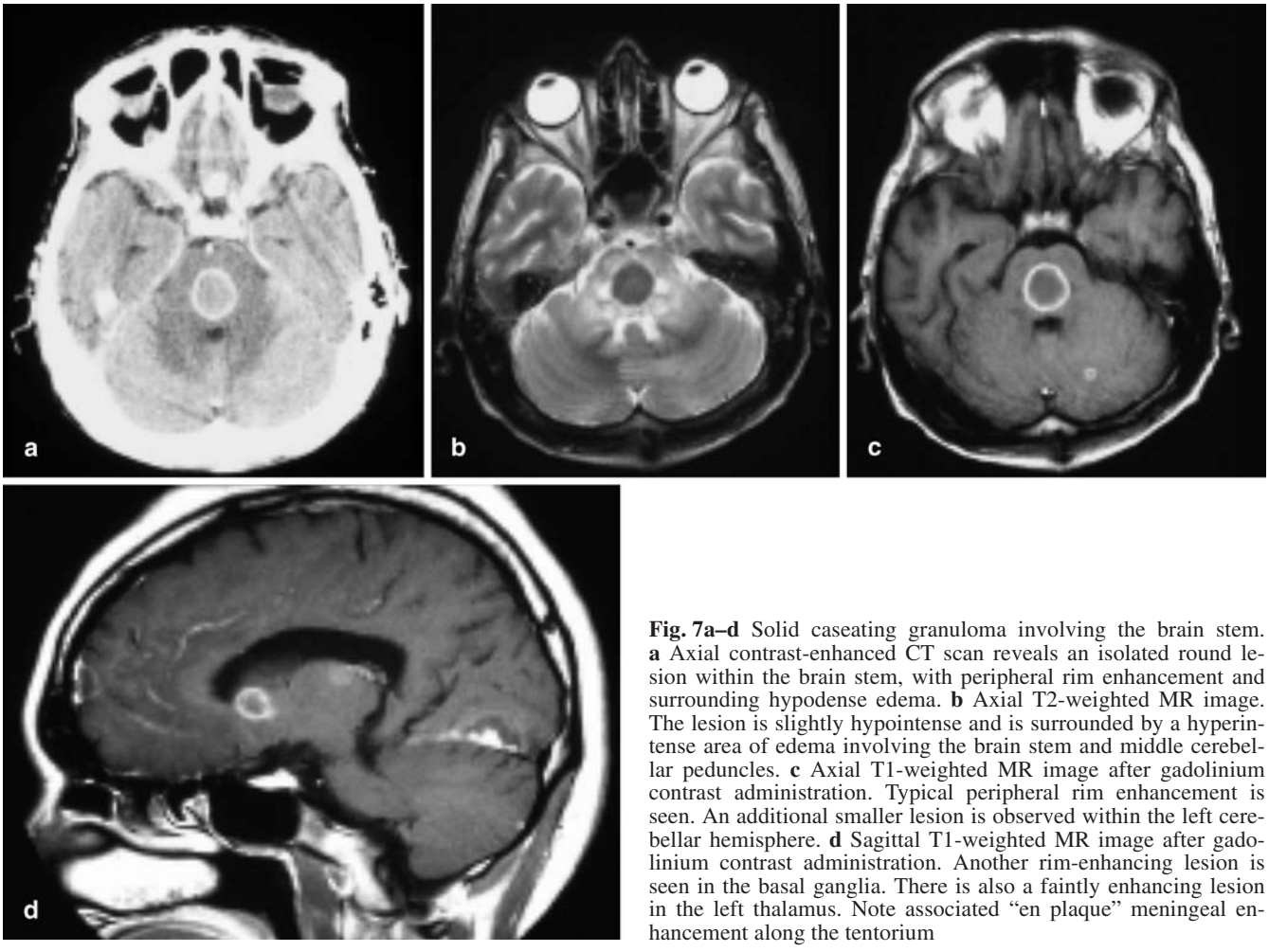


**Fig. 7a–d** Solid caseating granuloma involving the brain stem. **a** Axial contrast-enhanced CT scan reveals an isolated round lesion within the brain stem, with peripheral rim enhancement and surrounding hypodense edema. **b** Axial T2-weighted MR image. The lesion is slightly hypointense and is surrounded by a hyperintense area of edema involving the brain stem and middle cerebellar peduncles. **c** Axial T1-weighted MR image after gadolinium contrast administration. Typical peripheral rim enhancement is seen. An additional smaller lesion is observed within the left cerebellar hemisphere. **d** Sagittal T1-weighted MR image after gadolinium contrast administration. Another rim-enhancing lesion is seen in the basal ganglia. There is also a faintly enhancing lesion in the left thalamus. Note associated "en plaque" meningeal enhancement along the tentorium

