CME Article

Manifestations of cerebral tuberculosis

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ABSTRACT

Intracranial tuberculosis continues to be a serious problem in both the developing and developed world, with significant morbidity and mortality. It has protean manifestations and at times, poses significant diagnostic challenges to both the radiologist and the treating physician. This pictorial essay aims to acquaint the radiologist with the varied imaging spectrum of intracranial tuberculosis, both the common and uncommon appearances.

Keywords: meningitis, miliary, tuberculoma, tuberculosis

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INTRODUCTION

Tuberculosis continues to be an important cause of morbidity and mortality throughout the world. According to the 13th annual report on global control of tuberculosis published by the World Health Organization, an estimated 9.27 million cases of tuberculosis were discovered in 2007, with the number of cases showing an upward trend.[1] Overall, both the incidence and prevalence of tuberculosis continue to be higher in developing countries.

Although tuberculosis most commonly involves the lungs, one with the involvement of the central nervous system (CNS) is the most serious type of systemic tuberculosis due to its high mortality rate, common neurological complications and sequelae.[2] The involvement of the CNS occurs in 2%–5% of all patients with tuberculosis and in 10% of those with acquired immunodeficiency syndrome (AIDS)-related tuberculosis. Synchronous extraneural tuberculosis is reported in up to 50% of cases of neurotuberculosis, and may be an important clue to the diagnosis of CNS tuberculosis, if present.[2,3]

PATHOLOGY

Tuberculous infections of the brain are most commonly caused by haematogenous spread of *Mycobacterium tuberculosis* secondary to a disease focus elsewhere in the body, such as the lung or the gastrointestinal tract, usually due to an affected lymph node eroding into a vessel.[2,4] The initial tuberculous lesions may develop either in the brain parenchyma or the meninges, and are known as Rich foci when they occur in the CNS.

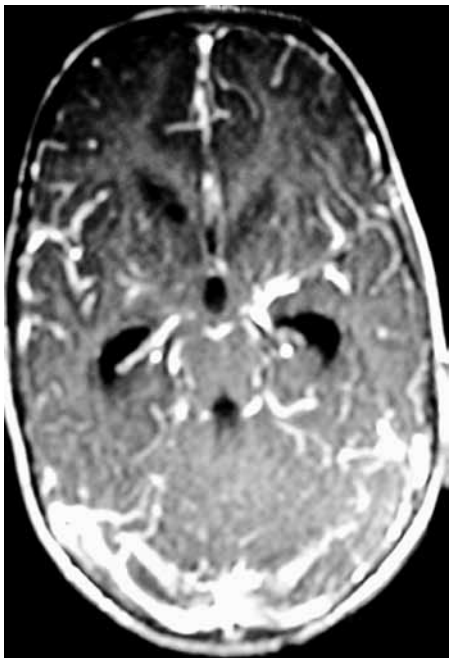


Fig. 1 Gadolinium-enhanced axial MR image in a known case of tubercular meningitis shows marked leptomeningeal enhancement along the sylvian fissure and tentorium. Mild ventricular prominence is also seen.

Intracranial manifestations of tuberculosis include meningeal and intraparenchymal diseases. Intraparenchymal disease usually presents as solitary or multiple tuberculoma. Meningitis may or may not be present.[4-6] Other possible forms of intraparenchymal manifestations include tuberculous abscesses, cerebritis and tuberculous encephalopathy. Tuberculous meningitis is believed to be caused by cerebrospinal fluid seeding from the rupture of pial or subependymal granuloma.[7] Involvement of a vessel in the subarachnoid space may also lead to subsequent involvement of the surrounding meninges.[2] Rarely, meningeal involvement may be due to contiguous spread from tubercular involvement of the mastoids or sphenoid sinuses.[2,6]

CRANIAL MENINGEAL TUBERCULOSIS

Patients with leptomeningeal tuberculosis show abnormal meningeal enhancement and basal exudates. Meningeal enhancement (Fig. 1) has been found in up to 90% of cases and is considered to be the most sensitive feature of tubercular meningitis.[8,9] On computed tomography (CT) images, obliteration of the basal cisterns by isodense or mildly hyperdense exudates is a common finding in cranial

