Central nervous system tuberculosis in children: neuroradiological patterns, complications and pitfalls

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Learning objectives

To describe and illustrate imaging features of tuberculous meningitis (TBM) on computed tomography (CT) and gadolinium-enhanced magnetic resonance (MR) studies based on a series of 30 children with clinical suspicion of TBM.

In this poster, we discuss our own experience with TBM in children and summarize the current literature.

Background

Central nervous system (CNS) tuberculosis is endemic in certain regions of the world, and, recently, the prevalence of tuberculosis (TB) has been on the rise worldwide as a result of the increased number of AIDS cases. TBM can be seen at any age, predominantly in young children and adolescents, because of their relative inability to contain the infection at sites beyond the lung. In fact, it is an important cause of childhood morbidity and mortality even in non-immunosuppressed children.

TBM is closely associated with miliary TB and a pathogenetic relationship is suspected, although it has been proposed that the two processes are unrelated. Inoculation with Mycobacterium tuberculosis occurs on inhalation of bacilli into pulmonary alveoli.
Hematogenous dissemination then occurs during the first week after infection, as the bacilli enter the bloodstream directly from the pulmonary vessels or from pulmonary lymphatics via the thoracic duct. The bacilli are distributed within the brain and meninges throughout the CNS but do not multiply as readily as they do in other organs. Involvement of the CNS usually becomes clinically apparent within 6 months of the initial infection. Meningitis probably results from rupture of small tuberculomas in the cortex, spinal cord, or leptomeninges; tuberculomas of the coroid plexus may be another source of infection. In TBM, a gelatinous exudate fills the pia-arachnoid along the basal cisterns, particularly the prepontine cistern (Figure 1 on page ), where it infiltrates and produces inflammation along the walls of the meningeal blood vessels. The small cortical blood vessels and perforating vessels are involved as the exudates spreads into the Virchow-Robin spaces. The basal ganglia and thalamus in the region of the lenticulostriate and thalamo-perforating arteries are involved by this vasculitis in almost half the cases. The thick exudate blocks the subarachoid spaces, causing hydrocephalus. The perineurium of the cranial nerves is infiltrated, causing neuropathies, particularly of cranial nerves II, VI, and VII. Small tubercles may lay over the convexity of the brain or in the periventricular area.

Fig.: Tuberculosis basilar meningitis in a 5-year-11-month-old girl. (A, B)Photographs of a gross specimen reveal thick purulent exudate, most predominantly in the basilar cisterns, especially around the circle of Willis.

References: L. N. Delfino; Radiology, Ospedale Bambino Gesù, Roma, ITALY

Post-primary CNS tuberculosis may manifest as diffuse pattern (leptomeningeal granulomatosis), focal pattern (cerebritis, granuloma, tuberculoma and abscess) and mixed pattern. TBM is the most common presentation of CNS infection.

After an insidious onset of nonspecific symptoms such as fever, nausea, vomiting and headache, the clinical progression of TBM tend to be rapid specially in infants and young children, with acute hydrocephalus, seizures, and cerebral edema. Early diagnosis
of TBM may be difficult due to these often non-specific signs and symptoms and inconclusive laboratory results.

Radiographic studies may aid in the early diagnosis of TBM, playing a critical role in patient management. CT and MR imaging are the main imaging techniques used in its localization and characterization. The imaging features overlap with other intracranial diseases, such as cysticercosis, metastases, and primary brain neoplasm.

**Imaging findings OR Procedure details**

In TBM, the common triad of neuroradiological findings is:

1. hydrocephalus;
2. basal meningeal enhancement;
3. infarction due to vasculitis.

**Hydrocephalus** is one of the most common complications of TBM occurring in up to 85% of children with the disease. It is more frequent and severe in children than in adults and also occurs at an earlier stage in the disease process. The hydrocephalus results primarily from obstruction of the basal cisterns by inflammatory exudate. It can be divided into two types: communicating, which is common, secondary to an obstruction of the basal cisterns by inflammatory exudates, and obstructive, which is less common and either secondary to a focal parenchymal lesion causing mass effect or due to the entrapment of a part of the ventricle by granulomatous ependymitis. Periventricular hyperintensity on proton density and T2-weighted images (T2WI) is due
to the seepage of the cerebral spinal fluid (CSF) across the white matter and usually suggests hydrocephalus under pressure, which is an indication for CSF diversion surgery to decompress the ventricular system (Figure 1 on page 18, 2 on page 19). Chronic hydrocephalus may result in atrophy of the brain parenchyma.