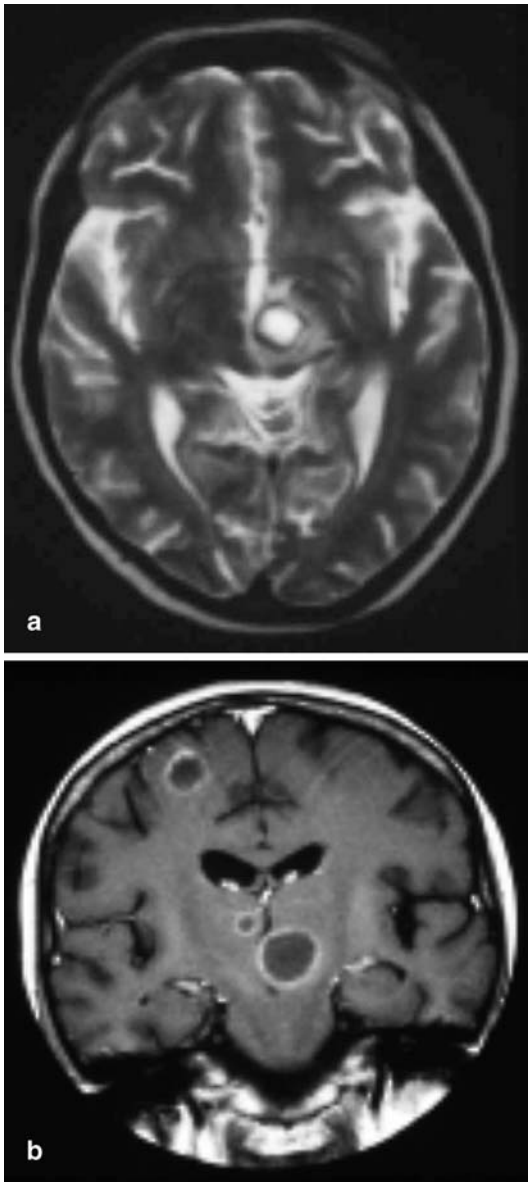


**Fig. 8a, b** Caseating granuloma with a liquid center. **a** On axial T2-weighted MR image, a hyperintense lesion in the left thalamus with hypointense rim is seen. The lesion impinges upon the third ventricle, and is surrounded by a halo of edema. Differential diagnosis in this stage includes a pyogenic abscess. **b** Coronal gadolinium-enhanced T1-weighted MR image demonstrates three rim-enhancing lesions with central hypointense area at the corticomedullary junction of the right parietal lobe, and within the right and the left thalamus, along the wall of the third ventricle

According to McGuinnes [10], the target sign, defined as a central nidus of calcification or central enhancement surrounded by a ring of enhancement, is a pathognomonic finding of CNS tuberculosis; however, recent studies have suggested that only the target sign with central calcifications is pathognomonic of tuberculoma, whereas the target sign with a central enhancing dot does not necessarily correspond to tuberculoma [35]. Such cases may represent reactivation of chronic calcified parenchymal lesions [29].

Miliary CNS tuberculomas usually are associated with TBM and many of these patients have a primary pulmonary focus of tuberculosis [1, 10]. Histologically, 2- to 3-mm granulomas are demonstrated. Miliary CNS tuberculosis generally occurs as a relatively silent clinical event [36]. The CECT and T1-weighted images after gadolinium administration may show numerous enhancing foci which are hyperintense on T2-weighted images [10, 37]

The differential diagnosis for parenchymal tuberculomas includes mainly other granulomatous processes (e.g., sarcoidosis, fungal lesions, parasitic disease such as cysticercosis and toxoplasmosis), multicentric primary neoplasms (e.g., hemangioblastomata, gliomata), as well as metastatic neoplasms [1, 4, 17]. Of additional help in the differential diagnosis may be the characteristic T2 shortening (Fig. 6), which is not found in most other space-occupying lesions [33]; however, imaging characteristics of tuberculomas may remain nonspecific. If such is the case, a high clinical index of suspicion for diagnosis of TB is provided by consideration of history and clinical findings, the use of serological investigations, and especially of follow-up under therapy [38]. As a rule, the radiological response can be monitored on CT and MRI within 4–6 weeks [6, 27]. Failure to make clinical or radiological improvement raises the suspicion of either drug resistance or misdiagnosis [10].