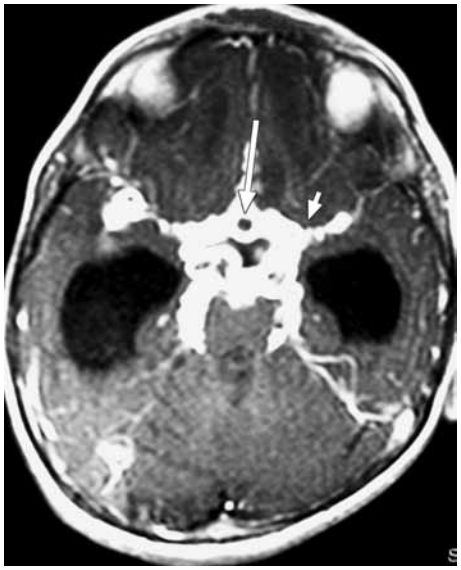


Fig. 2 Post-contrast axial MR image shows diffuse homogenous enhancement predominantly involving the basal cisterns (arrowhead). Associated ring-enhancing tuberculomas are also seen in the suprasellar cistern (arrow) and right sylvian fissure. Dilatation of the temporal horns is due to obstructive hydrocephalus at the level of the aqueduct (not shown).

tuberculous meningitis (CTBM).[2,6,10] The presence of hyperdense basal cisterns on non-contrast imaging was found by Andronikou et al to be the most specific feature of CTBM (100%).[8]

Meningeal involvement may not be appreciated on non-contrast magnetic resonance (MR) images, but is usually well demonstrated on post-contrast T1-weighted images. Recently, some authors have suggested the role of contrast-enhanced fluid-attenuated inversion recovery (FLAIR) imaging in the cases of leptomeningitis, including tuberculous meningitis. A recent study by Parmar et al suggested that post-contrast FLAIR images may have similar sensitivity but higher specificity compared to contrast-enhanced T1-weighted images for detection of leptomeningeal enhancement. Post-contrast FLAIR thus might be a useful adjunct in the evaluation of patients with suspected tuberculosis.[11]

In the basal cisterns, these exudates are most severe around the circle of Willis (Fig. 2), often extending to the ambient, sylvian and pontine cisterns, and around the optic chiasm.[2,6,10] Exudative meningitis may result in necrotising panarteritis, with secondary thrombosis and occlusion of small- and medium-sized vessels at the base of the brain, particularly the lenticulostriate and thalamoperforating arteries, vessels which perfuse the so called medial TB zone.[12] Consequent ischaemic infarcts that occur are a common complication of CTBM, and have been found by Dastur et al in 41% of cases in an autopsy series.[13] Bilateral involvement is also a useful distinguishing feature.

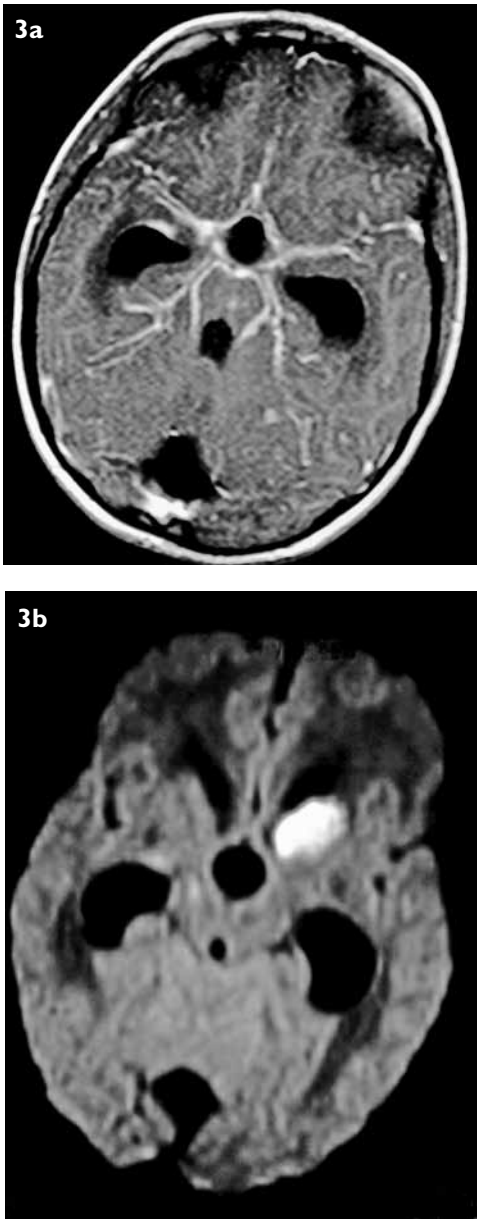
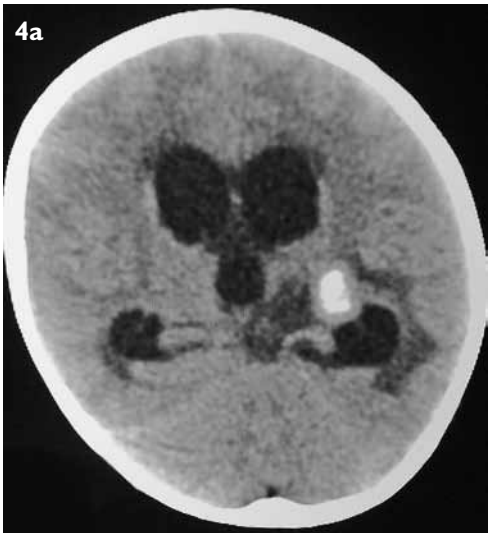


