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CASE REPORT

Evolving Stroke in Tuberculous Meningitis

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ABSTRACT

Tuberculous meningitis (TBM) is the most severe form of extra-pulmonary tuberculosis which carries high mortality with 100% mortality without treatment. A neurological complication of TBM includes hydrocephalus, brain abscess and stroke. In this report, we would like to illustrate a case of stroke in a patient with TBM. In this case, a 37-year-old man initially presented with fever for 1 week associated with severe headache and occasional vomiting. Computed tomography (CT) of the brain showed leptomeningeal enhancement and lumbar puncture findings consistent with infective in nature. His MARAIS score was 13 and was treated as tuberculous meningitis with anti-tuberculous therapy. While in the ward, he developed right-sided body weakness with evolving CT brain findings. His condition then stabilized with anti-tuberculous treatment which consists of isoniazid, rifampicin, pyrazinamide and streptomycin. Dexamethasone was also initiated. On follow up, his condition further improves and is functionally independent. In conclusion, tuberculous meningitis is an aggressive disease with high morbidity. Stroke can occur as a result of TBM. Timely initiation of treatment is important in improving the outcome of the patients.

INTRODUCTION

Tuberculosis is one of the leading causes of death worldwide. World Health Organisation estimated 10 million people were infected by tuberculosis and a total of 1.5million people died from tuberculosis in 2018 (World Health

Organisation [WHO], 2019). Tuberculous meningitis (TBM) is the most severe form of tuberculosis, which carries the most significant mortality and morbidity, particularly among patients with HIV. The absolute incidence of TBM and the overall proportion of meningitis cases that are attributable to TBM vary greatly by location and are influenced by the overall incidence of tuberculosis, age structure and HIV-1 prevalence in a population (Wilkinson et al., 2017). Patients with TBM often present with typical symptoms and signs of meningitis such as fever, headache and stick neck. Importantly, the meningeal sign may be absent in the early stages (Chin, 2014). Some patients may go on and develop complications as a result of TBM. The neurological complications of TBM include stroke, hydrocephalus, tuberculoma formation, cranial nerve palsies, myeloradiculopathy, epileptic seizures and visual impairment (Anderson et al., 2010; Zhang et al., 2019). A stroke occurs in around 20% of TBM patients, either symptomatic or asymptomatic (Anuradha et al., 2010). Here, we would like to illustrate a case of evolving stroke in a patient with TBM.

CASE PRESENTATION

A 37-year-old previously healthy man presented to a local health clinic with fever for 1-week with chills and rigours. He also complained of persistent severe headaches with occasional vomiting. Otherwise, he denied cough, difficulty in breathing, abdominal pain or diarrhoea. There was reduced appetite and weight loss for the past 1week. He has no history of tuberculosis and denied any previous tuberculosis contact. On examination, his blood pressure was 110/60 mm Hg, pulse rate was 105 bpm, temperature 38.1°C. He was alert and conscious. Neurological examination showed reactive pupils and power of 5/5 in both upper and lower limbs. There was no neck stiffness. Kernig's and Brudzinski signs were both negative. He was referred to the hospital for suspected meningitis.

Upon arrival to the hospital, a computed tomography (CT) of the brain was done which showed ill-defined hypodensity at the left head of the caudate nucleus and internal capsule (Figure 1). There was leptomeningeal enhancement upon contrast with no hydrocephalus. His chest radiograph did not show features of tuberculosis. His cerebrospinal fluid (CSF) examination showed 100 total white blood cells (90% lymphocytes), protein 5g/l and a glucose ratio of 0.33. His CSF Genexpert and cryptococcal antigen were negative. CSF for mycobacterium culture was sent and came back as negative later on (Table 1). His MARAIS score was 13. He was then treated as TBM and started on anti-tuberculous (anti-TB) therapy which consisted of oral isoniazid 300mg daily, oral rifampicin 600 mg daily, oral pyrazinamide 1.25 g daily and intramuscular streptomycin 900 mg daily. He was also started on dexamethasone 0.4 mg per kg daily with a tapering dose to treat for TBM.