The activity of a tuberculoma may be judged by the degree of contrast enhancement on follow-up CT or MR imaging studies [10]. Occasionally, newly developing or enlarging intracranial tuberculomas may be observed despite appropriate antituberculous therapy [3, 5, 10, 31]. A possible explanation is the chemotherapy induced destruction of acid-fast bacilli and liberation of tuberculoprotein, resulting in an inflammatory reaction and swelling of the focus [31]. As a consequence, patients on antituberculosis therapy who develop signs of raised intracranial pressure or new neurological signs should have urgent neuro-imaging to exclude the development of new lesions or the enlargement of existing granulomas located in close proximity to strategic points of possible CSF obstruction [28].

Late changes include calcifications and regional atrophy, although many lesions leave no radiological traces following successful medical treatment [10, 29].

## Tuberculous abscess

Tuberculous abscess formation is a rare complication, observed in less than 10% of all patients with CNS tuberculosis [12]. A tuberculous abscess develops from pa-

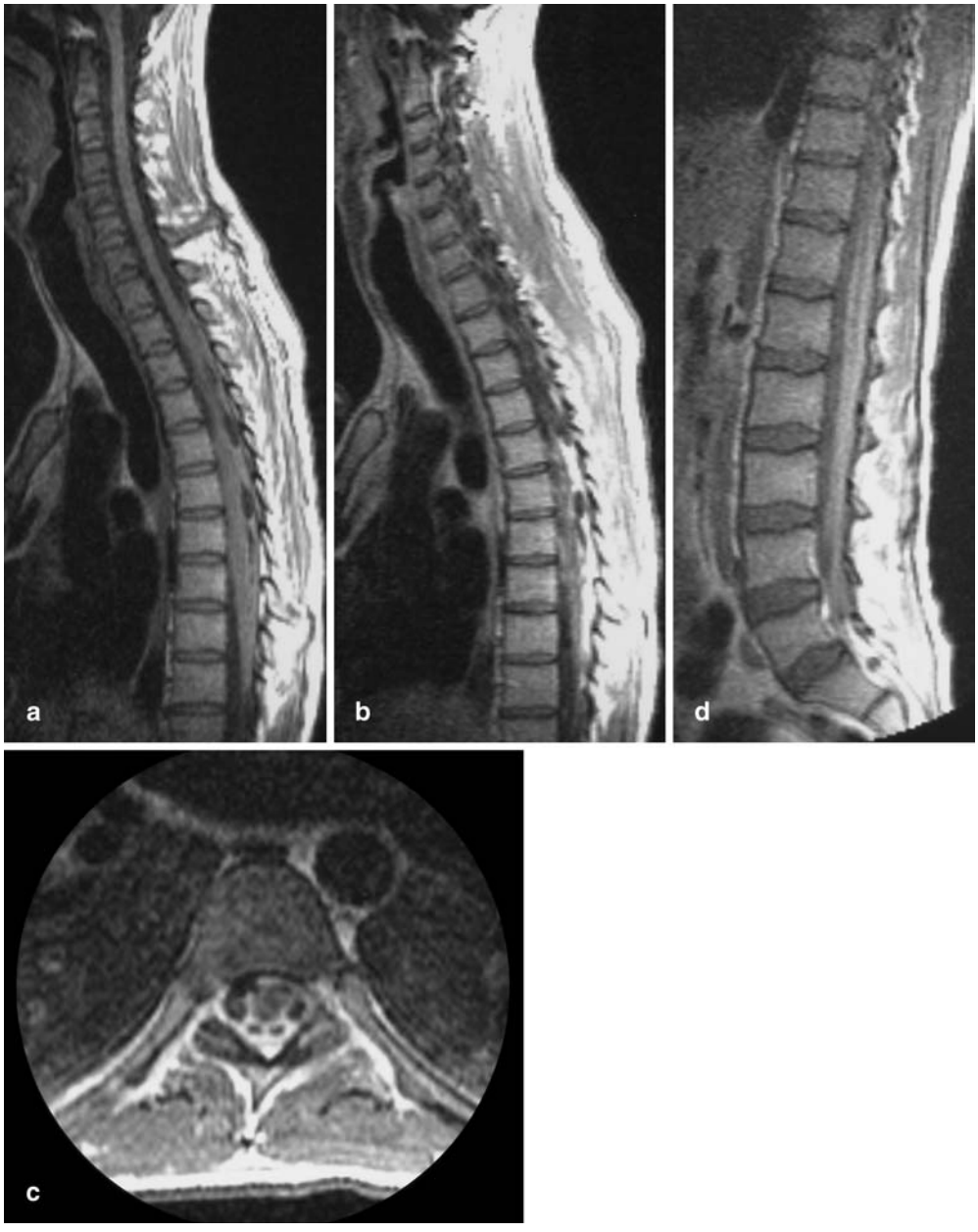


**Fig. 9a–d** Tuberculous radiculomyelitis. **a** Sagittal T1-weighted MR image of the cervico-thoracic spine demonstrates loss of definition between the thoracic spinal cord and the surrounding subarachnoid spaces, with heterogenous intermediate signal intensities. Areas of low signal intensity behind the thoracic cord are due to CSF loculations. **b**, **c** Sagittal and axial gadolinium-enhanced