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Case report

Magic Dr.T? Tuberculous brain lesions in an immunocompetent patient-A case report ☆,☆☆

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ABSTRACT

Tuberculomas in the form of multiple ring-enhancing brain lesions is an uncommon occurrence in immunocompetent patient. Central nervous system tuberculosis may manifest as meningitis, tuberculoma, or abscess and can even occur in patients with or without active respiratory tract infection. In the case of active infection, specific antibiotic combinations and dosing duration are required, and respiratory isolation/precautionary measures must be taken by the health care workers and members of the family. Most literature has reported Central nervous system tuberculosis in patients with immunosuppression such as from HIV infection or solid organ transplantation; however, in endemic areas, CNS tuberculoma should be a differential consideration even for immunocompetent patients presenting with ring enhancing lesion (s). Our case highlights the importance of maintaining this clinical suspicion. Early diagnosis and management of our patient helped prevent potentially serious neurological sequelae.

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Introduction

Central nervous system tuberculosis (CNS TB) is a rare complication of Mycobacterium tuberculosis. It is commonly seen in developing countries in patients with already heightened

risk, such as from HIV-coinfection, use of immunosuppressive agents, alcoholism, and/or malignancy [1].

Droplet inhalation of Mycobacterial tuberculosis provides an entry to the human body, which subsequently causes a cascade of inflammatory reactions, protective immunity, and primary complex formation. Primary infection can also result in bacteremia, allowing spread to various organ systems including the central nervous system. Seeding of the CNS results in

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tuberculomas, which are usually preceded or accompanied by meningitis [2].

Given non-specific clinical symptoms and radiological findings, CNS TB often poses a diagnostic dilemma [3].

We present a case of CNS TB in an immunocompetent patient that illustrates the value of always considering TB in endemic areas.

Clinical presentation

A 22-year-old female presented with a 2-month history of progressive memory loss, vision abnormalities, and intermittent tonic-clonic seizures. The seizures occurred at least weekly and involved alternating extremities for 5–10 minutes. Eye rolling and severe headache followed the seizure episodes. She reported no fever, cough, night sweats, or weight loss.

Her past medical history was unremarkable with no known underlying chronic illness or use of medications.

Physical examination revealed an ill-appearing female without focal neurological deficits.

The patient was the first born in a family of eight members. She lived with both parents. There was no family history of chronic illnesses, and contact with any known cases of tuberculosis.

Investigation/imaging findings

Laboratory investigations revealed a high erythrocyte sedimentation rate (40 mm/hr), negative HIV test, mild thrombocytosis (329000 per microliter of blood), unremarkable liver and renal function tests, Sputum culture isolating normal flora-negative, Xpert MTB/RIF (genexpert) -negative and normal Adenosine deaminase serum.

Contrast enhanced brain MRI revealed multiple ring-enhancing lesions clustered in the left parietal lobe, the largest measuring 2.1cm. A smaller lesion was seen in the right occipital lobe. The central contents of the lesions were heterogeneous on T2WI and isointense on FLAIR without blooming on SWI. No evidence of restricted diffusion was seen on DWI. There was marked T2WI/FLAIR hyperintensity surrounding the lesion from vasogenic edema. No leptomeningeal enhancement seen on post-contrast images.

[Figure 1](#)

Differential diagnosis

Entities within the “MAGIC DR” mnemonic, was considered for the cerebral ring enhancing lesions [4]. Of these, metastases and glioblastoma multiforme seemed most fitting because of multiplicity, grey-white matter junction location, marked vasogenic edema as well as the absence of internal restricted diffusion. Abscess was considered unlikely due to absence of central restricted diffusion, normal blood counts, and absence of fever. Clinical history and lesion distribution eliminated

contusion and radiation necrosis. The duration of symptoms, presentation, and sparing of the overlying grey matter made subacute infarct unlikely. The complete ring-enhancing morphology did not seem to fit demyelinating process, which is more likely to have an incomplete (“horse shoe”) ring. Initially, CNS TB was not offered as a differential consideration.

Treatment

Craniotomy for tumor excision and biopsy was performed 3 weeks after initial presentation. Intra-operatively, the surgeons found a nonhemorrhagic mass, with a caseous core. There was extensive surrounding brain edema.