Fig. 3 (a) Post-contrast axial MR image shows enhancing basal exudates with associated hydrocephalus. (b) Diffusion-weighted MR image of the same patient reveals acute infarct in the left caudate nucleus. The triad of basal exudates, infarctions and hydrocephalus is considered highly specific for tuberculous meningitis.

Communicating hydrocephalus, the most common complication of CTBM, is usually secondary to obstruction of cerebrospinal fluid flow caused by meningeal exudates in the basal cisterns.[2,4] In some cases, the hydrocephalus may be non-communicating, resulting from obstruction due to tuberculomas or rarely, tuberculous abscess. The presence of basal exudates, infarcts and hydrocephalus is considered the diagnostic triad of tubercular meningitis.[2] It is considered almost 100% specific but has lower sensitivity (Fig. 3).[8]

Cranial nerve palsies can also occur in CTBM, most commonly affecting the third, fourth and sixth cranial



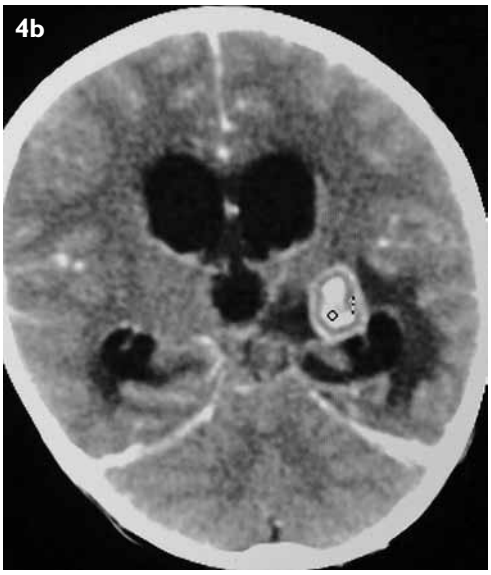
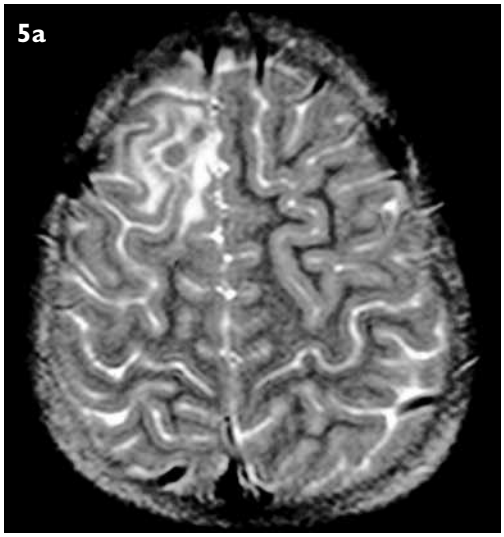


Fig. 4 (a) Axial non-contrast CT image shows a calcified lesion in the left periventricular region, with associated hydrocephalus. (b) Contrast-enhanced axial CT image shows ring enhancement around the calcified lesion, suggestive of Target sign.