T1-weighted MR images depict heterogenous enhancement of the dura-arachnoid complex with anterior displacement of the spinal cord. Note absence of enhancement within the CSF loculations posterior to the thoracic cord. **d** Sagittal gadolinium-enhanced T1-weighted MR image of the lumbar spine reveals thickening, enhancement, and clumping of the nerve roots of the cauda

renchymal tuberculous granulomas or the spread of tuberculous foci in the meninges to the brain substance in patients with TBM [10]. In contrast to a tuberculoma, which contain few bacilli, a TB abscess is formed by semiliquid pus that is teeming with tubercle bacilli. The wall lacks the giant cell epithelioid granulomatous reaction of a TB granuloma [7, 12].

The TB abscesses have a more accelerated clinical course than tuberculomas, usually presenting acutely with fever, headache, and focal neurological signs [4].

As previously mentioned, tuberculous abscesses may be indistinguishable from caseating granulomas with a liquid center. On imaging studies they might differ from tuberculomas by their generally larger size (often >3 cm in diameter), thin walls, more rapid course, multiloculation, and often solitary nature [7, 11, 12].

## Focal tuberculous cerebritis

Focal tuberculous cerebritis is an infrequent clinicoradiological pattern reported in non-AIDS patients, presenting as intense focal gyral enhancement [39]. Microscopically, it is characterized by microgranulomata, lymphocytic infiltrate, Langerhans' giant cells, epithelioid cells, and variable evidence of scarce tubercle bacilli [3].