Histopathological analysis revealed confluent granulomas replacing brain tissue. These had extensive areas of caseous necrosis surrounded by Langhan's type giant cells as shown in [Figure 2](#). The findings were suggestive of tuberculoma.

Anti-TB antibiotics (Rifampicin/Isoniazid/Pyrazinamide/Ethambutol, a.k.a. RHZE) were prescribed, three times a day for one year. The patient was instructed to follow up monthly at an outpatient neurosurgery clinic.

Followup

On monthly follow up clinic visits, the patient reported marked improvement. By six months her vision had returned, her memory had improved and she had fewer episodes of convulsions reported that were mostly controlled by carbamazepine.

Six month follow up MRI scan showed left parietal encephalomalacia with gliosis and mild gliosis of the right occipital lobe as shown in [Figure 3](#), which was compatible with resolving of tuberculomas.

Discussion

CNS TB in the form of meningitis, tuberculoma, or abscess has mostly been reported among patients with immunosuppression due to HIV infection or solid organ transplantation [5]. However a few case reports have reported CNS TB in immunocompetent patients with and without lung infections and mostly among young adults below age of 30 in Sub-Saharan countries [6].

Genetic susceptibility factors such as defects in the interleukin-12 (IL-12) and interferon-gamma pathways are reported in patients presenting with extensive forms of the disease [7].

Most literature have described adult intracranial tuberculomas to be commonly seen in the supratentorial location of the frontal and the parietal lobes however few cases in children have shown involvement in the infratentorial region [8].

Clinical manifestations are similar to those seen in other lesions of the brain parenchyma. In our patient, preoperative symptoms of loss of memory and vision can be explained by

