

Tuberculous encephalopathy mimicking limbic encephalitis and large intraparenchymal mass: A case report

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Abstract

We report a 17-year-old gentleman presented with acute encephalopathy and neuropsychiatric disturbances. Contrast-enhanced CT and MRI brain revealed bilateral enhancing grey matter lesions involving both basal ganglia with perilesional oedema. The peculiarity of the lesions raising confusions whereby limbic encephalitis and intracranial masses were initially given consideration hence causing a delay in treatment. Tuberculous encephalopathy has different imaging appearances depending on the stage of maturity which will be further discussed here. Definitive treatment for this patient comprises of daily 10-months dose of anti-tuberculous drugs with prompt neurosurgical intervention if required. However, these should be delivered at a timely fashion to improve the outcome for both survival and neurological sequelae.

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Introduction

Being the most devastating clinical manifestation of tuberculosis due to its high mortality and distressing neurological sequelae, CNS TB accounts for 1% of all TB cases and approximately 5-10% of extrapulmonary TB (Cherian & Thomas, 2011). Risk factors for CNS TB includes age (children > adult), HIV co-infection, malnutrition, recent measles in children, alcoholism, malignancies, the use of immunosuppressive agents in adults and diseases prevalence in the community (Cherian & Thomas, 2011). However, Dastur only first described TB encephalitis as an autopsy finding in 1960 (Hee-Jin *et al.*,

2011). Unfortunately, no prevalence of TB encephalitis and large intraparenchymal mass was well documented to date in comparison to the more recognized form of CNS TB which includes tuberculoma, meningitis (accounting for 90% of CNS TB) and less commonly tuberculous abscess and miliary form (Taheri *et al.*, 2011). The uniqueness of this uncommon imaging manifestation of a very common disease as well as it being misleading towards limbic encephalitis and intraparenchymal mass may pose diagnostic challenges for clinicians.

Case Report

Our patient is a young 17-year-old previously well gentleman presented with

acute encephalopathy and neuropsychiatric disturbance comprising of general unwellness, lethargy and headache for the past 1 month. Apart from previous travel history to Selangor and Johore, patient denied previous history of high risk behaviours and worked as a garbage collector. On general examination patient was noted to be dysphonic, drowsy and lethargic with Glasgow Coma Score (GCS) of 11/15. Further physical examination revealed slight neurological deficit whereby power of all 4 limbs of 4-5/5, up-going right plantar reflex and significant neck stiffness.

Except for raised total white blood count with neutrophil predominance and raised CK, the rest of the blood investigations are normal. Contrast-enhanced computed tomography (CT) of the brain demonstrated bilateral enhancing grey matter lesions involving both basal ganglia with perilesional oedema (Figure 1). No abnormal leptomeningeal enhancement is observed. Gadolinium-enhanced MRI showed multiple enhancing lesions at deep grey matter with haemorrhages (Figure 2). Patient was treated as cerebritis, but unfortunately took at-own-risk discharge home.

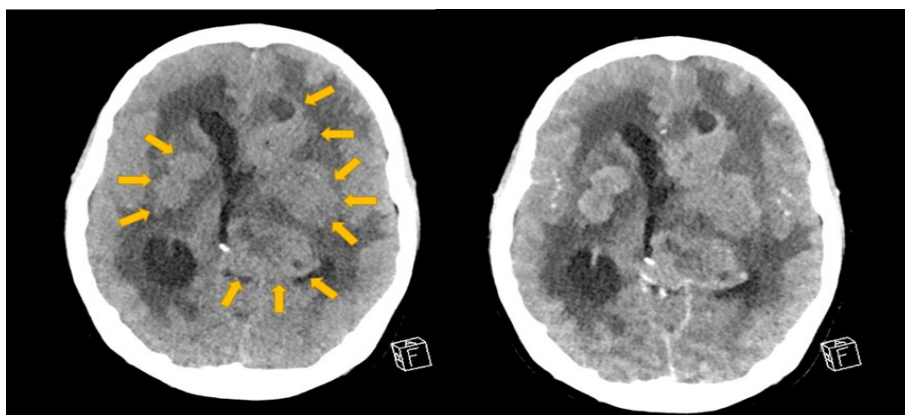


Figure 1. Unenhanced and contrast-enhanced axial CT brain showing isodense bilateral basal ganglia lesions with involvement of the left thalamus (yellow arrow) and causing extensive vasogenic oedema. Homogenous enhancement post contrast is noted.