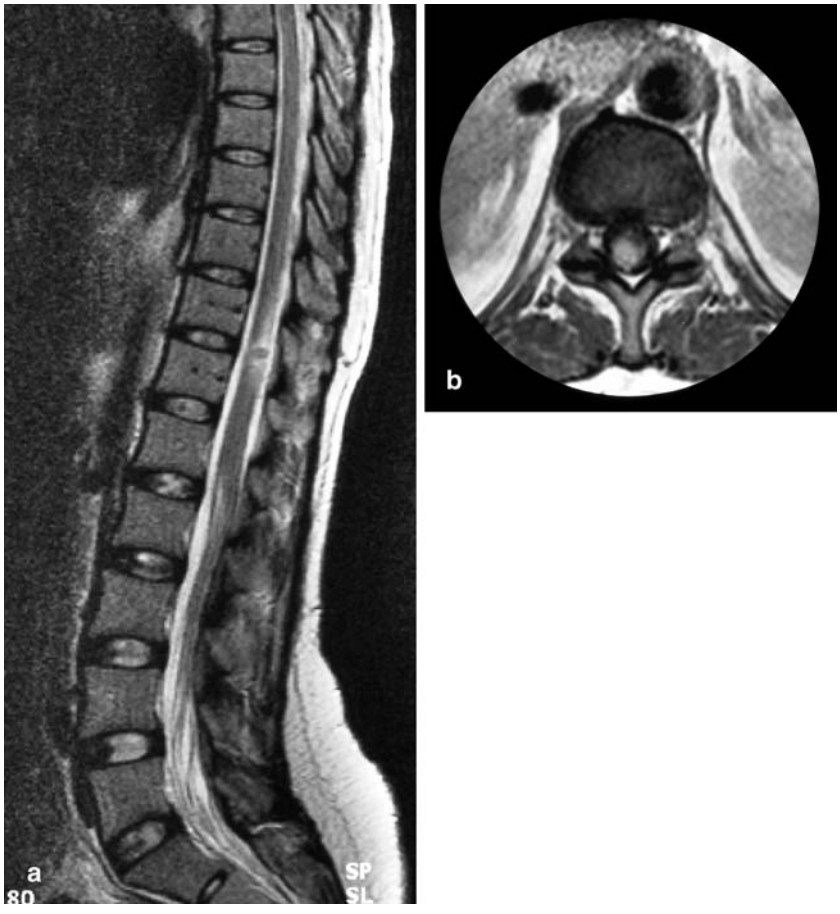


**Fig. 10a, b** Intramedullary TB granuloma involving the thoracic spine. **a** On a midsagittal T2-weighted MR image, a hypointense intramedullary lesion with surrounding hyperintense edema is seen at the Th11–Th12 level. There is mild fusiform cord enlargement. **b** Axial gadolinium-enhanced T1-weighted MR image demonstrates a focal enhancing intramedullary nodule

### Tuberculous encephalopathy

Tuberculous encephalopathy is a diffuse cerebral disorder usually occurring in young children or infants with pulmonary TB. Extensive damage to the white matter may occur together with the infrequent onset of perivascular demyelination on the basis of an "allergic" delayed type-IV hypersensitivity mechanism due to cell-mediated immunity to tuberculoprotein.

Drowsiness and coma supervene early in this diffuse cerebral disorder, whereas meningitic signs and vascular changes are absent, mild, or delayed.

In the diagnostic work-up, CSF shows only mild inflammatory changes. Severe brain edema may be seen on CT or MR imaging which may at times be referred more to one cerebral hemisphere. Death often occurs within 1–2 months of onset of neurological illness despite antituberculous medical treatment [13].

## Spinal tuberculosis

With the advance of MRI techniques, increasingly more cases are discovered of spinal TB. As opposed to other spinal infections, TB tends to involve all the intraspinal elements simultaneously [40, 41]. Spinal TB may take a variety of forms, including tuberculous radiculomyelitis, myelitic tuberculoma, epidural phlegmon, and abscess. Clinically, a patient with tuberculous infection of the spinal canal may present acutely with back pain, paresthesia, muscular weakness, and sphincter dysfunction; however, a more insidious onset can occur, with a progressive pattern of symptoms mimicking intraspinal tumor, polyradiculopathy, or spinal demyelinization [8, 40]. The TB bacilli are rarely found in the CSF [40, 41]; therefore, imaging plays once again a pivotal role in suggesting the correct diagnosis. Magnetic resonance imaging should be the primary imaging modality in the screening of patients with suspected intraspinal TB, since MRI better delineates the extent of leptomeningeal disease than CT myelography and allows direct evaluation of intramedullary lesions and associated epidural or osseous pathology of the spine [41, 42].

### Tuberculous radiculomyelitis

Tuberculous leptomeningitis in the spinal canal frequently involves the spinal cord and nerve roots. This condition is known as tuberculous radiculomyelitis (TBRM).