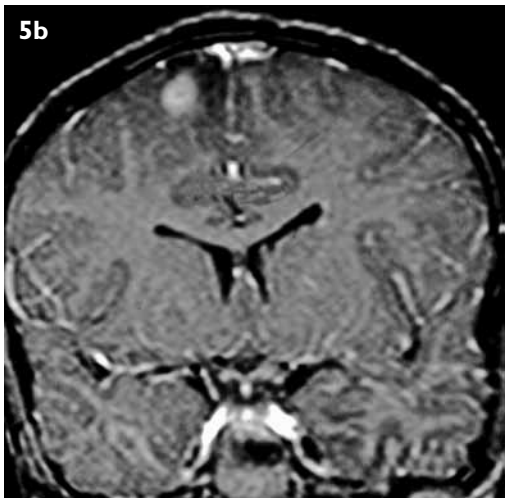


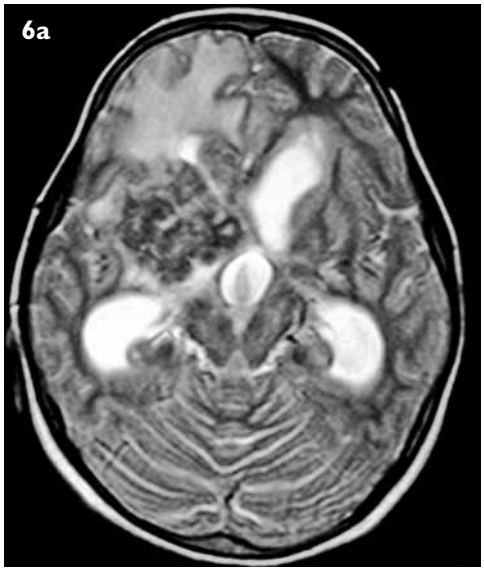
Fig. 5 Non-caseating tuberculoma. (a) T2-W axial MR image shows isointense nodular lesions in the right high parietal region, with associated perilesional oedema. (b) Post-contrast coronal image shows an enhancing nodular granuloma.

nerve, although other nerves may also be involved.[6] Cranial nerve impairment may result from vascular compromise, leading to ischaemia, or may be due to entrapment of the nerve in basal exudates. The proximal portion of the nerve at the root entry zone is the most susceptible, and may show thickening and enhancement on post-contrast T1-weighted images.[2]

INTRACRANIAL TUBERCULOMAS

Intraparenchymal tuberculomas are thought to be secondary to an infective focus elsewhere in the body.[6] In adults, they are commonly multiple and occur in the frontal and parietal lobes. Children, on the other hand, have a predominance of infratentorial lesions.[2,6,10,14] On CT, tuberculomas have variable appearances, and may appear hypo- or hyperdense to the brain parenchyma. In rare cases, a ring-enhancing lesion with a hypodense centre may reveal a central calcification. This is known as the 'target sign' (Fig. 4) and is considered characteristic of tuberculoma by some authors, while others consider it to be nonspecific and leading to erroneous diagnoses.[6,7]

Due to its inherently superior soft tissue contrast, the MR appearance of intracranial tuberculomas is usually more specific than the CT appearance. Non-caseating tuberculomas are hypointense to brain parenchyma on T1-weighted images, hyperintense on T2-weighted images and show intense nodular enhancement on post-contrast images (Fig. 5). In most cases, subsequent caseous central necrosis develops, which is initially solid. The lesion then appears hypo- to isointense on T1-weighted images and hypointense on T2-weighted images. As the central caseating component is avascular, ring enhancement is seen on post-contrast images (Fig. 6). In some cases,



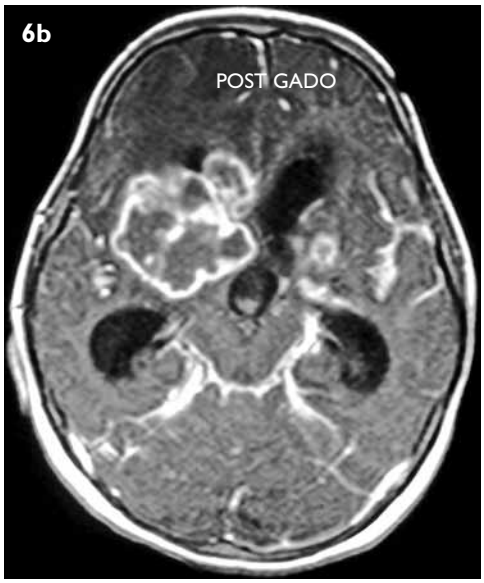
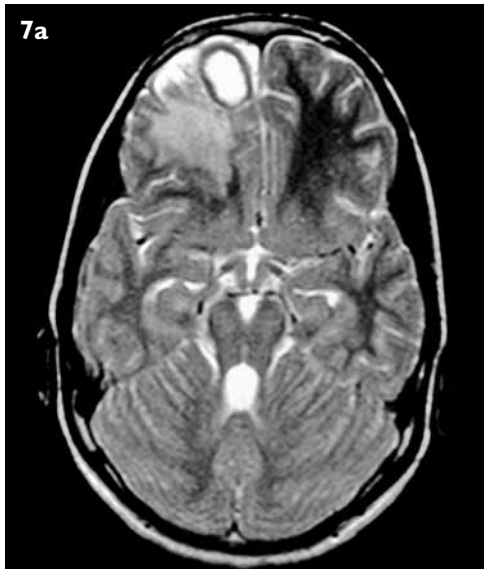


Fig. 6 Caseating tuberculoma without liquefaction. (a) T2-W axial MR image shows hypointense lesions in the bilateral ganglia-thalamic regions (more on the right side), with perilesional oedema. Note the associated hydrocephalus. (b) Post-contrast axial image shows multiple ring-enhancing lesions, along with abnormal leptomeningeal enhancement.