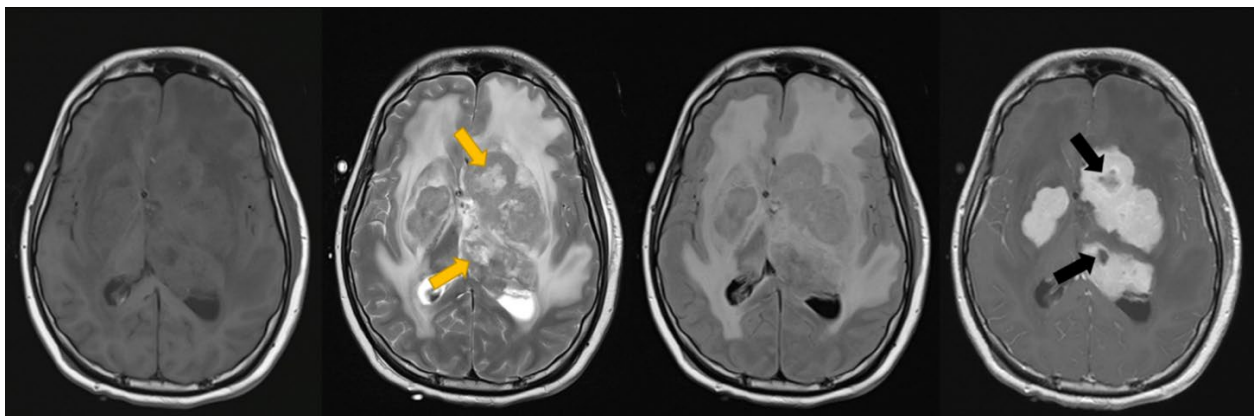


Figure 2. Axial images of MRI brain T1, T2, T2 FLAIR and T1 post contrast. Note the appearance of the basal ganglia lesions which are isointense on T1, T2 and T2 FLAIR with homogenous enhancement post contrast. Note also the appearance of central T2 hyperintensity (yellow arrow) with minimal or no contrast enhancement (black arrow) which likely represent caseating tuberculomas with liquefied centre.

However, the patient was readmitted in the ensuing month for worsening neurological deficit with otherwise similar GCS. Infectious screenings are normal with increased level of CRP and LDH. FBP showed mild anisopoikilocytosis, neutrophilia and lymphopenia with no evidence of abnormal lymphoid cells. CSF fluid revealed high total protein, positive globulin and lymphocytosis. Repeat MRI revealed more extensive involvement of the lesions involving medial part of temporal lobe, possibly due to limbic encephalitis (Figure 3). The lesions also had progressively

worsened with masses-like appearance with areas of liquefaction (Figure 4). Contrast enhanced CT thorax, abdomen and pelvis was also performed to look for primary tumour considering paraneoplastic encephalitis as a possible diagnosis but no significant mass was found. Repeated brain biopsy was carried out which eventually yielded positive AFB hence the patient was immediately commenced on anti-tuberculous medication. However, patient eventually succumbed due to nosocomial pneumonia.