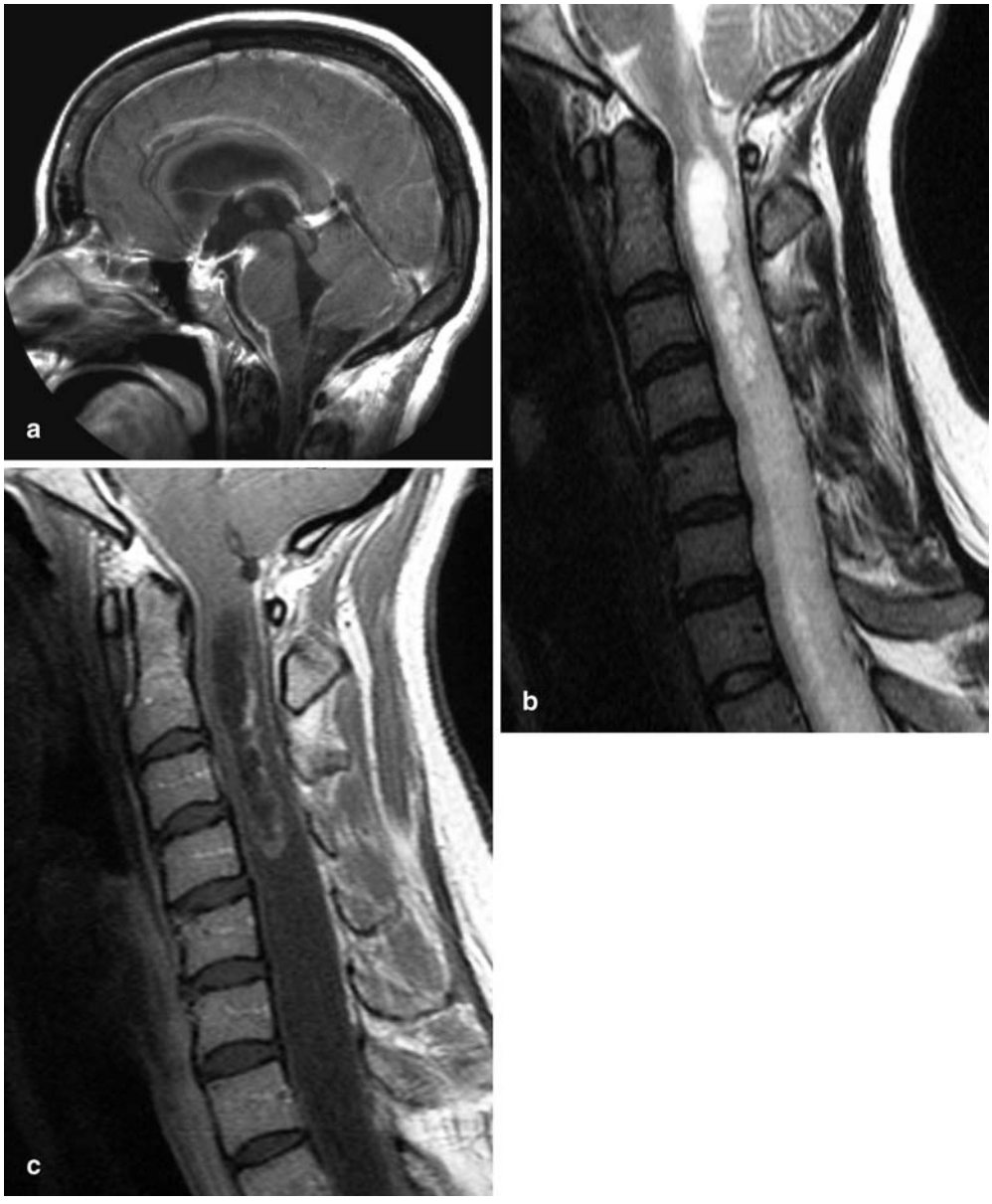


**Fig. 11a–c** Intramedullary tuberculoma indistinguishable from an abscess at the level of the cervical spine. **a** Midsagittal gadolinium-enhanced T1-weighted MR image through the brain. Prominent leptomeningeal enhancement in the prepontine and suprasellar cisterns is seen. Note the thickening and enhancement of the pituitary stalk. **b** Sagittal T2-weighted MR image of the cervical spine reveals diffuse cord swelling and a focal intramedullary central cavitating granuloma or abscess extending from C1 to C4. **c** Gadolinium-enhanced T1-weighted MR image demonstrates peripheral enhancement of the intramedullary lesion. Additionally, the cord is outlined by linear areas of leptomeningeal enhancement, which are continuous with the enhancing prepontine cisterns

It frequently accompanies intracranial disease and should be suspected whenever a patient with TBM develops spinal cord symptoms [4, 40, 43]. The thoracic cord is most commonly affected, followed by the lumbar and the cervical regions [4, 15].

The pathogenesis of TBRM can be explained in three ways:

1. As a primary tuberculous lesion from hematogenous spread from a source outside the CNS
2. Via secondary extension of cranial tuberculous meningoencephalitis
3. By secondary intraspinal extension from tuberculous spondylitis [1, 8]

Pathologically, it is characterized by a gross granulomatous exudate that fills the subarachnoid space and extends over several segments. Vasculitis of the spinal arteries may lead to spinal cord ischemia. The cord and nerve roots may become also inflamed and are edematous. With time, exudates get organized and fibrin-coated nerve roots can become adherent to each other as well to the thecal sac [4, 40].