![Image of CT scans showing hydrocephalus](image)

**Fig.:** Hydrocephalus in a 1-year-2-month-old boy with fever, nausea, vomiting and drowsiness. (A, B) Non-contrast CT scan demonstrates hydrocephalus involving the lateral, third and fourth ventricles. (B) Note the marked widening of the temporal horns of the lateral ventricles.

**References:** L. N. Delfino; Radiology, Ospedale Bambino Gesù, Roma, ITALY
Fig.: Hydrocephalus in a 9-month-old girl who presented nausea, vomiting and fever. (A-C) Axial T2-weighted images show ventricular dilatation and a high-intensity periventricular hydrostatic edema (black arrows). Hyperintensity in the left caudate and putamen corresponds to infarcts (blue arrows). (D) Sagittal T1-weighted image shows upward bowing of the corpus callosum.

References: L. N. Delfino; Radiology, Ospedale Bambino Gesù, Roma, ITALY

Meningeal contrast medium enhancement is supposed to occur due to extravasation of the contrast medium from the vascular endothelium, which is disrupted because of the activity of lymphocytes. The patterns of enhancement of the different layers
of the meninges are divided into two types: leptomeningeal (pia and arachnoid) and pachymeningeal (dura). Meningeal enhancement can be focal or diffuse in TBM. The diffuse enhancement of the meninges in early stages of the disease cannot be considered to result from widespread and diffuse tubercles (Figure 3 on page 20). In fact, it is thought that diffuse meningeal contrast fixation occurs because of an "allergic" reaction due to cell mediated immunity in patients with pulmonary tuberculosis. Tuberculoproteins are known to cause tuberculous encephalopathy on the basis of a delayed type IV hypersensitivity reaction. As this reaction declines over time, meningeal involvement becomes limited to the basal areas where the bacilli are numerous. Focal linear enhancement occurs due to the contrast fixation of the exudate in the subarachnoid space or on the pial surface. The predilection of the basal areas for enhancement has not yet been explained (Figure 4 on page 21, 5 on page 22). It may be because basal areas are gravity dependent, and the interpeduncular cistern, the boundaries of which comprise the pons inferiorly and cerebral peduncles laterally, is the only cistern that remains gravity dependent in both the erect and supine positions. It is also thought that this area is less affected by CSF pulsations. Because of these features, it is likely that tuberculosis bacilli sediment in this area. Pial tuberculomas cause the nodular form of meningeal enhancement seen in TBM.
**Fig.**: (A-F) Diffuse leptomeningeal contrast enhancement in a 5-year-11-month-old girl with fever and headache. Gadolinium enhanced axial T1W images show linear and nodular meningeal enhancement. Note the surface of the mesencephalon and middle cerebral artery cisterns (D).

**References:** L. N. Delfino; Radiology, Ospedale Bambino Gesù, Roma, ITALY

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**Fig.**: (A, B) Tuberculous meningitis in a 4-year-old boy. Contrast medium-enhanced CT demonstrates marked abnormal basal enhancement within the suprasellar cistern, preoptin cistern, ambient cistern, middle cerebral artery cisterns, and anterior interhemispheric fissure. Note the "Y" sign at the junction of the suprasellar cistern and middle cerebral artery cistern (orange arrow). There is also hydrocephalus.

**References:** L. N. Delfino; Radiology, Ospedale Bambino Gesù, Roma, ITALY

On noncontrast CT or T1-weighted images (T1WI), the exudate appears as soft tissue density that fills the cisterns. The exudate may be easily overlooked on T2WI because the high intensity CSF signal will obscure the cisternal disease. Pachymeningitis may exist as focal or diffuse involvement of the dura. Focal pachymeningitis appears isointense on T1WI, iso- to hypointense on T2WI, hyperintense in FLAIR and enhanced on postcontrast images. In contrast to focal lesions, diffuse involvement may appear hyperintense on T2WI.
**Fig.**: The same patient of figure 4. Gadolinium enhanced coronal T1W image shows the double line sign in the middle cerebral artery cisterns.