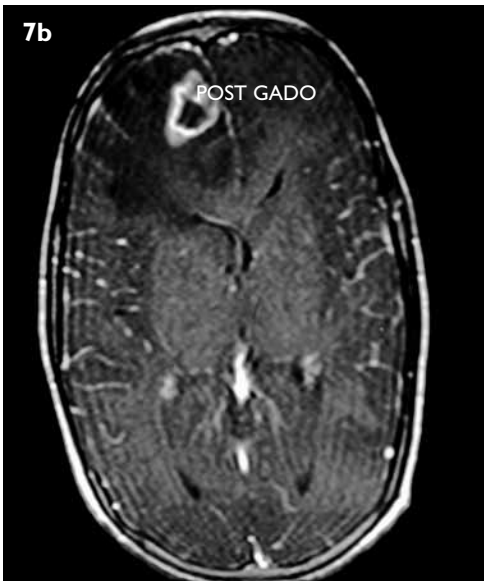


Fig. 7 Caseating tuberculoma with liquefaction. (a) T2-W axial MR image shows a centrally hyperintense granuloma with a peripheral hypointense rim. There is associated perilesional oedema. (b) Gadolinium-enhanced T1-W axial image shows peripheral ring enhancement of the same lesion.

the solid core eventually liquefies, and the tuberculoma then appears hypointense on T1-weighted images and hyperintense on T2-weighted images, with a peripheral hypointense capsule, representing tuberculoma capsule. These granulomas again show ring enhancement on post-gadolinium images (Fig. 7).

Less common but distinctive tuberculomas include en plaque meningeal and intraventricular forms. An en plaque meningeal tuberculoma is rarely seen, manifesting as a dural-based, mass-forming localised meningeal process, which may superficially resemble en plaque meningioma or secondary meningeal neoplastic disease.[7] En plaque tuberculomas are more common along the frontal and parietal convexities, but have also been reported along the tentorium, in the posterior fossa and interhemispheric fissure.[15]

On non-contrast CT images, these lesions appear hyperdense. On T1-weighted images, they appear isointense to brain parenchyma. Their appearance on T2-weighted images depends on the presence or absence of central necrosis, with those having central caseation appearing hypointense. On post-contrast images, the lesions may show homogenous or peripheral enhancement, depending on the presence or absence of central caseation (Fig. 8). Broad dural attachments may be seen occasionally, with prominent feeding meningeal vessels.[16]