The TBRM should be suspected whenever a patient with TBM develops spinal cord symptoms [43]. Although the contents of the spinal canal may be difficult to see on CT, some CT findings have been reported in TBRM, such as gross volume changes of the myelum, pear-shaped cross section in the lower thoracic region,

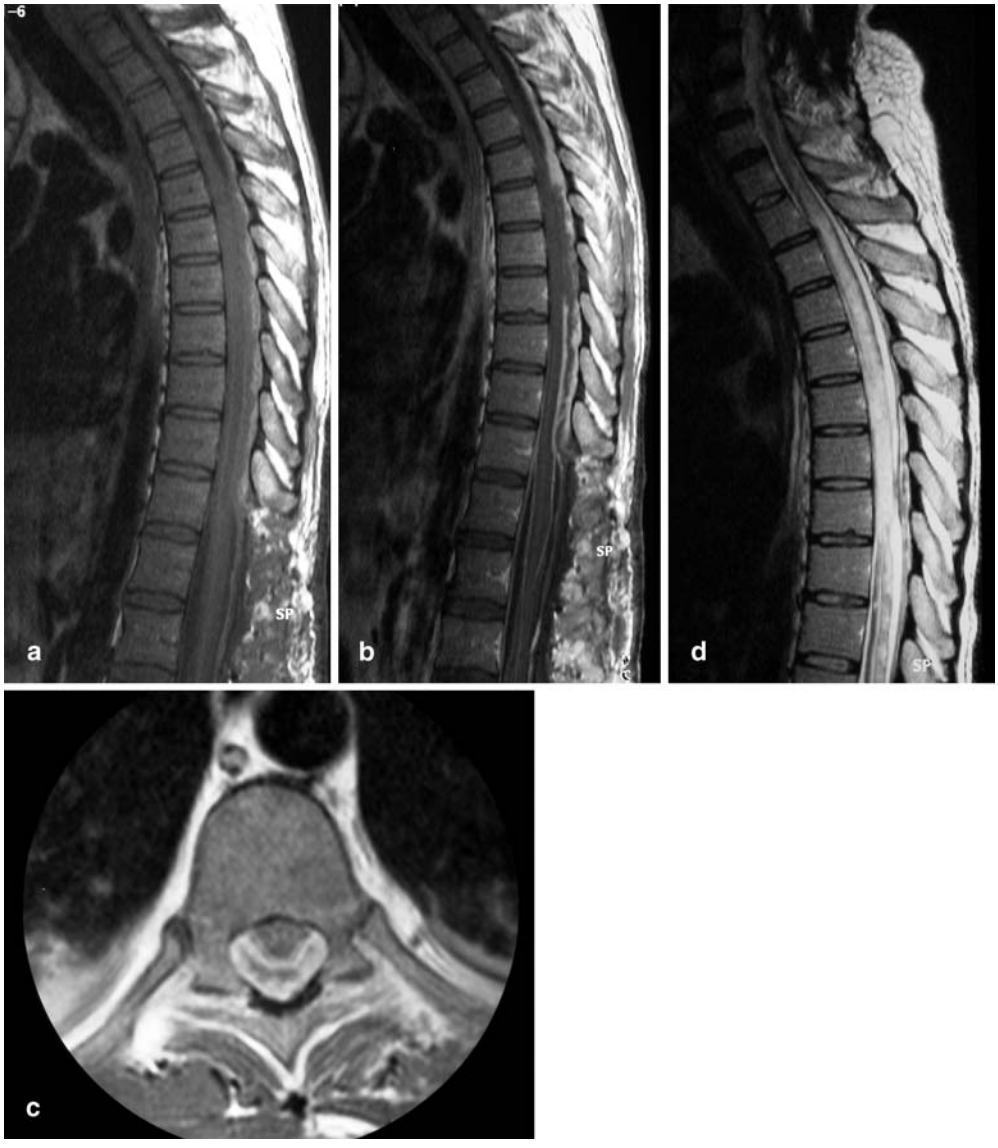


**Fig. 12a–d** Recurrent thoracic epidural abscess with associated radiculomyelitis. **a** Sagittal T1-weighted MR image demonstrates poor outline of the spinal cord, due to a combined thickening of the posterior epidural space and the dura-leptomeningeal complex, which is of relatively high signal intensity compared with the spinal cord. Note the presence of a laminectomy defect at the thoraco-lumbar junction. **b** On this gadolinium-enhanced midsagittal T1-weighted MR image an epidural empyema with associated radiculomyelitis is noted. The conus medullaris and thoracic cord are outlined by pial enhancement. **c** Axial gadolinium-enhanced T1-weighted MR image. A peripheral enhancing extradural mass displaces the spinal cord anteriorly. Note also faint enhancement of the leptomeninges. **d** Sagittal T2-weighted MR image 1 month after start of treatment reveals a heterogenous high signal intensity within the spinal cord due to progressive myelitis

