Egyptian Journal of Radiology and Nuclear Medicine

RESEARCH Open Access

The many faces of intracranial tuberculosis: atypical presentations on MRI—a descriptive observational cohort study

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Abstract

Background Atypical MRI findings of cranial tuberculosis can lead to prolonged delay in diagnosis resulting in high costs to evaluate for alternative diagnoses. The aim of this study was to describe a series of cranial tuberculosis patients with spectrum of MRI features, other than hydrocephalus, parenchymal tuberculomas, and leptomeningeal thickening. The final diagnosis was made based on CSF findings, clinical findings, and/or marked improvement after antitubercular treatment.

Results A total of 39 patients met the inclusion criteria and were diagnosed with vasculitis ($n=15$), tubercular abscess ($n=5$), miliary tuberculosis ($n=3$), tubercular cerebritis ($n=9$), sellar and parasellar tuberculosis ($n=7$), mass forming tuberculosis ($n=1$), choroid plexitis ($n=2$), and intraventricular tuberculomas ($n=1$).

Conclusion A significant number of patients of cranial tuberculosis can have variable presentations and may be misdiagnosed. This analysis helps to reinvestigate the spectrum of MRI findings.

Keywords Tuberculosis, Brain, MRI, Imaging spectrum

Background

Central nervous system (CNS) involvement is one of the most disastrous manifestations of tuberculosis (TB), seen in 5–10% of extra-pulmonary TB cases [1]. It carries a high mortality and neurological morbidity. Imaging, especially MRI, can frequently provide a considerable diagnostic clue for a definitive diagnosis of cranial tuberculosis. In conjunction with CSF analysis and clinical findings, imaging findings aid in the diagnosis of cranial tuberculosis without a biopsy.

Cranial tuberculosis in its typical form presents as tubercular meningitis (TBM), hydrocephalus, or focal tuberculoma on MRI [2]. Meningeal thickening of basal subarachnoid cisterns and abnormal leptomeningeal enhancement along the cerebral hemispheres, sylvian fissures, or the tentorium are the most common findings suggestive of TBM [3]. Hydrocephalus encountered in TBM is usually of the communicating type caused due to blockage of CSF resorption by inflammatory exudates in the basal subarachnoidal cisterns [4]. Occasionally, the hydrocephalus can be of the obstructive type, secondary to narrowing of the aqueduct or a ventricle by a focal parenchymal lesion and mass effect or due to entrapment of a ventricle by granulomatous ependymitis [5]. Tuberculomas are frequent manifestations of brain tuberculosis, presenting as either homogenously enhancing nodules (non-caseous granuloma) or ring-enhancing lesions (caseating granuloma) [6].

Although most cases of cranial tuberculosis can be confidently diagnosed based on the typical imaging findings, a small number of cases present a diagnostic

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challenge that can result in a delay in diagnosis or misdiagnosis. The purpose of this study is to evaluate and describe the constellation of atypical MRI features of cranial tuberculosis.

Methods

Subjects

This was a prospective, observational, cohort study carried out for two years in a university-based tertiary care hospital. The study was approved by the Institute's ethical committee at the outset, and an informed consent was obtained from each patient/legal guardian.

Diagnosis

We included the patients with a diagnosed case of TB based on one or more of following positive test results: (a) CSF culture, CSF ADA > 10 U/L, CSF PCR, CSF study (cellularity, protein, glucose, chloride) consistent with tubercular etiology, (b) patients showing definite clinical and radiological improvements after antitubercular treatment (ATT).

MR imaging and interpretation

MRI was done on a 1.5 T superconducting magnet (Magnetom Avanto, Siemens medical system, Erlangen-Germany). The routine sequences acquired were T1 axial, T2 axial, T2 sagittal and coronal, T2 FLAIR axial, diffusion-weighted images (DWI), T1 Post-Gadolinium Turbo Spin Echo sequences. Additional MR techniques were also obtained according to findings, as and when required. Magnetization transfer sequence was obtained in a suspected tubercular abscess which involved an addition of saturation pulse immediately before the 90-degree radiofrequency pulse to saturate the magnetization of protons with restricted motion. MR images were interpreted by two radiologists in tandem with 9 years and 17 years of experience, respectively. We excluded the patients who had only. hydrocephalus, leptomeningitis, basal-enhancing exudates, and parenchymal tuberculomas. In cases of vasculitis, the distribution of infarcts was analyzed in details and an attempt was made to classify the infarcts into "TB zone" and "ischemic zone" originally described by Hsieh et al. [7]. The ischemic zone supplied by lateral striate, anterior choroidal, and thalamo-geniculate arteries consists of lentiform neucleus, posteriorlimb of internal capsule, and thalami, whereas TB zone supplied by medial striate and thalamo-perforating arteries consists of caudate and anterior limb of internal capsule. Lesions involving sellar and parasellar regions were evaluated based on the involvement of pituitary and other structures, enhancement pattern and mass effect. Ring-enhancing lesions were evaluated for the presence of diffusion restriction at the center of the lesion to identify tubercular abscess. MR spectroscopy carried out for distinguishing these lesions from pyogenic abscesses using image-guided, single-voxel, point-resolved MR spectroscopy (PRESS; repetition time [TR] 1500 ms and echo time [TE] 35 ms and 135 ms) was used. The presence of lipid/lactate peak at 1.3 ppm and the absence of an amino acid peak at 0.9 ppm were suggestive of the tubercular lesion.

Results

A total of 39patients of cranial tuberculosis were included in the study with a mean age of 28 years. The most common age group in the present study was 21–30 years. Female predominance was noted with male: female ratio of 17:23. The clinical features, coexisting tubercular involvement of other sites, other coexisting illnesses, results of laboratory investigations are summarized in Table 1. CSF evaluation and sputum culture were done in all the patients while PCR was performed in 24 patients. The diagnosis was confirmed in 60% cases ($n=24$) and was probable in the rest of the cases ($n=15$). Fever was the most common presenting complaint, followed by headache and altered sensorium. Pulmonary tuberculosis was present in 43% of our patients and abdominal tuberculosis in 20% cases, whereas Potts's spine was coexistent in 25% cases. Seven out of 39 were positive for HIV.

Table 1 Clinical features in 39 patients of our study

	Patients ($n=39$)
Age (mean)	27 years
Gender (*n*, %)	
Male	17 (42.5%)
Female	22 (57.5%)
Clinical features (*n*, %)	
Fever	30 (76%)
Headache	27 (67%)
Altered sensorium	26 (65%)
Loss of appetite	18 (45%)
Loss of weight	15 (38%)
Hemiparesis/paraparesis	12 (30%)
Neck stiffness	12 (30%)
Other TB sites (*n*, %)	
Pulmonary tuberculosis	17 (43%)
Pleural tuberculosis	4 (10%)
Tuberculous disease of spine	10 (25%)
Abdominal tuberculosis	8 (20%)
Other medical illnesses (*n*, %)	
HIV	7 (18%)
Diabetes	5 (13%)
Hypertension	4 (10%)
Others	8 (20%)

Based on the MRI appearances, our cohort presented with following findings: vasculitis ($n=15$), tubercular abscess ($n=5$), miliary tuberculosis ($n=3$), tubercular cerebritis ($n=9$), sellar and parasellar tuberculosis ($n=7$), mass forming tuberculosis ($n=1$), choroid plexitis ($n=2$), and intraventricular tuberculomas ($n=1$).