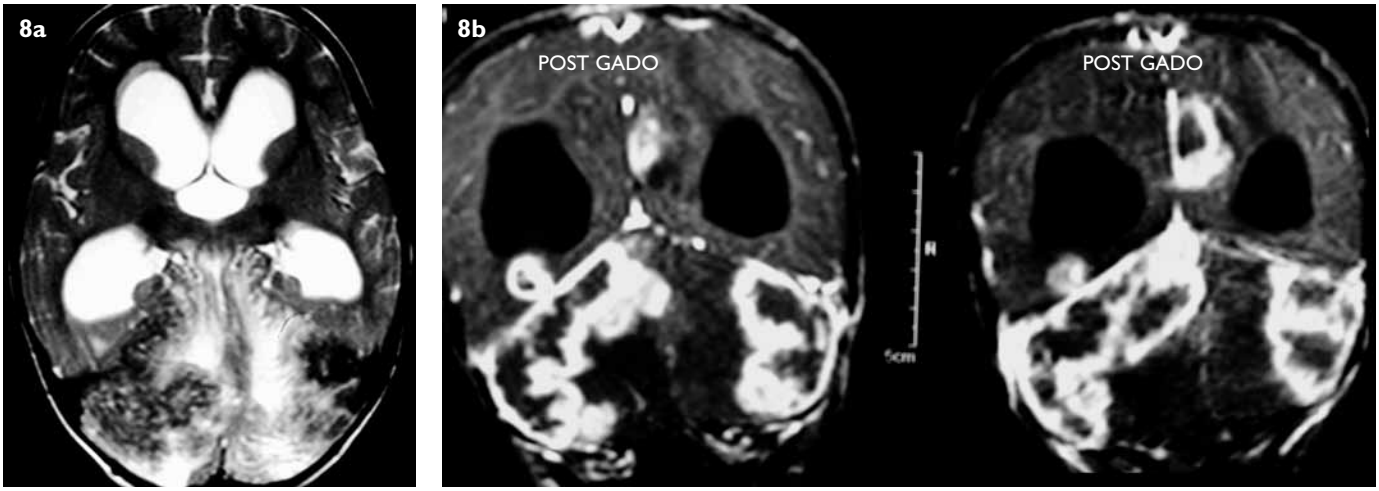


Fig. 8 En plaque tuberculoma. (a) T2-W axial image shows predominantly hypointense dural-based masses along the tentorium, with associated cerebellar oedema. (b) Gadolinium-enhanced coronal images show a peripheral rim of enhancement in the lesions. A similar lesion is also noted along the falx. Note the associated obstructive hydrocephalus.

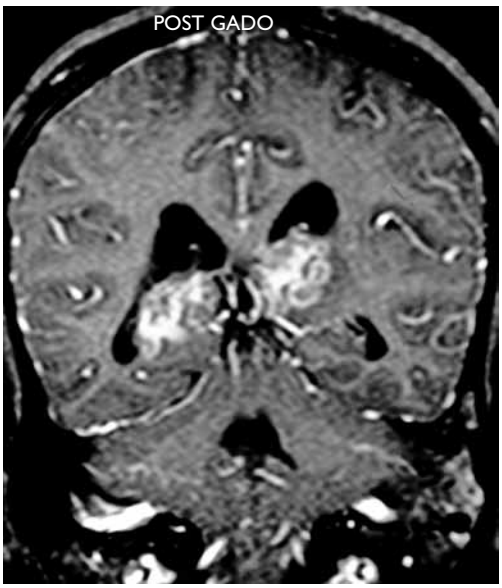


Fig. 9 Post-gadolinium coronal image shows poorly defined ring-enhancing conglomerate tuberculomas involving the choroid plexus of the bilateral lateral ventricles. Note the mild leptomeningeal enhancement along the cerebral convexity and tentorium on the right side due to meningitis.

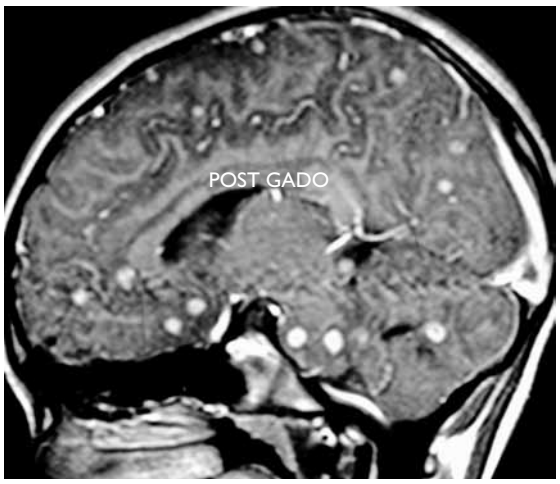


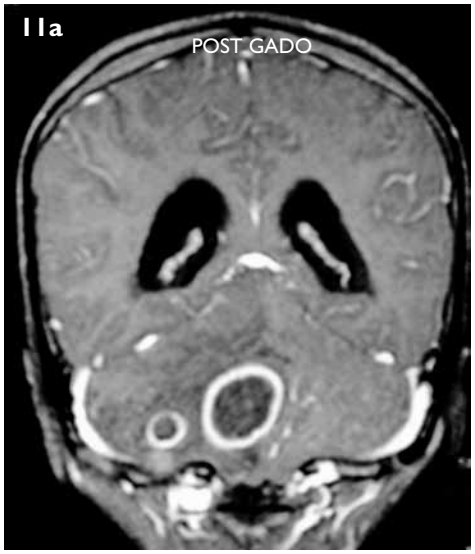
Fig. 10 Gadolinium-enhanced T1-W sagittal image shows multiple nodular-enhancing lesions scattered throughout the brain parenchyma, suggestive of disseminated tuberculomas. This patient also had miliary nodules on chest radiograph (not shown).