related extra-axial mass lesions, and associated spinal tuberculous osteomyelitis. Administration of intravenous contrast may be of value in enhancing epidural tuberculous granulation tissue or any paravertebral abscess [8]. The MR imaging features of spinal tuberculous meningitis include cerebrospinal fluid loculations, obliteration of the spinal subarachnoid space with loss of outline of the spinal cord in the cervicothoracic spine (Fig. 9a), and thickened, clumped nerve roots in the lumbar region. The spinal cord can be directly or indirectly affected, with diffuse high signal intensity changes on T2-weighted images representing edema, cord infarction, or myelitis. Contrast-enhanced MR imaging reveals a linear or nodular enhancement coating the nerve roots and spinal cord or a thick intradural enhancement completely filling the subarachnoid space (Fig. 9b–d). Contrast-enhanced MRI is helpful in differentiating active tuberculous granulomatous disease from chronic fibrotic adhesions and in separating tuberculoma from surrounding edema, as areas of both fibrotic tissue and edema fail to enhance [2, 4, 8, 15, 39, 42].

Syringomyelia is a well-known complication of TBRM. Inflammatory edema and spinal cord ischemia appear to be the underlying mechanisms in the early cases, whereas chronic arachnoiditis underlies late-onset cases [4]. Indeed, focal scarring in the subarachnoid spaces impedes free circulation of CSF, thus forcing CSF into the central canal of the spinal cord via Virchow-Robin spaces. Focal cystic dilatations in the cord eventually coalesce to form a syrinx [44]. On MRI syringomyelia presents as a central cavity that is isointense to CSF on both pulse sequences and does not enhance [2].

Tuberculous arachnoiditis can mimic other infections as well as neoplastic, granulomatous, demyelinating, and iatrogenic conditions [8]. It is different from other types of arachnoiditis in that it frequently involves the spinal cord, meninges and the nerve roots simultaneously [8, 40, 41]. The most important differential diagnosis is meningeal carcinomatosis, which may be associated with multiple intracranial metastatic masses [40].

### Myelitic tuberculomas

Myelitic tuberculomas are very rare. The ratio of intracranial to intraspinal tuberculomas ranges between 20:1 and 42:1 [1]. They arise from hematogenous dissemination [2]. The MR findings are similar to the characteristic appearance of intracranial tuberculomas (Figs. 10, 11) [45]. Infrequent cases of intramedullary tuberculous abscesses have been reported [46].

Neuroimaging findings are nonspecific and the differential diagnosis of intramedullary tuberculomas includes neoplastic, inflammatory, demyelinating, vascular, and other granulomatous lesions. Correlation of clinical findings, history, and the peculiar hypo- or isointensity on T2-weighted images within the spinal cord can help in making the diagnosis of intramedullary tuberculoma [45].

### Extrinsic tuberculous involvement

Extrinsic tuberculous involvement of the spinal cord is usually secondary to epidural abscess formation. They often extend directly from infections of the spinal column. Epidural TB lesions generally appear to be isointense to the spinal cord on T1-weighted (Fig. 12a) and of mixed signal intensity on T2-weighted images. Enhancement after gadolinium will be uniform if the TB inflammatory process is phlegmonous in nature or peripheral if true epidural abscess or caseation has occurred (Fig. 12b, c) [1].

## Conclusion

A CNS infection with *Mycobacterium tuberculosis* occurs either in a diffuse form as basal exudative leptomeningitis or in localized forms as tuberculoma, abscess, or cerebritis. Tuberculosis of the central nervous system is still a major cause of death or significant neurological disability. Consequently, prompt diagnosis and early treatment are of utmost importance to reduce morbidity and mortality. Imaging is a cornerstone in early diagnosis. Generally, MR imaging appears to be superior to CT in the detection and assessment of CNS tuberculosis. Sequential imaging is recommended to monitor therapy response and to identify unexpected or asymptomatic complications of TB during treatment.

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