Vasculitis

A total of 15 patients in our study showed evidence of vasculitis predominantly in the form of vasculitic infarcts. Basal ganglia, internal capsule, and thalamus were the most common sites of involvement (Fig. 1). All of the 15 patients with features of vasculitis showed involvement of either or all these three sites. 20% of the

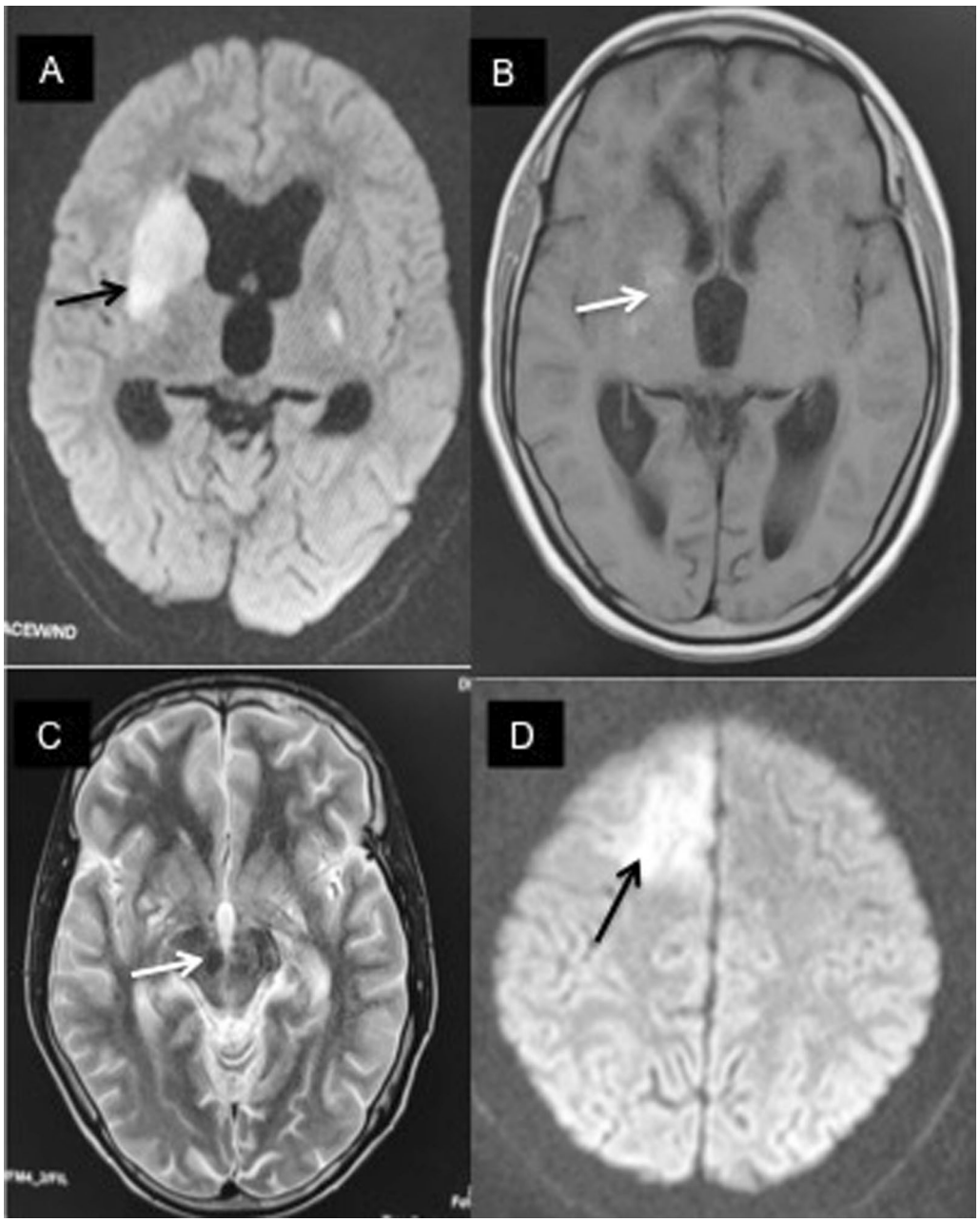

Fig. 1 Tubercular vasculitis. Axial diffusion-weighted image (**A**) shows hyperintense lesion in right caudate and lentiform nuclei (black arrow) and left globus pallidus suggestive of vasculitic infarcts. T1 (**B**)- and T2 (**C**)-weighted images of another patient showing T1 hyperintense areas in right globus pallidus and internal capsule (white arrow) and T2 dark areas in midbrain (**C**) (white arrow) consistent with hemorrhages. DWI image of another patient (**D**) showing lobar infarct in right frontal lobe (black arrow)

cases showed involvement confined exclusively to the ischemic zone, whereas the majority (80%) showed the involvement of both ischemic and TB zones. One of the patients showed hemorrhagic foci as well as infarct (Fig. 1). The infarcts mainly involved the lateral lenticulostriate arteries (7/15), medial lenticulostriate arteries (5/15), perforators from the posterior cerebral artery (5/15) & terminal perforators from basilar arteries (6/15) with 1 case each of involvement of superior cerebellar and anterior inferior cerebellar artery territories.

Sellar/Parasellar region tuberculosis

A total of 7 patients in the present study showed tuberculosis of the sellar & parasellar region in forms other than basal exudates found commonly in the related region. Of these 7 cases, 3 showed involvement of pituitary, whereas 4 were supra or intrasellar tuberculomas without the involvement of pituitary. Table 2 summarizes the sellar involvement of tuberculosis in our study (Figs. 2 and 3).

Tubercular abscess

Five cases of the tubercular abscess were found in our study. Table 3 shows the imaging features found in 5 cases of tubercular abscess. Three cases presented as lesions showing T1 hypointensity and T2 hyperintensity with peripheral T2 hypointense rim showing ring enhancement (Figs. 4 and 5). Mass effect and perilesional vasogenic edema were present in all these cases. Two cases presented with multiple lesions. On conventional MR imaging, they were thin-walled showing peripheral ring enhancement. All the lesions showed central diffusion restriction with low ADC value and lipid, lactate peaks, and absence of amino acid peak characteristic of TB. Magnetization transfer pre-contrast T1-weighted sequences showed a strongly hyperintense rim in these lesions.

Tubercular cerebritis

In our study, 9 cases were affected by tubercular cerebritis (Table 4). Out of these, 6 cases also showed adjacent meningeal thickening. We found an ill-defined area of

Table 2 Imaging features of cases of sellar tuberculosis

SL No	Age/sex	Diagnosis	Structures involved	MRI features
1	54 Y/F	Tubercular stalkitis	Infundibular stalk	Homogenously enhancing stalk thickening with normal pituitary
2	16 Y/F	Tubercular Infundibulohypophysitis	Pituitary gland and stalk	Homogenously enhancing thickened stalk and bulky pituitary
3	24 Y/F	Intrasellar tuberculoma	Pituitary involvement	Peripherally enhancing lesion, T2 hypointense
4	21 Y/F	Intrasellar tuberculoma	Without pituitary involvement with suprasellar extension	Homogenously enhancing lesion
5	35 Y/F	Intrasellar tuberculoma	Without pituitary involvement with suprasellar extension	Ring-enhancing lesion
6	26 Y/M	Suprasellar tuberculoma	Suprasellar cistern	Ring-enhancing lesion
7	26/F	Suprasellar tuberculoma	Suprasellar cistern extending between stalk and mammillary body	Ring-enhancing lesion

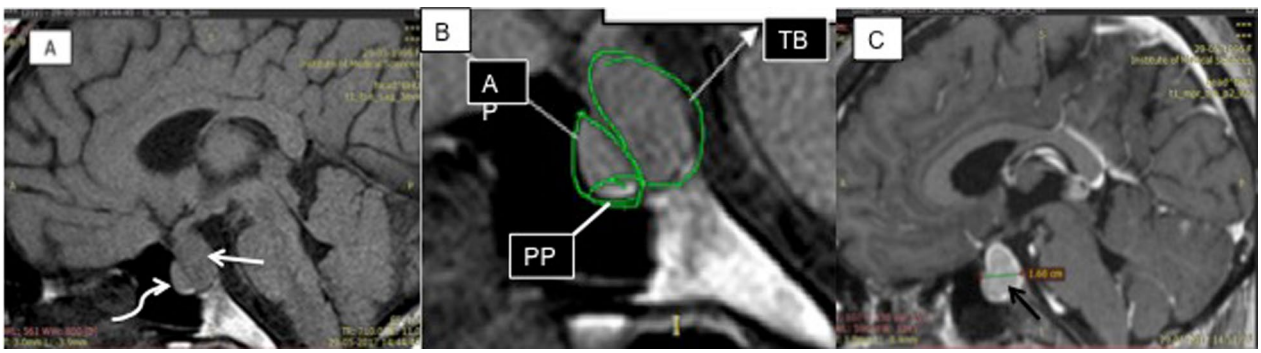

Fig. 2 Sellar tuberculosis. Sagittal T1-weighted image (**A**) of a patient showing a sellar mass (white arrow) with anterior displacement of pituitary gland (curved arrow). Magnified view (**B**) of sagittal T1 image clearly demarcates anterior pituitary (AP) and posterior pituitary (PP) separate from tubercular mass (TB), which appears mildly hypointense compared to normal pituitary. Sagittal post-contrast image (**C**) of this patient shows homogenously enhancing mass in the sella (black arrow) suggestive of non-caseous granuloma