Intraventricular tuberculomas are also rarely reported, and may be associated with hydrocephalus, meningitis and ependymitis.[7] The exact route of entry of tubercle bacilli into the ventricles is controversial. Haematogenous spread through the choroid plexus appears to be the most likely mechanism. Tuberculomas usually occur in the lateral ventricles (Fig. 9). Intraventricular tuberculous abscesses have also been reported but are again extremely rare.[17]

Miliary CNS tuberculomas occur when there is diffuse infiltration of the brain by small granulomas that are less than 5 mm.[6] Contrast-enhanced CT, which may show multiple enhancing lesions and non-contrast MR are often suboptimal to detect intracranial miliary tuberculomas.[2,10] These are best appreciated on post-gadolinium images (Fig. 10).[6]

CRANIAL TUBERCULOUS ABSCESS

Tubercular abscesses are rare and seen in less than 10% of all patients with CNS tuberculosis.[2,10,18] They may be solitary or multiple and are more common in the geriatric age group or in those with compromised immune status.[7] On imaging studies, abscesses are commonly found at the junction of the gray and white matter in the supratentorial compartment.[6] A tubercular abscess may be indistinguishable from a caseating tuberculoma, a pyogenic abscess or a caseating tuberculoma with



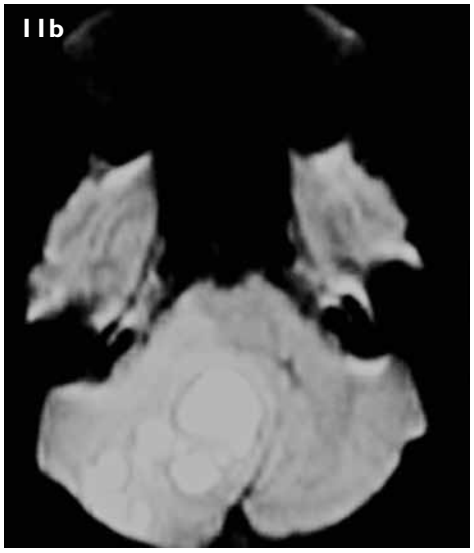


Fig. 11 Tubercular abscess. (a) Gadolinium-enhanced T1-W coronal image shows a large abscess, with peripheral enhancement and multiple smaller, similar surrounding lesions involving the right cerebellar hemisphere. (b) The lesions show restricted diffusion on diffusion-weighted images.

liquefaction (Fig. 11).[2,6] However, a tubercular abscess is more likely to show uniformly thin and enhancing smooth walls. It is usually larger than 3 cm in diameter and commonly has a multilocular appearance.[10]

FOCAL TUBERCULOUS CEREBRITIS

This entity was described as a unique clinicoradiologic pattern of involvement of the brain parenchyma by Jinkins based on a retrospective analysis of five patients.[19] CT imaging shows intense focal gyral enhancement (Fig. 12). On MR imaging, focal tuberculous cerebritis appears hypointense on T1-weighted and hyperintense on T2-weighted images, with post-contrast images showing small areas of patchy enhancement.

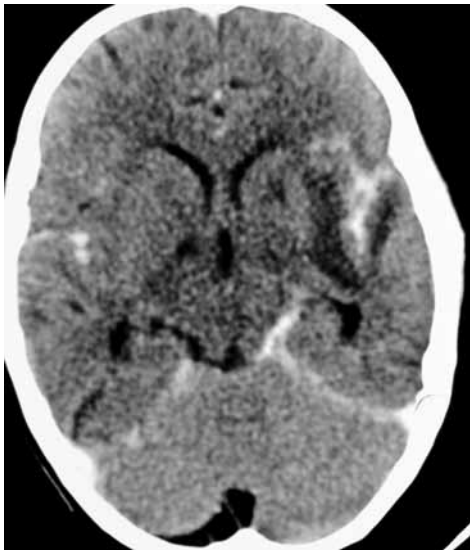
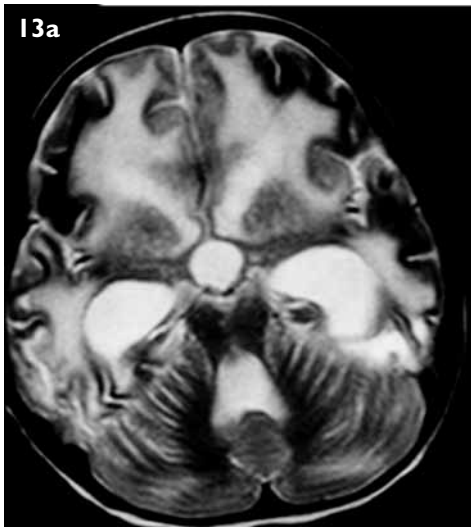


Fig. 12 Post-contrast axial CT image shows intense focal gyral enhancement in the region of the left sylvian fissure, with surrounding cerebral oedema, suggestive of focal cerebritis.