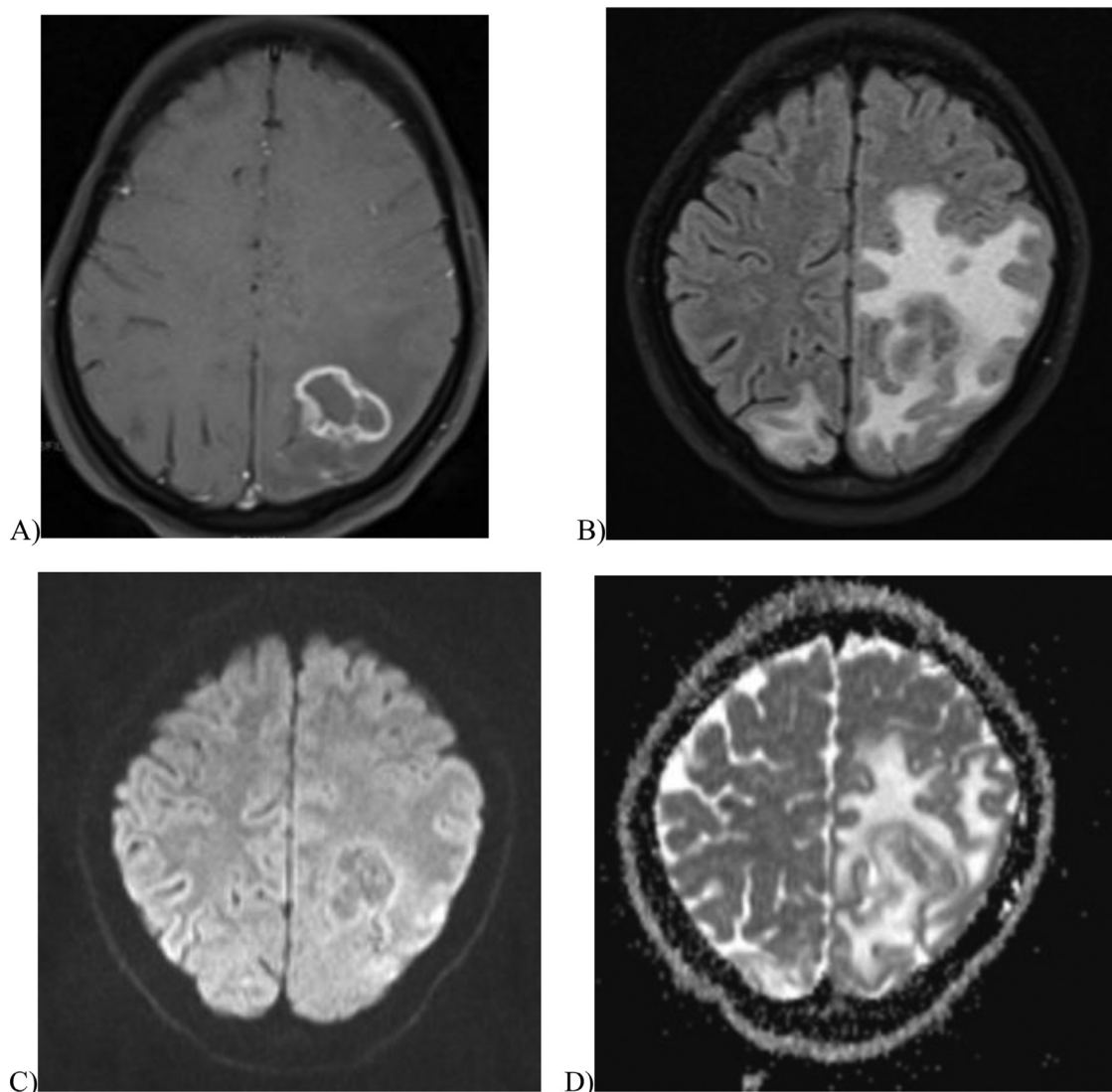


Fig. 1 – MRI images at initial presentation: (A) Axial T1-weighted post contrast images show an irregular thick rim-enhancing lesion at the left parietal lobe without leptomeningeal enhancement. (B) Axial FLAIR images show extensive perilesional vasogenic edema. (C & D) Axial DWI and ADC map show no corresponding restricted diffusion in the left parietal lobe lesion.

location of the lesion in the parietal and occipital lobe respectively [3].

Histopathology findings in parenchymal tuberculomas show a typical granulomatous reaction around a central area of caseating necrosis [9].

Conventional imaging techniques cannot differentiate tuberculoma from other intracranial masses. On pre-contrast brain CT the lesion can be of variable density and on post contrast images they typically demonstrate rim enhancement with perilesional vasogenic edema [6].

MR imaging helps in early diagnosis of the lesions due to its inherent specificity and sensitivity. T1WI demonstrate the non-caseating tuberculomas to be iso/hypointense while T2WI shows them to be hyperintense. There is homogeneous enhancement on post contrast images. Caseating solid tuberculomas appear hypo-intense on T1WI and T2WI which is

thought to be due to granulation tissue and compressed glial tissue in the central core resulting in greater cellular density than the brain parenchyma. On post gadolinium, these also demonstrate rim enhancement [8].

Tuberculoma with central liquefaction appears hypointense on T1, and hyperintense on T2-weighted images with a peripheral hypo-intense rim on T2W images. The low signal intensity of the capsule can be due to a layer of collagenous fibers with high protein concentration and low water content and a layer of outer inflammatory cells [10].

On MR spectroscopy, high fatty-acid spectra are seen in tuberculomas, making it a useful technique to differentiate them from other intracranial mass lesions. MR spectroscopy can therefore be used as an alternate/adjunctive option to biopsy, though this was not pursued in our case.