**References**: L. N. Delfino; Radiology, Ospedale Bambino Gesù, Roma, ITALY

Meningeal enhancement is nonspecific and has a wide differential diagnosis that includes meningitis from other infective agents, inflammatory diseases such as reumathoid arthritis and sarcoidosis, and neoplastic causes, both primary and secondary (Figure 6 on page 23).
Fig. Primary leptomeningeal melanomatosis in a 1-year-old girl with fever, nausea, vomiting and drowsiness. (A) Axial T1WI and (B) T2WI show a high signal intensity focus in the left periventricular white matter. (C) Gadolinium enhanced axial T1WI shows linear and nodular diffuse enhancement in the basal cisterns, middle cerebral artery cistern and cortical and cortical-white matter junction nodular foci. There is also hydrocephalus.

References: L. N. Delfino; Radiology, Ospedale Bambino Gesù, Roma, ITALY

Vasculitis is a complication that is commonly seen at autopsy in TBM. The adventitial layer of small and medium-sized vessels develops changes similar to those of the adjacent tuberculous exudates. The intima of the vessels may eventually be affected or eroded by fibrinoid-hyaline degeneration. In later stages, the lumen of the vessel may get completely occluded by reactive subendothelial cellular proliferation. Ischemic cerebral infarction resulting from the vascular occlusion is a common sequela of tuberculous arteritis. The middle cerebral and lenticulostriate arteries are most commonly affected. In fact, the majority of the infarcts are in the basal ganglia and internal capsule due to the involvement of these arteries. Cortical infarctions can result from involvement of cortical vessels but are less common. Infarctions continue to develop with continuing inflammation and even patients on treatment may show an initial deterioration related to progression of ischaemia. The differential diagnosis with cerebral small vessel disease, cardiac pathology, thrombotic process and collagen vascular disease should be done. It has been reported that the incidence of infarcts detected by CT scan varies from 20.5% to 38%. MR imaging detects more infarcts than does CT scan. The infarcts appear as low-density regions on CT (Figure 7 on page 24). On MR studies, acute infarct is hyperintense on DWI with or without hyperintensity on T2WI and iso- or hypointense on T1WI. ADC is low in the acute stage, variable in the subacute stage and high in the chronic stage. Perilesional edema/mass effect and intravascular/meningeal enhancement may
be seen with acute infarcts. Subacute infarcts may show parenchymal enhancement. Chronic infarcts are hyperintense on T2WI, iso to hypointense on DWI and hypointense on T1WI with no edema, mass effect or abnormal contrast enhancement (Figure 8 on page 25).

**Fig.**: (A, B) The same patient of figure 4. Non-contrast CT scan demonstrates low densities involving the caudate nucleus bilaterally (orange arrows), right putamen (green arrow) and left globus pallidus (blue arrow).

**References:** L. N. Delfino; Radiology, Ospedale Bambino Gesù, Roma, ITALY
Fig.: The same patient of figure 4. (A-B) Axial T2WI, (C) DWI and (D) ADC. Basal nuclei acute infarcts are hyperintense on T2WI, DWI and hypointense in ADC (blue and orange arrows). Chronic infarcts are hyperintense in ADC (green arrow in D).

References: L. N. Delfino; Radiology, Ospedale Bambino Gesù, Roma, ITALY
**Tuberculomas** are granulomas that result either from hematogenous spread or extension from cerebrospinal fluid infection via cortical veins or small penetrating arteries. The majority of tuberculomas are supratentorial and may be solitary or multiple; however, they can also be found in subdural, epidural, and subarachnoid spaces. Although no precise patterns of localization have been observed according to race, age or sex, children develop infratentorial tuberculomas more commonly than adults.