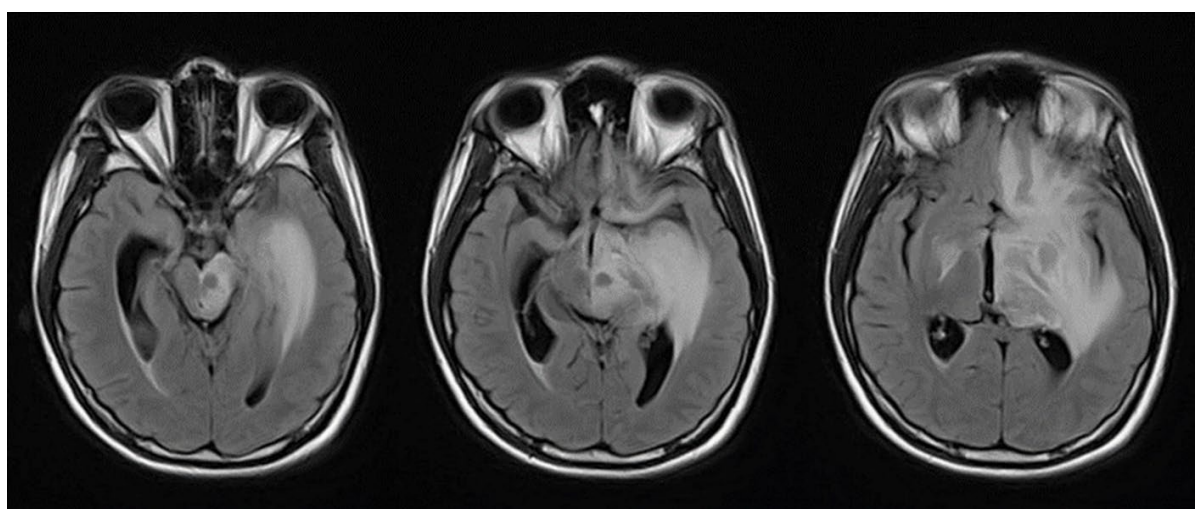


Figure 3. Axial MRI T2 FLAIR at different slices of temporal lobe. Note the white matter hyperintensity involving the medial aspect of the left temporal lobe which may mimic limbic encephalitis.

Discussion

Tuberculous encephalitis (TBE) is a much rarer form of CNS tuberculosis typically seen in young children (Cherian & Thomas, 2011; Taheri *et al.*, 2011). To date, only 13 cases of possible TBE had been reported since the initial report by Dastur *et al.* in 1966 (Hee-Jin *et al.*, 2011; Sharma, 2015; John, 1986; Fernando & Miguel, 2015; Vandana *et al.*, 2013; Venkatram *et al.*, 2017). In TB-endemic area like Malaysia, previous exposure to tuberculoprotein causes sensitization by ‘allergic’ or type IV direct hypersensitivity reaction due to cell-mediated immunity to tuberculoprotein.

Some literature also proposed that there is pathological similarity between this condition and other demyelinating disorders (Hee-Jin *et al.*, 2011; Fernando & Miguel, 2015). MR may show diffuse or focal hyperintense lesions in the white matter with marked gadolinium enhancement ((Hee-Jin *et al.*, 2011). Sometimes, gyriform pattern of contrast enhancement may also be demonstrable (John, 1986). Symmetrical basal ganglia hyperintensity on T2 and fluid-attenuated inversion recovery (FLAIR) sequences is demonstrated in basal ganglia encephalitis (Fernando & Miguel, 2015). Areas of restricted diffusion may also be manifested (Sharma, 2015). Nevertheless, our patient demonstrated only focal markedly enhancing tuberculous cerebritis predominantly involving both basal ganglia

regions. Otherwise, these changes were seen as rather asymmetrical in distribution as evaluated on T2-weighted and FLAIR sequences. Furthermore, neither gyriform pattern of enhancement post IV Gadolinium

administration nor areas of restricted diffusion on diffusion-weighted imaging was observed.

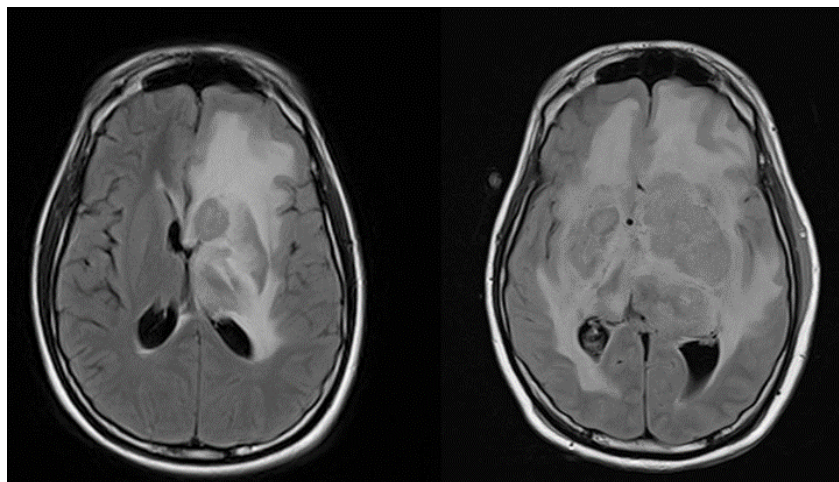


Figure 4. Axial MRI T2 FLAIR at initial presentation and repeat imaging at about 3 months later without proper treatment. The scan shows worsening of the bibasal ganglia and thalami lesions with extensive vasogenic oedema.