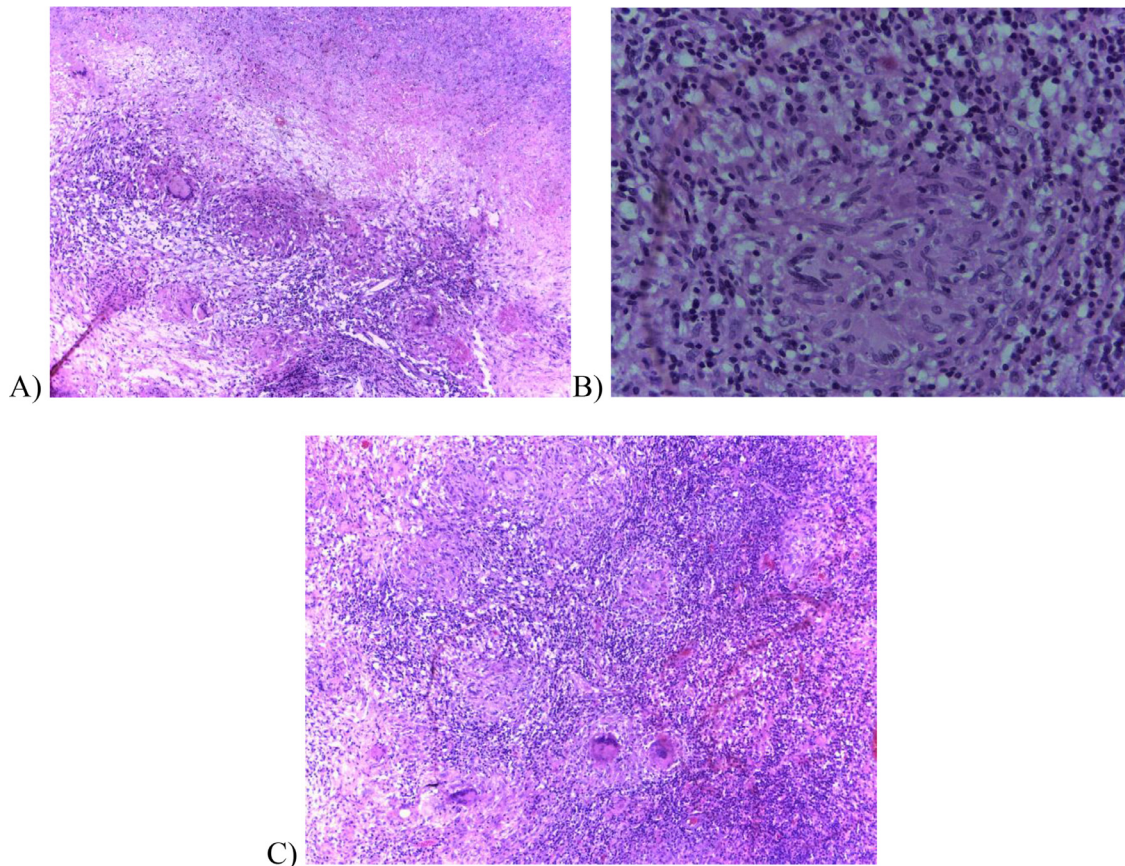


Fig. 2 – Representative histopathology sections with Haematoxyllin and Eosin staining showing (A) Granulomas with areas of caseous necrosis, Langhan’s multinucleated giant cells and rim of lymphocytes, original magnification; 10 x hpf. (B) Epithelioid cells and rim of lymphocytes, original magnification; 40 x hpf. (C) Replacement of brain tissue by multiple scattered granulomas, original magnification; 4 x hpf.

Ten months minimum treatment with anti-tubercular drugs is needed for tuberculomas. The recommended drugs are Isoniazid, rifampin, pyrazinamide, and ethambutol. In cases with perilesional edema or paradoxical progression during treatment, addition of corticosteroids is preferred [8].

Surgery is usually not indicated as the tuberculomas usually resolve with anti-tuberculous drugs and conservative treatment, but in case of a diagnostic dilemma or in cases of increased intracranial pressure despite treatment is when surgery is indicated [7]. This is well illustrated in our patient as the tuberculomas had completely resolved following 6 months treatment and surgery was only indicated because of the posed diagnostic dilemma thus necessitating a need for excisional biopsy.

If tuberculoma had been thought of as an early diagnosis in our patient, an extensive surgery may not have been required. Clinical testing for tuberculosis and/or more limited biopsy may have been able to establish a diagnosis and motivate medical therapy for tuberculosis.

Tuberculomas are seen to have resolved on follow up scans if they demonstrate calcifications or non-enhancement of previous enhancing lesions and these patients after completing therapy and do not have recurring symptoms then they don’t need to be followed up [8].

CNS TB is rare, especially in immunocompetent hosts. However, having a high clinical suspicion with ring enhancing lesions in endemic areas should raise a concern for this diagnosis. Early consideration may prevent unnecessary extensive surgical intervention as these will resolve with just medical management. In endemic areas, we therefore suggest that the differential diagnosis for rim enhancing lesions be remembered as “MAGIC DR. T” with tuberculoma representing the last letter in the modified mnemonic.

Learning points

- CNS TB is an important differential diagnosis in a patient presenting with ring enhancing lesions within the brain parenchyma.
- Immunosuppression is a known risk factor however immunocompetency should not exclude CNS TB especially in the developing countries where Mycobacterium tuberculosis infections are known to be endemic.
- Young patients presenting with CNS manifestations and brain lesions that don’t reach a clear diagnosis should raise the suspicion for a possible tuberculous infection.