On CT, they may be of high density and show a ring of enhancement after administration of contrast (Figure 9 on page 25). Depending on its stage of maturation, a tuberculoma's appearance varies on MRI, whether noncaseating, caseating with a solid center, or caseating with a liquid center. A **noncaseating tuberculoma** usually appears slightly hypointense on T1WI and hyperintense on T2WI. These granulomas show homogeneous enhancement after injection of paramagnetic contrast on T1WI (Figure 10 on page 27, 11 on page 27). A **solid caseating tuberculoma** appears relatively iso- to hypointense on both T1 and T2WI with an iso- to hyperintense rim on T2WI. In the presence of edema, the rim appears inseparable on T2WI, but it shows rim enhancement on postcontrast T1WI (Figure 9 on page 25). The degree of hypointensity of the solid caseating tuberculoma on T2WI depends on the complex relationship between the solid caseation, associated fibrosis/gliosis, macrophage infiltration, and perilesional cellular infiltrate. When the solid center of the **caseating lesion liquefies**, the center appears hyperintense with a hypointense rim on T2WI. The postcontrast T1WI show rim enhancement.
Fig.: Tuberculoma in the same patient of figure 1. (A) Non-contrast CT scan did not show the lesion. (B) After contrast medium administration, a ring-like tuberculoma is seen in the left pontocerebellar angle. Axial (C) T2W image and (D) FLAIR show a
hyperintense lesion, which is iso to hypointense on T1 MT WI (E). Ring-like contrast enhancement could also be seen on axial post-contrast T1 MT WI (F).

References: L. N. Delfino; Radiology, Ospedale Bambino Gesù, Roma, ITALY

Fig.: Brainstem tuberculoma in a 9-month old girl. (A) Axial T2WI shows a hyperintense tuberculoma in the right pons (blue arrows) that is isointense on T1WI (B) and shows homogeneous enhancement after administration of contrast medium on T1WI (C). There is also a cerebellar tuberculoma (green arrows). Note the prepontine contrast enhancement (orange arrow in C).

References: L. N. Delfino; Radiology, Ospedale Bambino Gesù, Roma, ITALY
MR imaging features of tuberculomas are known to overlap with those of other intracranial focal lesions, like the healing stage of neurocysticercosis, fungal granulomas, chronic pyogenic brain abscess, and lymphomas. Some gliomas and metastases may also have features similar to those of tuberculomas and should be considered in their differential diagnosis. In fact, sometimes, large tuberculomas mimic neoplastic lesions on MR studies as they appear predominantly hyperintense on T2WI, with mixed intensity on T1WI, and may show heterogeneous enhancement on postcontrast studies. In this cases, quantitative Magnetization Transfer (MT) imaging and proton MR spectroscopy may help in the differential diagnosis of tuberculomas. On MT T1WI, cellular components of the lesions appear brighter and relatively specific for the disease. In fact, the solid center should appears hypointense, with a hyperintense rim on this sequence.

Rarely, the central caseous component of the tuberculoma may liquefy, forming a tuberculous abscess. Abscesses are generally larger than tuberculomas, and usually elicit more vasogenic edema. Their imaging appearance differs from tuberculomas in that the central portion of tuberculous abscesses is hyperintense on T2WI, in contrast to the central T2 hypointensity seen in tuberculomas.

Miliary tuberculosis appears as multiple small foci of high intensity throughout the brain on T2WI; the foci enhance after IV administration of contrast. The primary locations are at the cortical-white matter junction and in the distribution of the perforating vessels (thalami, basal ganglia, brainstem). Other granulomatous meningitides such as those from cryptococcosis or coccidioidomycosis are extremely rare in the pediatric group. Their CT and MR appearances are similar to those of tuberculous meningitis.

Our population

We reviewed the brain CT scans and MR imaging studies of 30 patients who were admitted to our hospital from 1998 until 2009 with clinical findings of endocranic hypertension, such as nausea, vomiting, and headache. Children with an equivocal diagnosis of TBM or with no CT scan and or MRI were excluded. Included in the study were 7 patients with a Mycobacterium tuberculosis positive cerebrospinal fluid culture. There were 4 males and 3 females. Mean age was 38 months (9-90 months).

Scanning protocol:

CT
Axial images parallel to cantho-meatal line using 2.5mm to 7mm thickness.

**MR**

1.5-T system

Axial spin-echo (SE) T1WI (TR/TE 433/15ms)

Axial and coronal turbo spin-echo (TSE) T2WI (TR/TE 4,443/100ms)

Axial TSE FLAIR (TR/TE 11,000/140ms)

Field of view (FOV): 23X23

Imaging matrix: 256X256

Slice thickness: 5mm

Post contrast T1 MT multiplanar

**DWI:**

Single-shot spin echo planar imaging (EPI) (TR/TE 5700/139ms)