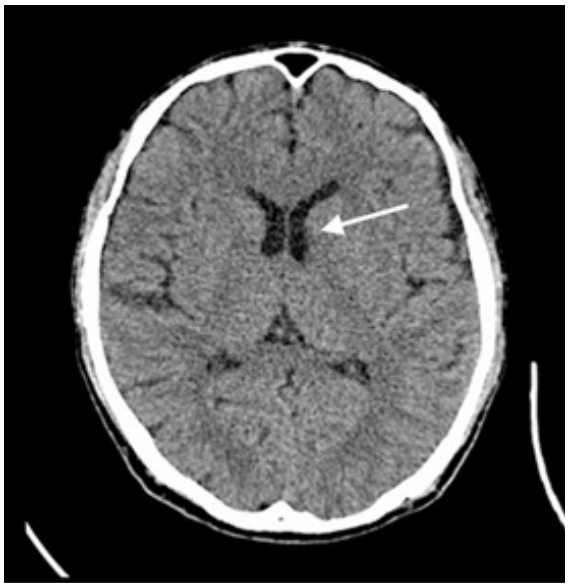

Figure 1 CT brain at day 1 showing ill-defined hypodensity at the left head of caudate nucleus.

Table 1 CSF results of the patient

CSF investigation	Results	Normal range
AFB	Negative	
Gram stain	Negative	
Protein	5 g/l	0.18 – 0.60 g/l
Cell count	100 TWBC (90% lymphocytes)	0 – 5 TWBC
Culture and sensitivity	No growth	
Glucose ratio	0.33	0.60
Geneexpert	Negative	
Cryptococcal antigen	Negative	

Two days into anti-TB treatment, the patient was noted to have been slow in response. Repeated CT brain showed more prominent hypodensities at the left caudate nucleus (Figure 2).

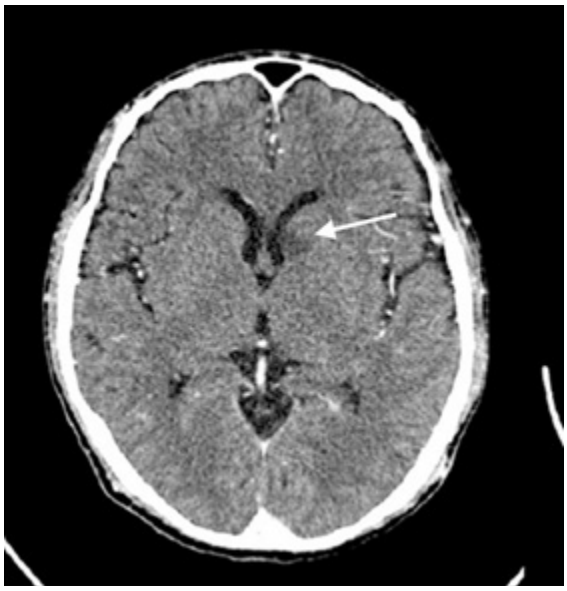

Figure 2 CT brain at day 3 showing more prominent hypodensity at the left caudate nucleus.

Two days later, the patient developed right-sided body weakness with a power of 3/5. A repeated CT brain showed worsening cerebral grey, white matter oedema (Figures 3 and 4). He was continued with anti-tuberculous therapy, dexamethasone with physiotherapy. His condition subsequently stabilized with treatment.

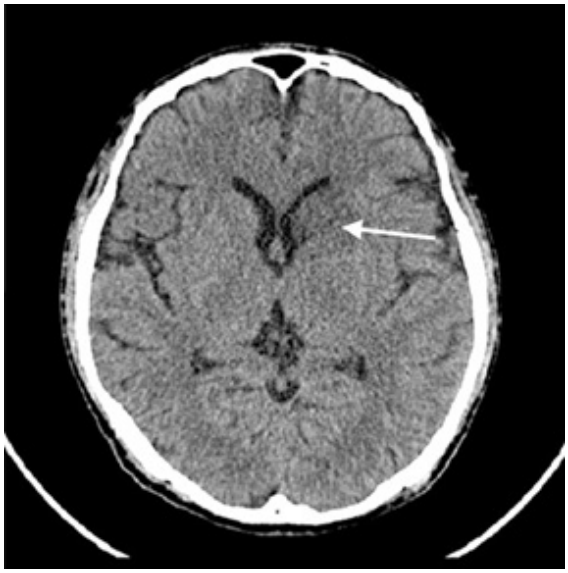

Figure 3 CT brain at day 5 showing evolving changes of basal ganglia with worsening grey white matter oedema