Involvement of the temporal lobe and limbic system prompts the diagnostic possibility of limbic encephalitis. This entity, however, remains a diagnostic challenge for clinicians since it may manifest a widely variable spectrum of clinical presentations. It can be further divided into 2 subgroups; paraneoplastic or non-paraneoplastic (Kelley *et al.*, 2017). MR findings typically include T2-FLAIR hyperintensities with/without restricted diffusion and contrast enhancement. To date, we have discovered case reports of two cases concerning tuberculous limbic encephalitis (Toudou, Obenda & Souirti, 2017; Daher, Monzer & Abi-Saleh, 2020). When compared to our 17-year-old patient, these two reported patients similarly presented with encephalopathic symptoms. However, these cases also demonstrated typical features of tuberculous meningitis and tuberculomas on MRI not predominant in basal ganglia; very much unlike our patient. The most recent case in 2020 also depicted pulmonary involvement when the patient synchronously developed unresolving upper lobe pneumonia with mediastinal lymphadenopathies yielding numerous acid-

fast bacilli from transbronchial needle aspiration.

CNS TB may also rarely present as a large intraparenchymal mass which may mimic a tumour (Sharma, 2015; Venkatram *et al.*, 2017). This could either be a giant tuberculoma or multiple tuberculomas forming a conglomerate mass (Sharma, 2015; Venkatram *et al.*, 2017). Uncommonly, tuberculomas predominate the basal ganglia region (Venkatram *et al.*, 2017) though this region is where high metabolic activity takes place making it susceptible to infections (John, 1986). As in our case, the confusion was oblivious due to symmetrical lentiform involvement of the lesions. Tuberculomas are known to exhibit different imaging profile based upon the stage of maturity (Rock *et al.*, 2008; Venkatram *et al.*, 2017; Khatri *et al.*, 2018). Referring to our case, two serial MRIs showed enlarging mass-like appearances of multiple tuberculomas at both basal ganglia regions which generally depicted as non-caseating tuberculoma and caseating tuberculoma with liquefied centre. Non-caseating tuberculoma is demonstrable as hypo- to isointense on T1, hyperintense

on T2 and subsequent homogenous enhancement post contrast. Whereas on the second MRI, caseating tuberculoma with liquefied centre is depicted as centrally

hypointense on T1 and hyperintense on T2. Table 1 summarizes the MR appearances of tuberculous brain lesions according to its stage of maturity (Khatri *et al.*, 2018).

Table 1. MR appearances of tuberculous brain lesions according to its stage of maturity (Khatri *et al.* 2018).

Stages of maturity	MR appearances
Non-caseating	Hypo- to isointense on T1, hyperintense on T2. Homogenous enhancement post contrast. Seen in the earliest imaging of our patient.
Caseating with solid centre	Hypointense on T1, strikingly hypointense on T2. Attributed to the granulation tissue and compressed glial tissue in the central core resulting in greater cellular density than the brain parenchyma.
Caseating with liquid centre	Centrally hypointense on T1, hyperintense on T2. This is demonstrated in the later imaging of our patient (Figure 2).
Capsule formation in caseating granulomas: peripheral hypointense rim on T2, rim enhancement post contrast, may be related to a layer of collagenous fibre with high protein concentration, low water content and a layer of outer inflammatory cells.	

The recommended first line treatment agents for CNS TB are daily 10-months doses of Isoniazid, Rifampicin, Pyrazinamide and Ethambutol. Patient should be treated for a minimum of 10 months (Cherian & Thomas, 2011). Extension to at least 12 months for failed responders or should treatment interruptions occur. Prompt neurosurgical referral is required should hydrocephalus or tuberculous brain abscess take place. Ventriculoperitoneal shunt or endoscopic third ventriculostomy may be opted if the duration of illness is more than 4 weeks. Patient with GCS of >8 and <14 are better off with early shunt procedure (Cherian & Thomas 2011). The single most important determinant of outcome for both survival and sequelae is the stage of the CNS TB at which treatment is started (Cherian & Thomas 2011).

Conclusion

TB encephalitis and large intraparenchymal mass are uncommon entities of CNS TB showing different radiological spectrum which needs to be considered by radiologists from the more common conventional tuberculoma or TB meningitis. The many faces of CNS TB in general should prompt this diagnosis to be included should atypical, intriguing imaging presentation is encountered. Failure in early recognition hence correct treatment at a timely fashion of CNS TB would result in considerable magnitude of the sequelae while the disease stage at which treatment is commenced is the single most important determinant for prognosis.

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