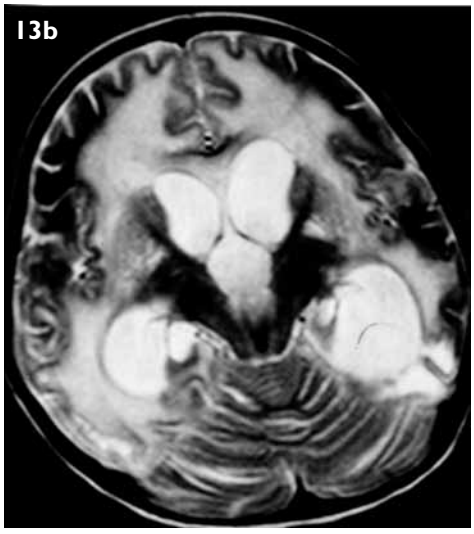


Fig. 13 (a & b) Axial T2-W MR images show diffused white matter oedema with gyral swelling. The patient had a history of anti-tubercular therapy for cerebral tuberculosis about six months prior to this presentation. Note the associated hydrocephalus.

TUBERCULOUS ENCEPHALOPATHY

The designation 'tuberculous encephalopathy' was first coined by Udani in 1958.[20] Its pathologic basis and probable pathogenesis were subsequently described by Dastur and Udani,[21] who suggested that the pathological basis of tuberculous encephalopathy was an allergic delayed type IV hypersensitivity reaction due to cell-mediated immunity to tuberculin protein. A distinctive feature of this entity is its occurrence in a younger child or infant with pulmonary tuberculosis. The brain examination reveals severe diffuse brain oedema and pallor, especially of the white matter. Brain imaging reveals severe unilateral or bilaterally asymmetrical brain oedema, especially of the white matter (Fig. 13).[2,10]

CONCLUSION

Tuberculosis of the CNS continues to pose challenges, both in diagnosis and management, with significant morbidity and mortality. It can have a myriad of imaging appearances, varying from meningitis to tuberculomas, tuberculous abscesses, focal cerebritis and tuberculous encephalopathy. Increased awareness of the imaging manifestations among radiologists would help suggest an early diagnosis and potentially contribute toward reducing morbidity and mortality.

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SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME
Multiple Choice Questions (Code SMJ 201102B)

	True	False
Question 1. Regarding tuberculomas:		
(a) They can have varying appearances on MR imaging based on the presence or absence of caseation and liquefaction.	☐	☐
(b) Children have a predominance of supratentorial lesions.	☐	☐
(c) They are commonly seen in the choroid plexus.	☐	☐
(d) They are commonly multiple.	☐	☐
Question 2. Regarding cranial meningeal tuberculosis:		
(a) Meningeal enhancement is the most sensitive feature of cranial tuberculous meningitis.	☐	☐
(b) It may be better seen on post contrast FLAIR images.	☐	☐
(c) It is usually more severe around the cerebral convexities.	☐	☐
(d) It is commonly associated with hydrocephalus and cerebral infarcts.	☐	☐
Question 3. Regarding cerebral tuberculosis:		
(a) It is commonly associated with synchronous extraneural tuberculosis.	☐	☐
(b) It may manifest as focal cerebritis.	☐	☐
(c) Tubercular abscesses are seen in up to 15% of all patients with CNS tuberculosis.	☐	☐
(d) Tubercular abscesses are more common in immunocompromised patients.	☐	☐
Question 4. Regarding en plaque tuberculomas:		
(a) They are common occurences.	☐	☐
(b) They may resemble meningiomas or meningeal neoplastic disease.	☐	☐
(c) They are never seen in the posterior fossa.	☐	☐
(d) They are usually hypodense on non-contrast CT images.	☐	☐
Question 5. Regarding miliary CNS tuberculomas:		
(a) There is diffuse infiltration of the brain by small tuberculomas.	☐	☐
(b) They are usually not seen on non-contrast CT.	☐	☐
(c) They are best seen on post-contrast CT.	☐	☐
(d) They may be associated with miliary pulmonary tuberculosis.	☐	☐

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RESULTS:
(1) Answers will be published in the SMJ April 2011 issue. (2) The MCR numbers of successful candidates will be posted online at www.sma.org.sg/cme/smj by 4 April 2011. (3) All online submissions will receive an automatic email acknowledgement. (4) Passing mark is 60%. No mark will be deducted for incorrect answers. (5) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council.

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