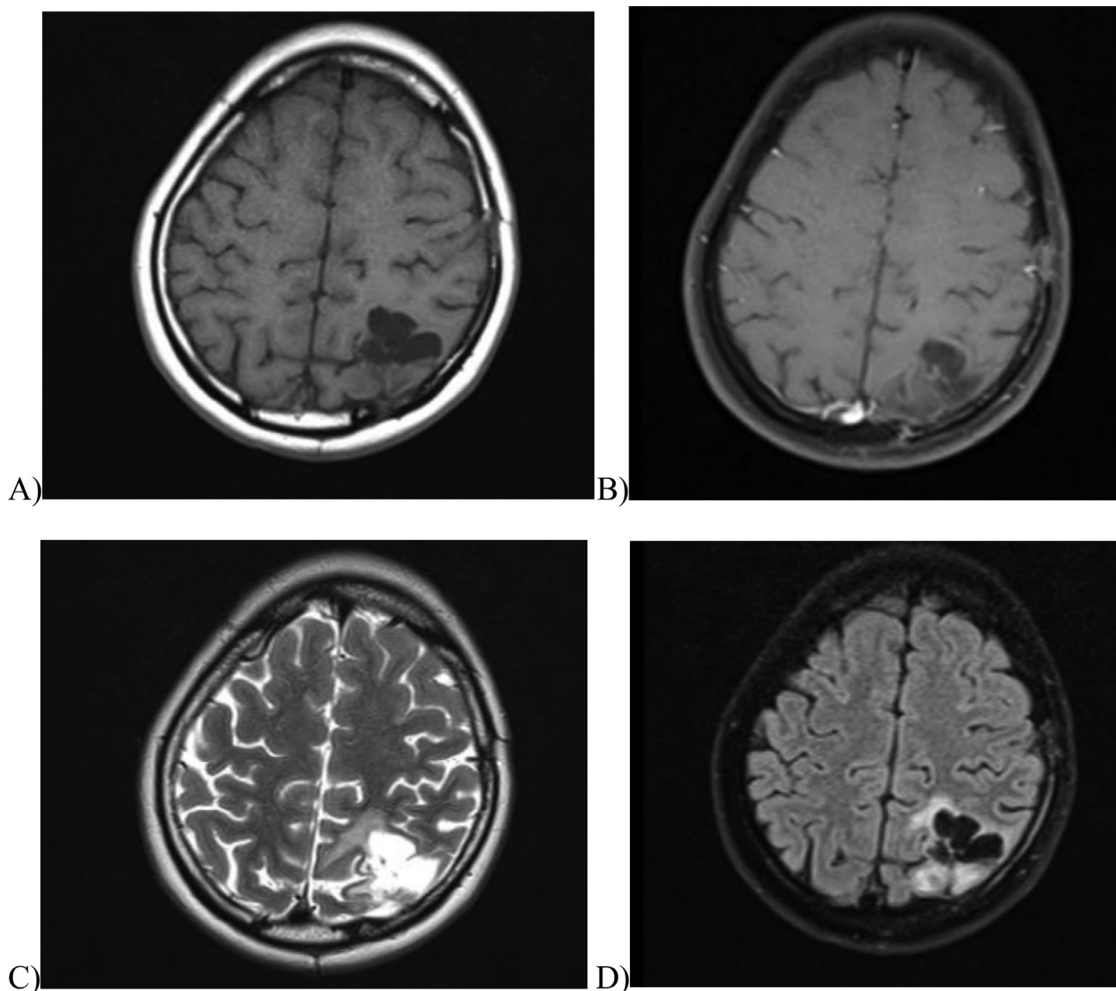


Fig. 3 – MRI images following 6 months of anti-TB treatment: (A) Axial T1-weighted pre contrast and (B) Axial T1-weighted postcontrast images show complete resolution of the previous irregular enhancing left parietal lobe lesion. (C) Axial T2-weighted and (D) Axial FLAIR images show resolution of previous perilesional vasogenic edema with residual encephalomalacia and gliosis.

- Remember – absence of restricted diffusion in ring-enhancing lesions *does not* exclude infectious etiology.

Patient consent

Informed consent was obtained from patient.

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