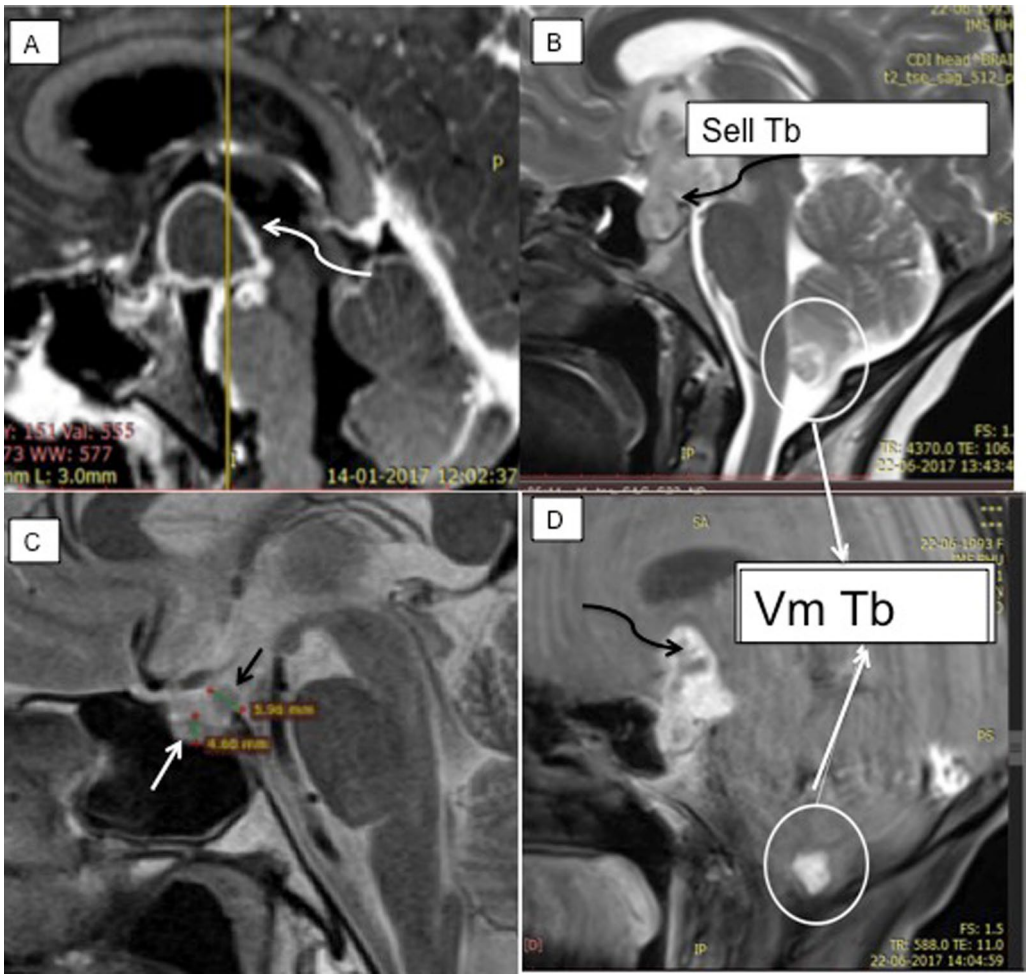

Fig. 3 Sellar tuberculosis. Sagittal T2 W (**A**) and post-contrast image (**B**) of a patient showing a T2 hypointense, peripherally enhancing suprasellar tuberculoma (white arrow). T2 W sagittal image (**C**) of another patient showing thickened pituitary stalk (black arrow) with normal pituitary (white arrow) suggestive of tubercular stalkitis. Sagittal (**D**) post-contrast T1W images of another patient showing T2 hypointense and peripherally enhancing (black arrow) sellar-suprasellar lesion involving pituitary. Also noted is another enhancing granuloma in inferior vermis (curved black arrow)

T1 iso-hypointensity and T2 hyperintensity with patchy enhancement in 1 case, and a gyral enhancement pattern was seen in 8 out of 9 cases. These lesions also showed restriction on DWI in all of the cases. Two of the cases also showed a "tree in bud" appearance similar to that obtained in pulmonary tuberculosis (Figs. 6 and 7).

Choroid plexitis and intraventricular tuberculoma

Primary involvement of the choroid plexus was the sole finding in 2 cases without any obvious evidence of secondary involvement of ventricular system/choroid plexus from adjacent parenchymal tubercular focus. First case (28 years male) who presented with headache and mild fever had left-sided involvement while 2nd case who (27 years male) presented with fever, neck rigidity, altered sensorium, and vomiting showed right-sided choroid plexitis. In both cases, there was a strongly enhancing lesion involving the choroid plexus with sequestration of the temporal horn of the ipsilateral lateral ventricle and asymmetrical hydrocephalus (Fig. 8a–c).

One of our cases presented with intraventricular tuberculoma involving septum pellucidum (Fig. 8d). The lesion did not abut the ependymal lining and there was no associated evidence of ventriculitis.

Miliary tuberculosis

Three patients in our study showed evidence of miliary tuberculosis. The lesions in the present study measured approximately 2–4 mm in diameter (Fig. 9). The lesions exhibited nodular enhancement on T1-weighted images

Table 3 Imaging features in cases of tubercular abscesses

Case	Age/sex	Location	Lesion No	Lesion size	Perilesional edema	Imaging parameters			MRS	
						T1W	T2W SI	DWI	Lipid lactate peaks	Amino-acid peaks
1	24/M	Left frontal lobe	Single	2.5 × 2.8 × 2.8 cm	Mild	Hypointense	Hyperintense center hypointense rim	Restriction	+	–
2	60/F	Right Parietal lobe	Single	2.4 × 3 × 3 cm	Moderate	Hypointense	Hyperintense center with hypointense rim	Restriction	+	–
3	7/F	Right occipital lobe	Two	1.5 × 1.5 × 1.5 cm (larger)	Moderate	Hypointense	Hyperintense center with hypointense rim	Restriction	+	–
4	3/F	Bilateral cerebellar hemisphere and vermis	Multiple	2 × 2 × 2 cm (largest)	Moderate	Hypointense	Hyperintense center with hypointense rim	Restriction	+	–
5	55/F	Left frontal lobe	Single	1.5 × 1.6 × 1.6 cm	Moderate	Hypointense	Hyperintense center with hypointense rim	Restriction	+	–

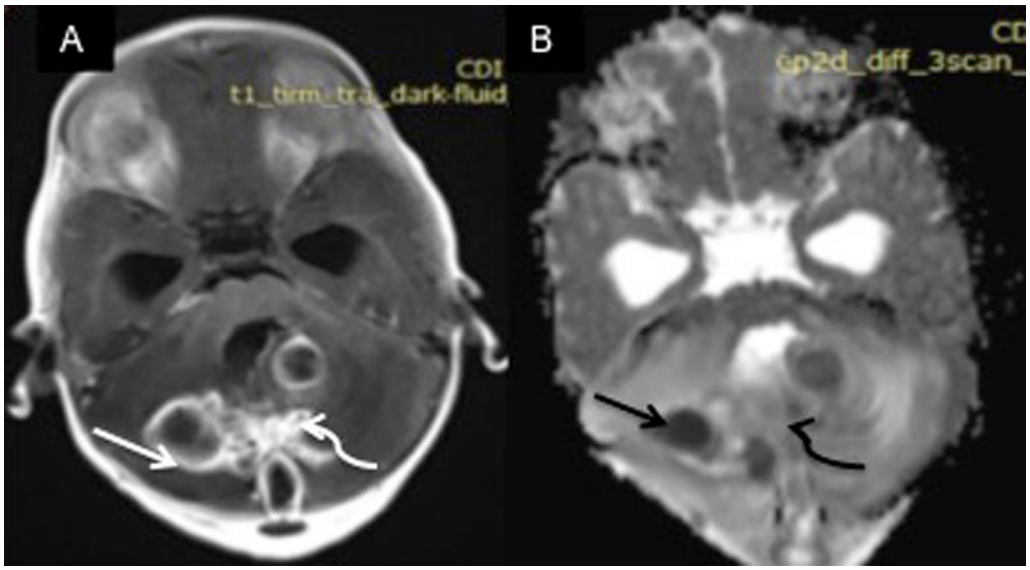

Fig. 4 Tubercular abscess. Axial post-contrast T1W (**A**) and ADC map (**B**) images of a patient showing multiple ring-enhancing lesions (white arrow) showing diffusion restriction (black arrow) suggestive of tubercular abscesses. Other conglomerated ring-enhancing lesions (white curved arrow) are noted showing no diffusion restriction (black curved arrow) representing tuberculomas

after gadolinium injection. Most were located at the corticomedullary junction. Clinically two of the patients exhibited mild clinical manifestations without typical systemic signs of TB infection. Only one of our 3 patients showed a disturbance of consciousness who exhibited the nodules close to the meningeal surface and concomitant meningeal thickening.