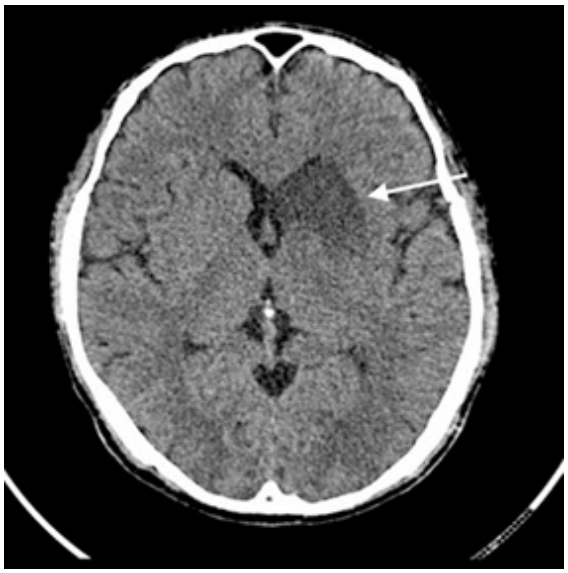

Figure 4 CT brain at day7 showing evolving changes of basal ganglia with worsening grey white matter oedema

On subsequent follow up in the clinic, the patient improved remarkably and functionally independent. Repeated CT brain on follow up 3 weeks later showed improvement of white matter oedema (Figure 5). CT brain after the intensive phase showed resolution of white matter oedema with encephalomalacic changes (Figure 6).

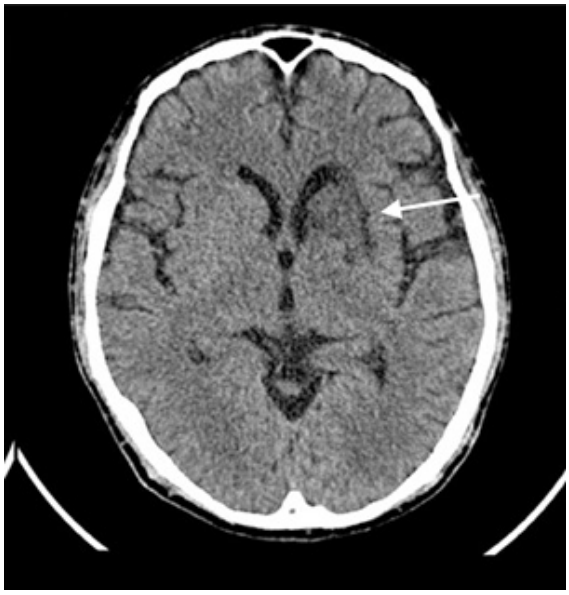

Figure 5 CT brain at 3 weeks showing improvement of white matter oedema

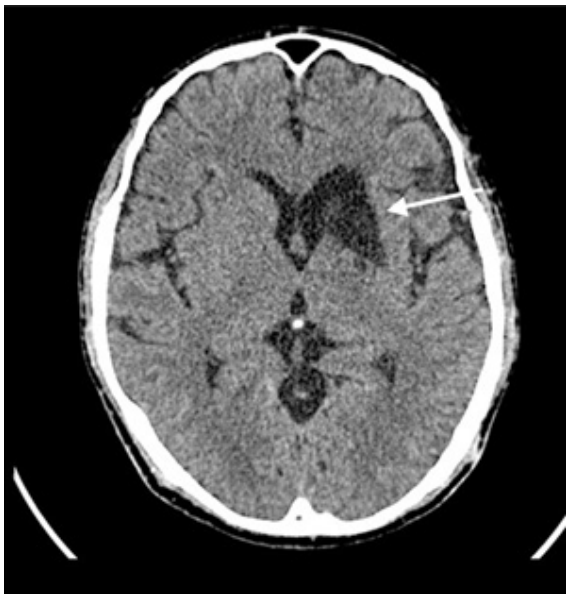

Figure 6 CT brain at 2 months of anti-TB showing resolution of oedema with encephalomalacic changes.