FOV: 24 X 24

Acquisition matrix: 96X200

Reconstruction matrix: 256X256

b values: 50, 500 and 1000mm²/s

NEX: 4

The most frequent radiographic findings were hydrocephalus and abnormal meningeal enhancement, most pronounced in the basal cisterns. This appearance is non-specific and has a wide differential diagnosis that includes meningitis from other infective agents, inflammatory diseases, and meningeal carcinomatosis.
**Fig. 1:** Hydrocephalus in a 1-year-2-month-old boy with fever, nausea, vomiting and drowsiness. (A, B) Non-contrast CT scan demonstrates hydrocephalus involving the lateral, third and fourth ventricles. (B) Note the marked widening of the temporal horns of the lateral ventricles.
Fig. 2: Hydrocephalus in a 9-month-old girl who presented nausea, vomiting and fever. (A-C) Axial T2-weighted images show ventricular dilatation and a high-intensity periventricular hydrostatic edema (black arrows). Hyperintensity in the left caudate and putamen corresponds to infarcts (blue arrows). (D) Sagittal T1-weighted image shows upward bowing of the corpus callosum.
Fig. 3: (A-F) Diffuse leptomeningeal contrast enhancement in a 5-year-11-month-old girl with fever and headache. Gadolinium enhanced axial T1W images show linear and nodular meningeal enhancement. Note the surface of the mesencephalon and middle cerebral artery cisterns (D).
Fig. 4: (A, B) Tuberculous meningitis in a 4-year-old boy. Contrast medium-enhanced CT demonstrates marked abnormal basal enhancement within the suprasellar cistern, prepontin cistern, ambient cistern, middle cerebral artery cisterns, and anterior interhemispheric fissure. Note the "Y" sign at the junction of the suprasellar cistern and middle cerebral artery cistern (orange arrow). There is also hydrocephalus.
**Fig. 5:** The same patient of figure 4. Gadolinium enhanced coronal T1W image shows the double line sign in the middle cerebral artery cisterns.
Fig. 6: Primary leptomeningeal melanomatosis in a 1-year-old girl with fever, nausea, vomiting and drowsiness. (A) Axial T1WI and (B) T2WI show a high signal intensity focus in the left periventricular white matter. (C) Gadolinium enhanced axial T1WI shows linear and nodular diffuse enhancement in the basal cisterns, middle cerebral artery cistern and cortical and cortical-white matter junction nodular foci. There is also hydrocephalus.

Fig. 7: (A, B) The same patient of figure 4. Non-contrast CT scan demonstrates low densities involving the caudate nucleus bilaterally (orange arrows), right putamen (green arrow) and left globus pallidus (blue arrow).
Fig. 8: The same patient of figure 4. (A-B) Axial T2WI, (C) DWI and (D) ADC. Basal nuclei acute infarcts are hyperintense on T2WI, DWI and hypointense in ADC (blue and orange arrows). Chronic infarcts are hyperintense in ADC (green arrow in D).
Fig. 9: Tuberculoma in the same patient of figure 1. (A) Non-contrast CT scan did not show the lesion. (B) After contrast medium administration, a ring-like tuberculoma is seen in the left pontocerebellar angle. Axial (C) T2W image and (D) FLAIR show a hyperintense
lesion, which is iso to hypointense on T1 MT WI (E). Ring-like contrast enhancement could also be seen on axial post- contrast T1 MT WI (F).

**Fig. 10:** Brainstem tuberculoma in a 9-month old girl. (A) Axial T2WI shows a hyperintense tuberculoma in the right pons (blue arrows) that is isointense on T1WI (B) and shows homogeneous enhancement after administration of contrast medium on T1WI (C). There is also a cerebellar tuberculoma (green arrows). Note the prepontine contrast enhancement (orange arrow in C).

**Fig. 11:** (A-F) Right pontocerebellar angle tuberculoma in a 1-year-3-month old boy (blue arrows).
Conclusion

Diagnosis of early tuberculous meningitis may be difficult due to the often non-specific presenting symptoms and inconclusive laboratory results. Delay in diagnosis and treatment is directly related to a poor outcome. Because prompt diagnosis results in earlier treatment, recognition of this disorder on radiological images may play a critical role in patient management. Contrast-enhanced sequences are essential in these patients.

Diffusion-weighted imaging has an advantage over conventional T2WI in patients with TBM. Amongst various MR imaging techniques, DWI plays a central role in detecting infarcts not demonstrated by CT and conventional MR imaging or demonstrating more extensive infarcts in unusual locations.

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