Focal pachymeningitis

One case of focal pachymeningeal mass-like thickening was included in this study who presented with a strongly enhancing meningeal mass in the left parietal region similar to meningioma (Fig. 10). Dural tail was present and there was secondary involvement and mild edema in the adjoining parietal lobe.

Tumor-like lesion

One of the 23-year-old male patients showed a strongly enhancing mass lesion in the right insular region with gross surrounding edema and mass effect (Fig. 11). The lesion showed restricted diffusion on DWI and MRS was inconclusive. The patient had coexisting miliary pulmonary tuberculosis as well as Pott's spine.

Discussion

Our study describes the extremely variable appearance of cranial tuberculosis on MRI with vasculitis, abscess, miliary tuberculosis, tubercular cerebritis, sellar and parasellar tuberculosis, tubercular encephalopathy, mass-forming tuberculosis, choroid plexitis and intraventricular tuberculomas. Although vasculitis is a known feature of tuberculosis, we have included vasculitis in our analysis to identify the pattern and distribution of involvement. The number of patients in our study suggests that these atypical forms are rare and are probably considerably under-reported. Despite their rarity, identification of clues to correctly diagnose them is critical, and based on our study we have developed a basic algorithm to diagnose atypical cases of cranial tuberculosis (Fig. 12).

Tubercular vasculitis

The presence of vasculitic infarcts in association with tubercular meningitis is a major factor contributing to residual neurological deficits or death. Early identification of cerebral infarcts in TBM can lead to early administration of aspirin, corticosteroid, and reduced morbidity [8]. It should be noted that even if there is no evidence of stroke on initial imaging, age > 25 years, cranial nerve involvement, sylvian fissure exudates, posterior fossa exudates, optic chiasmal exudates on the initial scan can act as predictors of subsequent stroke [9]. Furthermore, serial brain scans to monitor for worsening or new infarcts or vasospasm are also recommended. Vasculitis in TBM is initiated by direct invasion of the vessel wall by mycobacteria or may result from secondary extension of adjacent arachnoiditis. Also, the exudates at the basal region surround the arteries, leading to arterial narrowing or reactive vasospasm and subsequently stroke [10, 11].

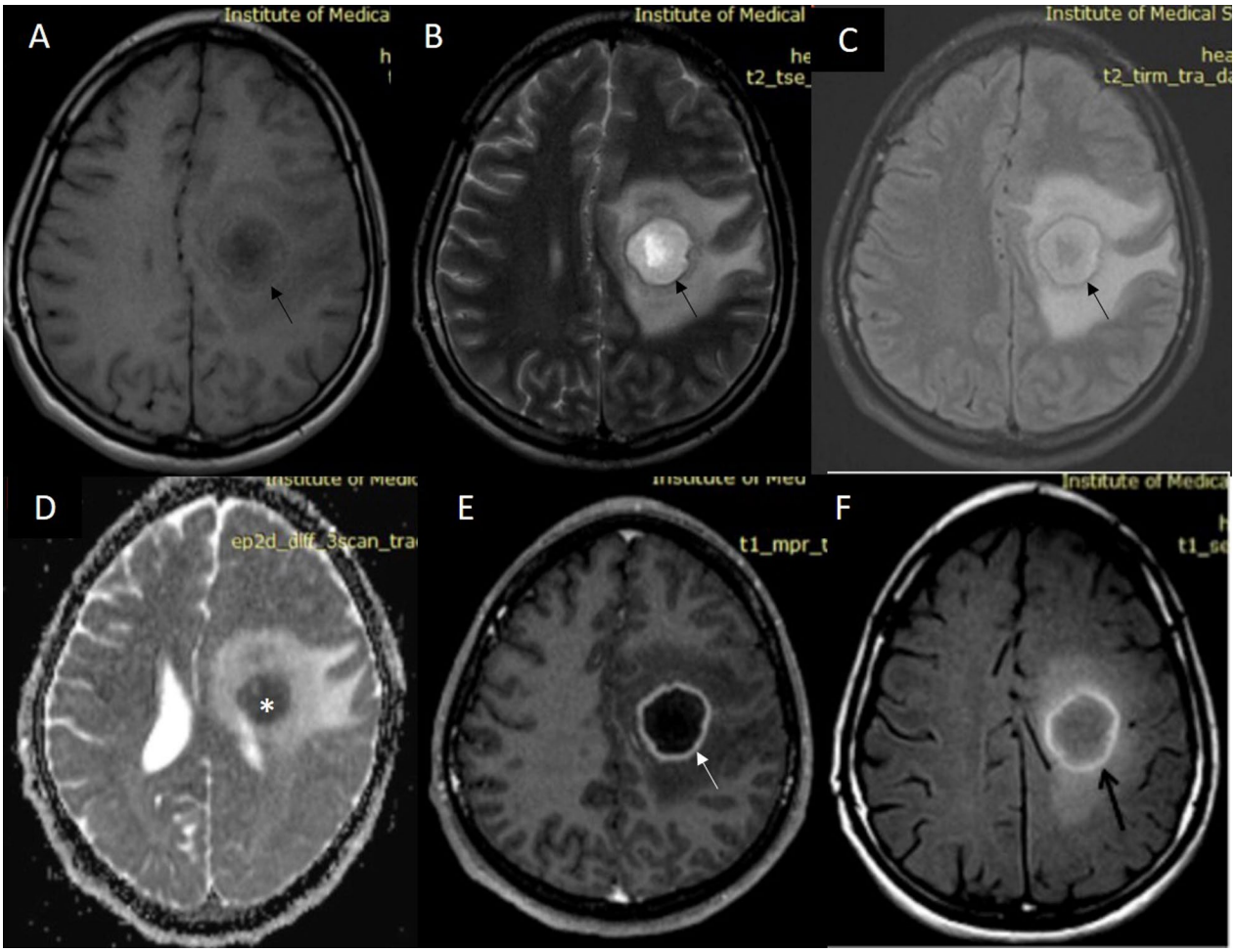

Fig. 5 Tubercular abscess. Axial T1 (**A**), T2 (**B**), FLAIR (**C**), ADC (**D**), post-contrast T1 (**E**), and magnetization transfer (MT) images (**F**) of a patient with tubercular abscess showing peripherally enhancing, T2 dark capsule with hyperintensity on MT images (arrows). The center shows diffusion restriction (*)

Similar to various previous studies, the most common sites of infarcts were in the basal ganglia, thalami, and internal capsules [8, 11, 12]. Distribution of the vasculitic infarcts in our study was not confined to "TB zone" described by Hsieh et al., and majority of strokes were distributed in combined ischemic (supplied by lateral striate, anterior choroidal, and thalamo-geniculate arteries) and TB zones (supplied by medial striate and thalamo-perforating arteries) [7]. Infarcts from total occlusion of major intracranial arteries were not seen among our patients, and various combinations of involvement of perforators and the terminal cortical branches were demonstrated in all cases.

Sellar tuberculosis

Sellar tuberculosis is extremely rare and when seen presents a diagnostic dilemma to the interpreting radiologists as it can mimic sellar neoplasms, especially pituitary macroadenoma, both radiologically and clinically. The correct diagnosis can be only obtained after surgical excision and histopathological evaluation which shows necrotizing granulomatous inflammation. Acid-fast bacilli (AFB) are rarely demonstrated which makes it difficult to distinguish from sarcoidosis or fungal infection [13]. Variable involvement of pituitary gland, stalk, sellar-suprasellar cisternal space was noted in our series with headache being the only symptom in the majority. Sharma et al. who reported 18 cases have described the largest series of sellar tuberculosis [14]. Rarely, tuberculoma in the pituitary gland can transform into pituitary abscess or can lead to pituitary apoplexy [15].