DISCUSSION

TBM is the most severe form of extra-pulmonary tuberculosis due to its morbidity and mortality with an estimated 50% of patients carry long term neurological deficits despite anti-tuberculous therapy. The diagnosis of TBM is often challenging as symptoms are often non-specific and can mimic other diseases. Marais case definition criteria and Thwaites diagnostic scoring have been developed to assist in the diagnosis of TBM (Luo et al., 2018). Reported neurological complications of TBM include stroke, tuberculoma formation, hydrocephalus, arachnoiditis, intracerebral haemorrhages, mycotic aneurysm, brain abscess, cranial nerve palsies and myeloradiculopathies (Anderson et al., 2010).

Stroke, on the other hand, occurs in about 20% of the patients with TBM (Azharuddin et al., 2016). Stroke in TBM is often ischemic in origin. Infarcts can be symptomatic or asymptomatic. TBM with stroke often presents with dense hemiplegia. Other neurological manifestations include ataxia, seizures and movement disorders. The exact pathophysiological mechanism of stroke in TBM is not well understood. The presence of basal inflammatory exudates can lead to vasculitis, arterial thrombosis, vasospasm and subsequently ischemia (Anuradha et al., 2010). Cytokines and hypercoagulable states during the early phase of TBM also play a role. Besides, the presence of classical risk factors of stroke such as hypertension, diabetes mellitus and dyslipidaemia increase the risk of stroke in TBM (Wasay et al., 2018).

In terms of neuroimaging, a cranial CT scan reveals infarction in 15%-57% of the patient with TBM. Magnetic resonance imaging (MRI) scan is a more superior imaging modality in detecting infarction in TBM (Misra et al., 2011). The common areas of cerebral infarctions include basal ganglia, thalamus, caudate and putamen (Zhang et al., 2019). Occasionally, infarct at the cortex, brainstem and cerebellum can also be seen. The pattern of cerebral infarctions is attributed to the involvement of medial striate, thalamotuberal and thalamostriate arteries. The presence of cerebral infarctions is often associated with poorer outcomes. Other common neuroimaging findings of TBM include leptomeningeal enhancement, hydrocephalus, tuberculoma and vasculitis. Leptomeningeal

enhancement is the commonest findings and it often occurs at basal areas such as prepontine cistern and ambient cistern (Tai et al., 2017).

In terms of treatment, there is no specific treatment for stroke in TBM. The patient should be started with anti-tuberculous therapy which is comprised of 2 months of intensive phase, followed by 10 months of maintenance phase (Azharuddin et al., 2016). Timely treatment improves the outcome of TBM. Empirical treatment should be considered even before microbiological confirmation when clinical features and CSF findings are suggestive of TBM. Besides anti-tuberculous therapy, the patient also should be given corticosteroid as an adjunct systemic therapy as it improves the outcome. On the other hand, the role of aspirin in TBM is still debatable (Kalantri et al., 2018). More studies are needed before any recommendations can be made.

CONCLUSION

In conclusion, TBM is an aggressive disease that carries high mortality and morbidity even with treatment. Cerebral infarctions is an important complication of TBM and often associated with poorer outcome. Neuroimaging is an important diagnostic tool in detecting complications of TBM. Timely initiation of anti-tuberculous treatment is paramount in improving the outcome of patients with TBM.

CONFLICT OF INTEREST

The authors declare that they have no competing interests in publishing this case.

CONSENT

Written consent was obtained from the patient to publish the case. A copy of the written consent is available for review by the Chief Editor.

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