Tubercular abscess

Tubercular abscesses are similar to tuberculomas on conventional T1W and T2W MR sequences presenting as ring-enhancing lesions. Unlike tuberculomas, the

Table 4 Imaging features in cases of tubercular cerebritis

SL No	Age/sex	Regions involved	Imaging features				Additional findings
			T1W SI	T2/FLAIR	DWI	Enhancement pattern	
1	24/M	Left occipital lobe	Isointense	Hyperintense	Facilitation	Gyral enhancement	Left frontal Tubercular abscess
2	33/F	Right temporo-parietal region	Hypointense	Hyperintense	Restriction	Gyral enhancement	Meningitis+, disseminated miliary tubercles with vasculitic infarct and thrombosis of corresponding right cortical MCA segment
3	24/M	Left Anterior temporal lobe	Hypointense	Hyperintense	Restriction	Patchy enhancement	Meningitis+, hydrocephalus+, vasculitic infarcts+
4	18/F	Bilateral cerebellar hemisphere	Hypointense	Hyperintense	Restriction	Gyriform enhancement	Meningitis+, vasculitic infarct involving thalamus and midbrain
5	3/F	Left frontal lobe	Isointense	Hyperintense	Restriction	Gyriform	Meningitis+, hydrocephalus+, left deep brain nuclei and fronto-temporo-parietal infarct
6	20/F	Left temporal lobe	Isointense	Isointense	Restriction	Gyriform	Meningitis+, vasculitic infarcts+
7	60/F	Left frontal lobe	Hypointense	Hyperintense	Restriction	Gyriform	–
8	55/M	Left parieto-occipital	isointense	Isointense	Restriction	Gyriform	Meningitis+, multiple tuberculomas+, vasculitic infarcts+
9	48/M	Bilateral cerebral and cerebellar hemispheres	isointense	Hyperintense	Restriction	Gyriform	Multifocal cerebritis

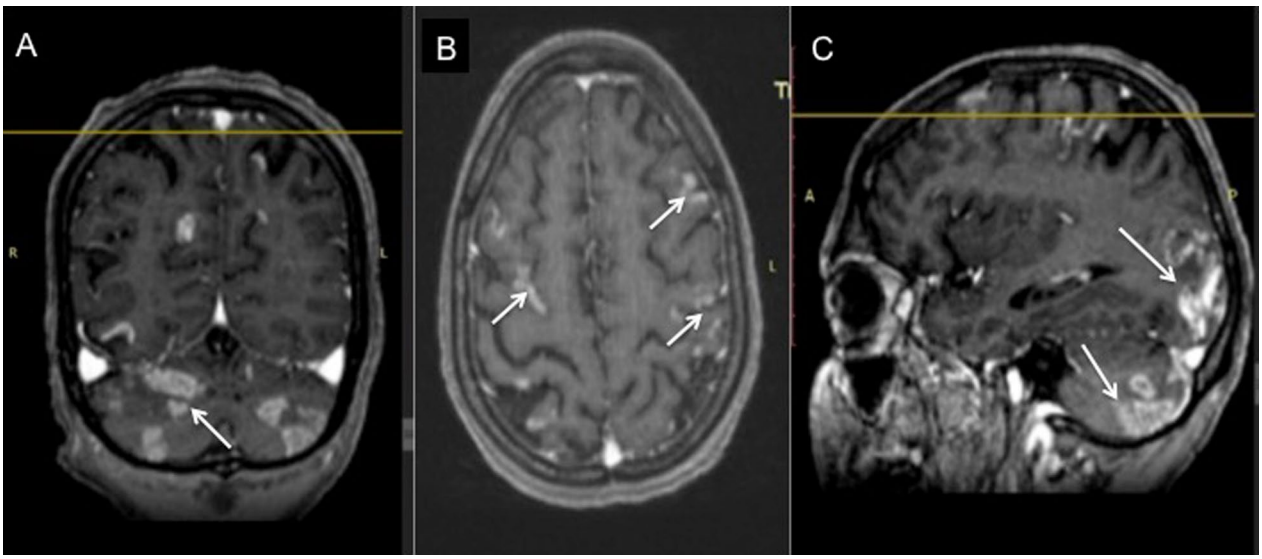

Fig. 6 Tubercular cerebritis. Coronal (**A**), axial (**B**), and sagittal (**C**) post-contrast T1W images of a patient with tubercular encephalitis showing multiple patchy gyriform-enhancing cortical lesions (arrows) in bilateral cerebral and cerebellar hemispheres. Also noted are adjacent meningeal thickening and few ring-enhancing lesions, consistent with tuberculomas

wall of abscesses lacks the granulomatous reaction and is visible as a low signal rim on T2-weighted images. The center contains semiliquid pus that is filled with tubercular bacilli which are visible as strongly T2 hyperintense contents that are not suppressed on FLAIR and show diffusion restriction. Tubercular granuloma contains only a few bacilli and majority show no diffusion restriction, although rarely tuberculomas can also restrict. Few studies suggest size >2 cm to be suggestive of abscess; however, in our study we encountered smaller multiple abscesses. Recognition of abscess is important in the setting of cranial tuberculosis because it has a more

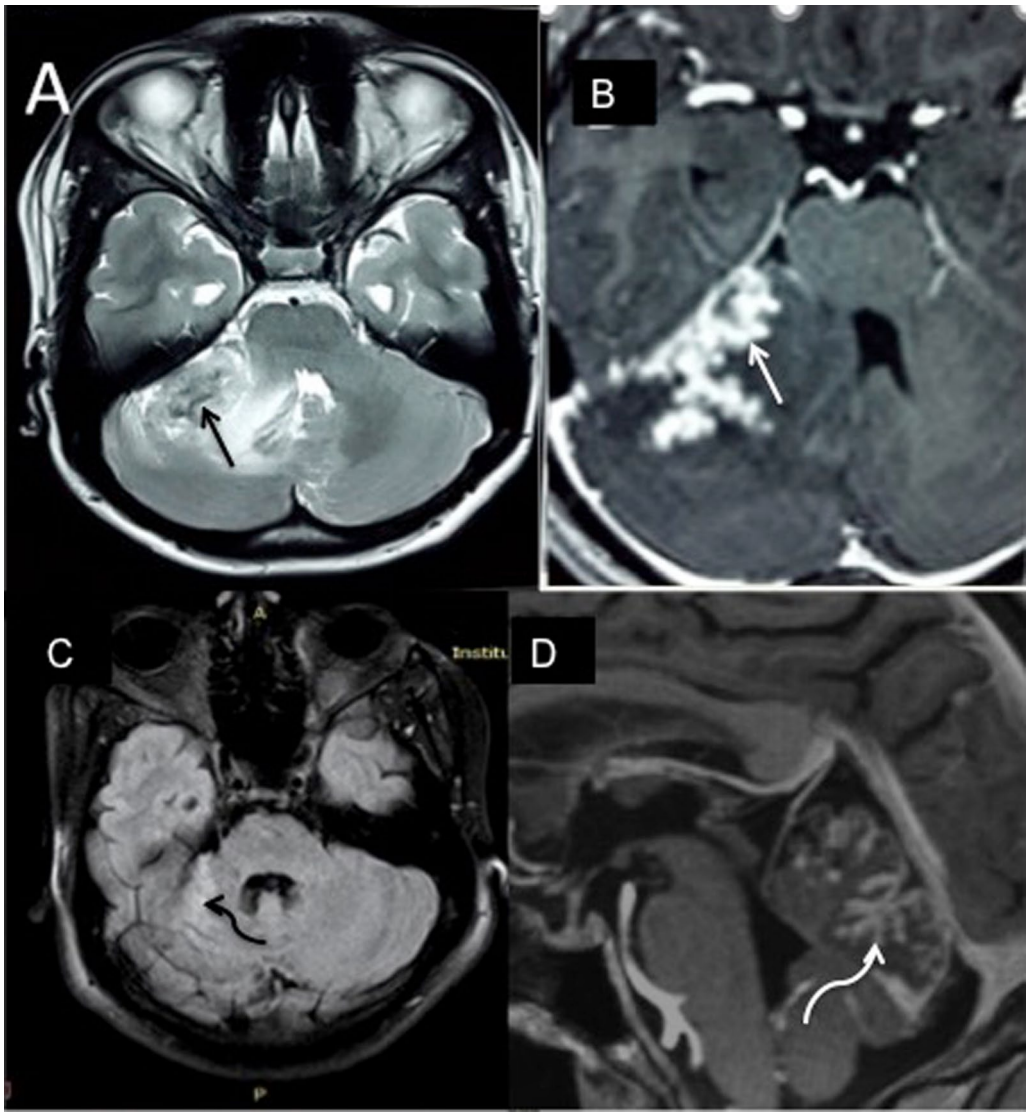

Fig. 7 Tubercular cerebritis. Axial T2W (**A**) and post-contrast T1 W (**B**) images show T2 hypointense lesion in right cerebral hemisphere (black arrow) with adjacent edema. The lesions show enhancing lesion involving cerebellar hemisphere extending to right cerebellopontine angle cistern with adjacent meningeal thickening. The lesions show micronodular thickening resembling "tree in bud" pattern (black arrow). Follow-up FLAIR axial image (**C**) after 8 months of therapy shows minimal residual gliotic changes (black curved arrow). Sagittal post-contrast image (d)of another patient of tubercular cerebritis showing tree in bud enhancement pattern (white curved arrow)

accelerated clinical course than tuberculomas and may require surgical drainage along with antitubercular treatment. The differential diagnosis of a tubercular abscess is pyogenic and fungal abscesses. Important MR features that distinguish tubercular abscesses from pyogenic and fungal abscesses are listed in Table 5 [16–19]. Magnetization transfer T1 (MT-T1) images can also be used to distinguish tuberculoma from tubercular abscess. In tubercular abscess, the hypointense peripheral T2 rim shows hyperintensity on MT T1, whereas, in tuberculomas, the T2 hypointensity is surrounded by a hyperintense rim on MT-T1, and that layer is not otherwise visible on T2-weighted images as this layer merges with edema [19].

Tubercular cerebritis

Tubercular cerebritis is a unique entity which is characterized by extensive inflammatory exudates, Langerhans' giant cells, reactive parenchymal changes, and caseating and noncaseating microgranulomas in the cortex. On MR images, it is seen as an area of gyriform post-contrast enhancement and corresponding

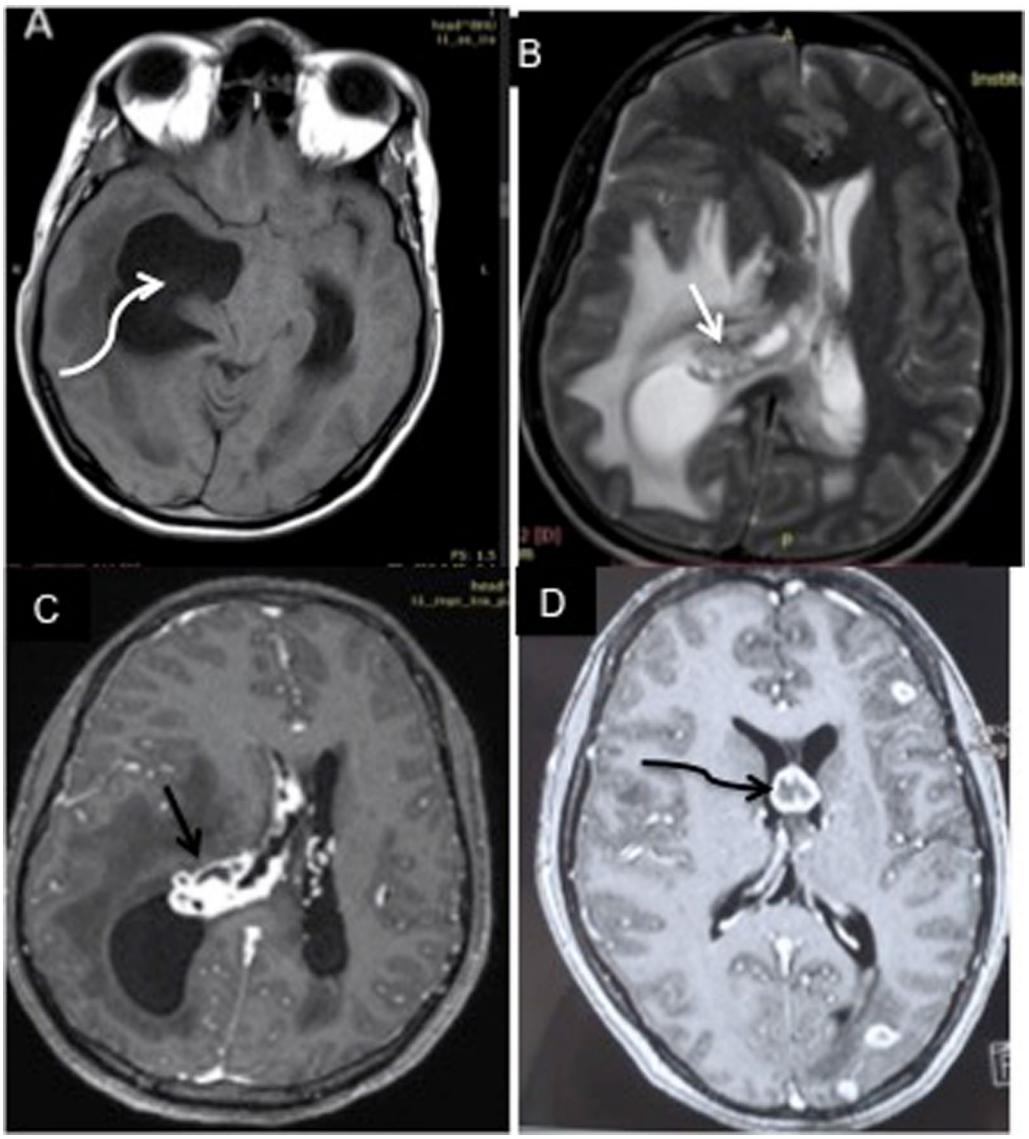

Fig. 8 Choroid Plexitis. Axial T1W (**A**), T2W (**B**), post-contrast T1W (**C**) images a patient showing strongly enhancing hetergenous and bulky right choroid plexus (black arrow) showing T2 hypointensity (white arrow). Sequestration and dilatation of right temporal horn are seen with periventricular ooze (curved white arrow). Post-contrast T1W image (**D**) of another patient shows a peripherally enhancing intraventricular tuberculoma (curved black arrow) centered at septum pellucidum. Also noted are multiple other tuberculomas in left cerebral hemisphere

hyperintensity on T2WI/FLAIR. In our study, we got 9 cases affected by tuberculous cerebritis with gyriform enhancement similar to previous studies [20]. Besides in two cases, both in the posterior fossa showed tree in bud pattern of enhancement with clusters of micro-granulomas (buds) attached to the enhancing gyrus (tree). The location of cerebritis of tubercular etiology is predominantly cerebral and cerebellar cortex in contrast with pyogenic cerebritis which involves the white matter and fungal cerebritis which involves basal ganglia and centrum semiovale [21].

Miliary tuberculosis

Disseminated miliary brain tuberculosis is characterized by numerous small (2–3 mm) nodules in the brain, which consists of caseating or non-caseating granulomas. On MRI, they show ring or nodular enhancement with a variable degree of adjacent edema. The imaging differentials are neurocysticercosis, metastasis, or fungal infection. Studies have shown that similar to miliary pulmonary TB, this imaging pattern results due to hematogenous spread from a preexisting primary focus [22, 23]. This type of brain tuberculosis exhibits a relatively mild

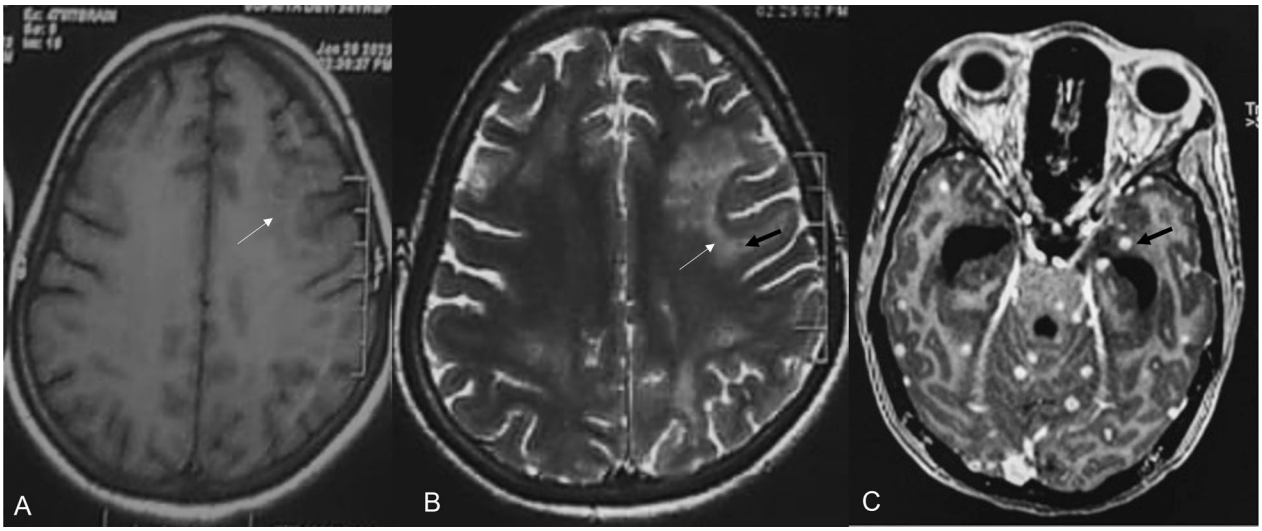

Fig. 9 Miliary tuberculosis. Axial T1 (**A**), T2 (**B**) and post-contrast T1W image (**C**) of a patient shows multiple T2 hypointense enhancing small nodules (black arrows) and adjacent edema (white arrows) in bilateral cerebral and cerebellar hemispheres consistent with miliary tuberculosis

clinical presentation without typical systemic signs of infection. Small lesions close to the ventricular ependymal wall or surface of the brain are prone to rupture causing severe TBM as seen in 1 of our patients [23].

Pachymeningeal tuberculosis

Rarely meningeal tuberculosis present as a predominantly dural-based mass-like lesion with secondary pial or parenchymal involvement also termed as en-plaque tuberculoma [24]. Both focal and diffuse forms exist. This entity is distinct from the inflammation in the dura mater adjacent to an intraparenchymal tuberculoma. These can present as isolated dural-based lesions or multiple lesions in which parenchymal involvement is caused by the dural inflammation. Isolated or focal lesions can mimic meningioma while diffuse pachymeningeal involvement can be similar to that in lymphoma, sarcoidosis, intracranial hypotension, Wegener's granulomatosis, or idiopathic hypertrophic pachymeningitis [23–25].

Tubercular choroid plexitis and intraventricular tuberculoma

The involvement of primarily choroid plexus was the sole finding in the present series of 2 cases who exhibited asymmetrically thickened enhancing choroid plexus with temporal lobe sequestration and dilatation similar to previously described cases [26, 27]. Choroid plexitis is thought to spread from the adjacent subependymal inflammatory focus of Rich, which eventually ruptures into the ventricle [26, 27]. The diagnostic differential may include choroid plexus papilloma; however, the hydrocephalus in papilloma is usually symmetrical on both sides with enlargement of the entire ventricular system.

Berthier et al. reported four cases of large intraventricular tuberculoma in children. Of these, three cases had tuberculoma in the frontal horn attached to the ependyma and the septum pellucidum and one had a thalamic tuberculoma extending into the ventricular body [28]. Besides two cases of choroid plexitis, we also came across a case of intraventricular peripherally enhancing tuberculoma centered at septum pellucidum.

Tumor-like presentation

A study by Algahtani et al. described a series of 9 cases of intra-axial tuberculosis whose clinical features and MRI suggested intra-axial tumors [29]. The study concluded that young age, history of tubercular contact, and presence of extracranial tuberculosis should suggest a non-neoplastic diagnosis in the space-occupying lesion. Ripamonti et al. reported 5 patients with a mass of tubercular origin in the brain [30]. The masses were markedly hypointense on T2-weighted images and showed strong post-contrast enhancement with few cases also revealing adjacent meningeal thickening and enhancement similar to our case. Radiological differentials are metastatic or primary intraaxial tumors such as glial tumors or lymphoma. A recent study has assessed the utility of MR perfusion study to distinguish between intracranial tubercular lesions and neoplastic lesions [31] and reported that tuberculomas/conglomerated tubercular lesions showed hypoperfused centers (rCBV 0.42 ± 0.25) and hyperperfused walls (rCBV 2.04 ± 0.61) while the

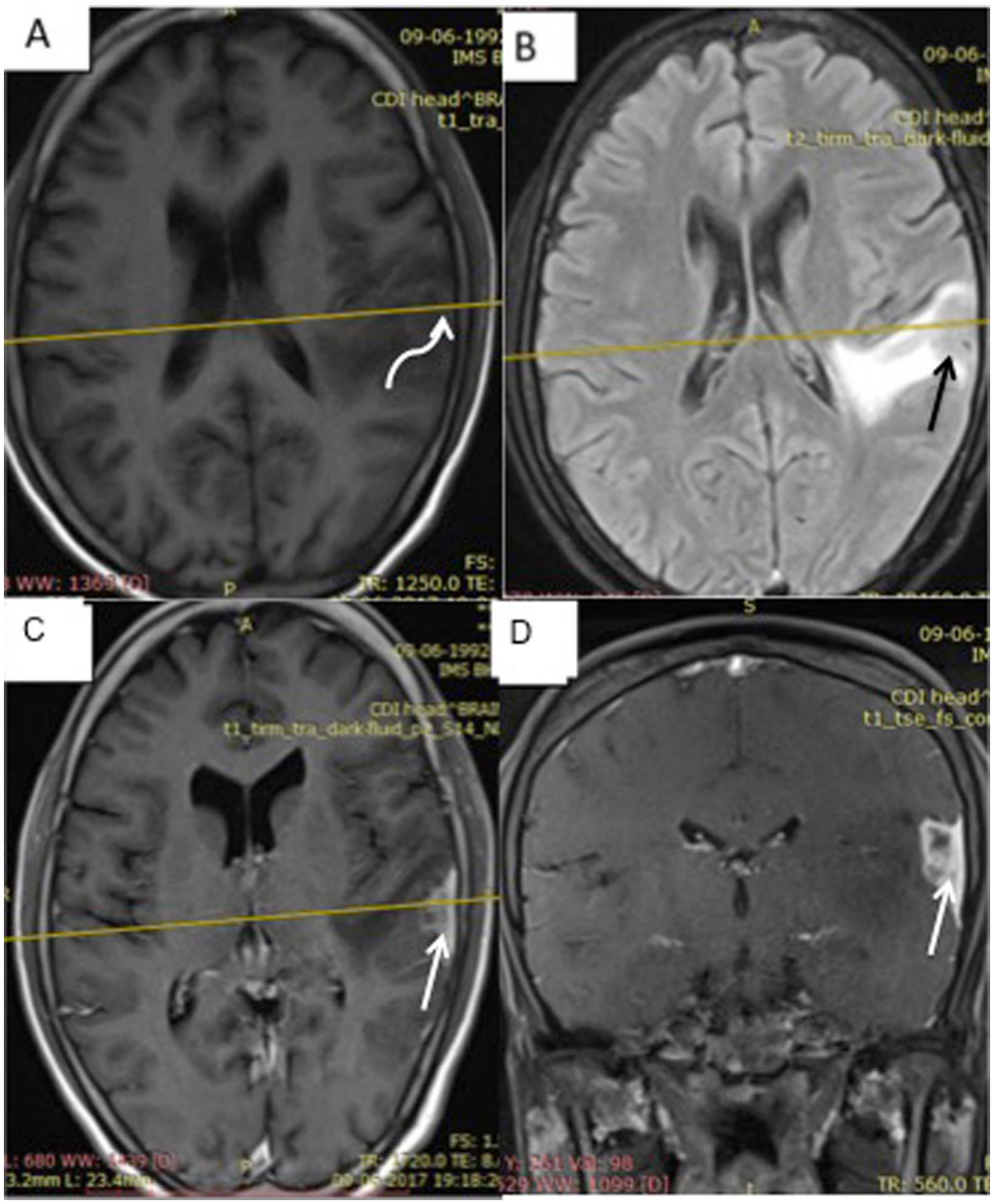

Fig. 10 Pachymeningeal tuberculosis. Axial T1W (**A**), FLAIR (**B**), post-contrast T1W (**C**), and coronal post-contrast T1W (**D**) images of a patient with showing T1 isointense (white curved arrow), T2/FLAIR hypointense (black arrow), strongly enhancing extraxial dural mass (white arrow) along left parietal lobe with secondary involvement of underlying parenchyma. The lesion shows small central non-enhancing area

rCBV of metastasis was significantly higher (5.43 ± 2.1). A cutoff value of ≥ 3.745 for peripheral wall rCBV was suggested for differentiating ring-enhancing metastases from ring-enhancing tuberculomas.

Figure 11 summarizes the variable presentation and imaging manifestations of cranial tuberculosis according to the location. Within the parenchyma, tuberculoma and vasculitic infracts are the most common presentation while cerebritis (gyriform cortical enhancement), abscess (diffusion restriction), and mass-like conglomerated granuloma. Tubercular encephalopathy (TBE) is an extremely rare form of tuberculosis caused due to delayed type IV hypersensitivity due to cell-mediated immunity to tuberculin protein [32, 33]. Only few reported cases have showed pathological and radiological similarity to acute disseminated encephalomyelitis with bilateral white matter disease [34]. Previous studies have identified a TBE in a 16-year-old girl with pulmonary TB

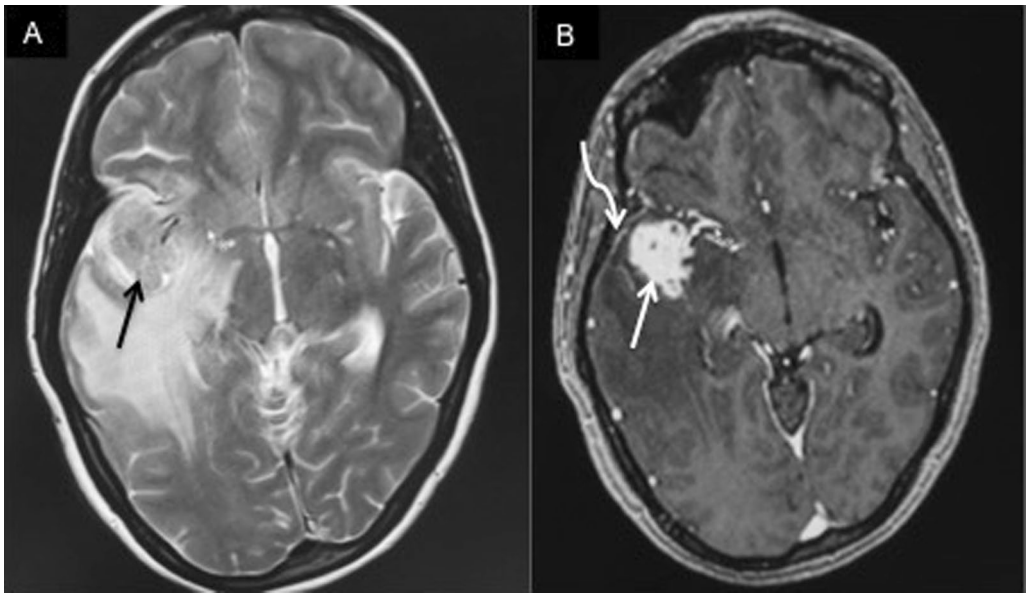

Fig. 11 Mass-like presentation. T2W (**A**) and post-contrast images (**B**) show T2 hypointense (black arrow), strongly enhancing intraaxial mass (white arrow) in right insular region mimicking intraaxial mass. Also noted was adjacent meningeal enhancement (white curved arrow)

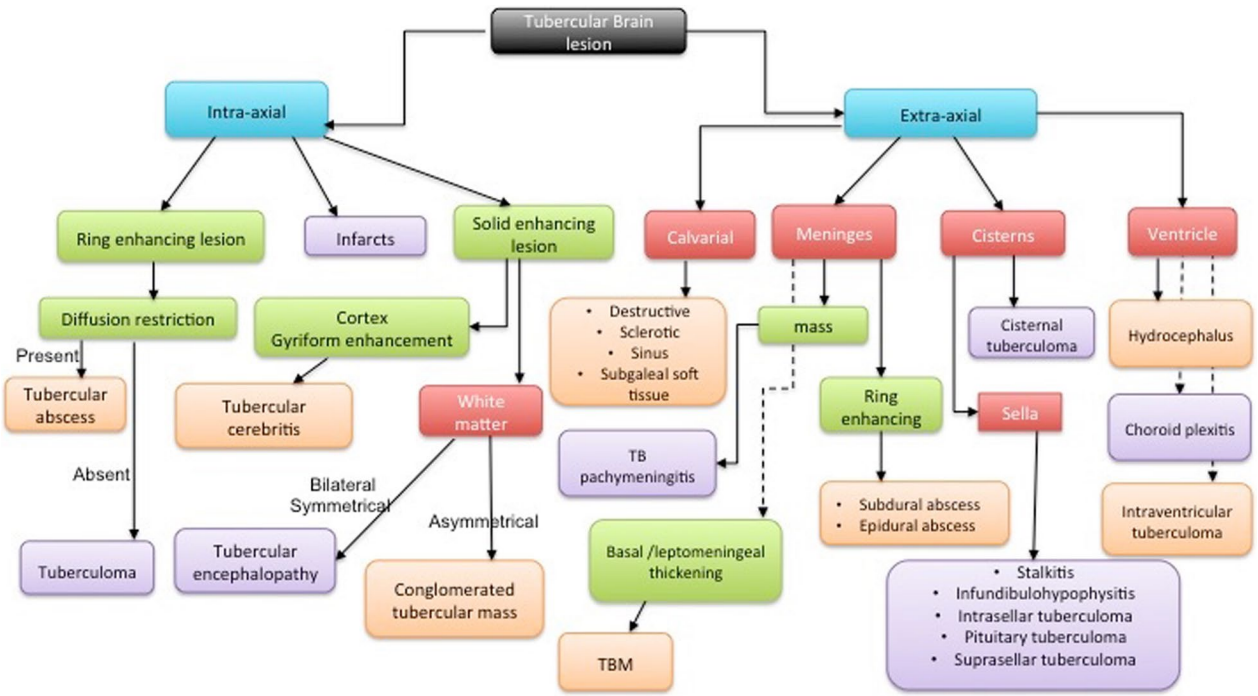

Fig. 12 Flow chart showing diagnostic algorithm in cases of cranial tuberculosis

who developed paraparesis and subsequent death 4 days after initiation of ATT for pulmonary tuberculosis, and post-mortem autopsy showed extensive demyelination of the brain [35]. Another case reported in the literature was a 45 year-old man with HIV infection and miliary TB [36] who developed a rapidly fatal hemorrhagic white matter disease. Varied presentation of extraaxial tuberculosis can occur in form of leptomeningtis, focal or diffuse pachymeningitis, epidural or subdural empyema, or calvarial lesions. Our study also demonstrates the spectrum

Table 5 Imaging features to distinguish between tubercular, pyogenic and fungal abscess

Features	Tubercular abscess	Pyogenic abscess	Fungal abscess
Morphology	Smooth lobulated or crenated wall	Smooth lobulated wall	Irregular wall with intracavitory projections
Diffusion	Low ADC in wall and cavity	Low ADC in wall and cavity	High ADC in cavity Low ADC in wall and projection
MRS	Lipid, lactate	Amino acid, acetate, succinate	Lipid lactate, amino acid, trehalose (3.6–3.8 ppm)
MTR	Low MTR of wall, (18–20) strong hyperintense rim on MT T1	High MTR of wall (25–30), minimal hyperintensity of wall on MT T1	

of sellar-suprasellar manifestations of TB. Ventricles can be affected in form of hydrocephalus, choroid plexitis, or intraventricular tuberculoma.

Our study has a few limitations. Firstly, this is a descriptive study and the findings may not be necessarily extrapolated to other populations. Secondly, the diagnosis in all cases could not be confirmed by the lab investigations and surgical biopsy in all cases and was presumptive in few cases based on the presence of evidence of coexisting cranial or extracranial tuberculosis. Thirdly, the number of cases included in our study is relatively small.

Conclusion

In conclusion, a significant number of patients of cranial tuberculosis can have atypical and misleading imaging manifestations. Our study highlights the variable and atypical imaging appearances of tubercular involvement of the brain. Familiarity with unusual presentations and their imaging findings is critical in ensuring prompt, accurate diagnosis, and treatment.

Abbreviations

MRI	Magnetic resonance imaging
TB	Tuberculosis
ADEM	Acute disseminated encephalomyelitis
ATT	Antitubercular treatment
CSF	Cerebrospinal fluid
TBE	Tubercular encephalopathy
TBM	Tubercular meningitis
HIV	Human immunodeficiency virus
DWI	Diffusion-weighted imaging
MRS	Magnetic resonance spectroscopy

Acknowledgements

The authors wish to acknowledge the contribution of the MRI technologist, Mrs Raichel Luyees in this study.

Author contributions

Data collection: SS, IK, TY. Manuscript initial drafting: AV, IK, PKS. Clinical analysis: PA. All authors read and approved the final manuscript.

Funding

No funding was obtained for this study.

Availability of data and materials

The datasets analyzed during the current study are available with the corresponding author.

Declarations

Ethics approval and consent to participate

The study was approved by the Institutional ethical committee of Institute of Medical Sciences, Banaras Hindu University. Written informed consent to participate in the study was obtained from all the patients/legal guardians included in the study.

Consent for publication

Written informed consent was obtained from all the patients/legal guardians (in case of minors) included in the study for the publication of the study.

Competing interests

The authors declare that they have no competing interests.

Received: 28 June 2022 Accepted: 21 June 2023
Published online: 07 July 2023

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