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Case Report

Tuberculous meningitis masquerading as acute ischemic stroke in young adult

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ABSTRACT

Tubercular meningitis (TBM) constitute 5% of all cases of extra pulmonary tuberculosis but a presentation leading to an ischemic stroke in a young adult is a rare clinical entity. In a case of TB vasculopathy, vasculitis, venous thrombosis and aneurysm may be the underlying events leading to a stroke. Stroke in TBM is seen in the tubercular zone which encompasses internal capsule, thalamus and caudate nucleus. Inflammatory mediators like TNF alpha, Interferon gamma and vascular endothelial growth factor have been implicated in the pathogenesis of arteritis. Imaging modalities like MRI show lesions which are usually bilateral in the territory of the perforating vessels. We report a case of 24 year old Asian male who presented with complaints of headache, projectile vomiting and altered sensorium. On examination his Glasgow Coma Scale (GCS) was 10/15, with left oculomotor and left facial nerve palsy, and hypotonia of all 4 limbs with bilateral plantar reflexes being mute. Contrast MRI of brain showed acute infarct, meningeal enhancement and basal exudates. He was started on Anti-tubercular therapy and steroids, but had a poor clinical outcome, due to his late presentation.

Keywords: Anti-tubercular therapy, Extra pulmonary tuberculosis, Stroke in young, TB meningitis, Vasculitis, Venous thrombosis

INTRODUCTION

Tuberculosis (TB) is a public health problem in the developing nations. The causative organism of tuberculous meningitis (TBM) is mycobacterium tuberculosis. Stroke is insidious in onset when associated with tuberculous meningitis. The incidence of tuberculous vasculitis varies between 6-41% amongst TBM cases.[1] TBM is characterized by exudates in the basal cisterns, brainstem, cerebellum and Sylvain fissure.[2] Exudates may enclose the cranial nerves and the arteries. Major vessels at the base of the brain are affected more. Patients with TBM may present with communicating, non-communicating or complex hydrocephalus.[3] Medical research council criteria divides the patients into stages based on their clinical presentation; Stage 1 is characterized by no focal neurological deficit, Stage 2 is associated with altered mental status without deficit and Stage 3 is associated with stupor, paraplegia and coma ($GCS \leq 10$).[4] Vasculitis in TBM may present as infarction, hemorrhage or aneurysm. Tubercular meningitis can cause vasculitis due to invasion of the vessels with inflammatory mediators which propagate thrombosis and vascular stenosis which can be seen on magnetic resonance angiogram (MRA) as narrowing of cerebral vessels leading to multiple small infarcts.[5] The pathology associated with vasculitis is pan arteritis leading to decreased caliber of the vessels.[1] Tubercular vasculitis can be suspected when there is a fall in the patient's sensorium and all the other causes have been ruled out. Infarcts in tuberculous meningitis may be due to vasospasm, intimal proliferation, thrombosis or stretch

of the vessel wall. Interferon gamma or tumor necrosis factor α have been implicated in the pathogenesis of stroke. Pathogenesis of vasculitis involves various processes in the initial period such as reversible vasospasm followed by inflammatory mediators infiltrating the adventitia causing fibrosis and strangulation of the arteries. Thrombosis of the lumen may be caused by infiltration of the intima finally leading to vascular necrosis which is a rare phenomenon.

Duration of treatment of TB meningitis is based on the clinical stage of the disease. In uncomplicated tuberculous meningitis, duration of treatment is 12 months and duration for complicated TBM varies from 12-24 months.[6] Dexamethasone when added to therapy can decrease the incidence of disability and death.[7] Stroke in TBM is associated with poor clinical outcomes.

This case report depicts the unusual presentation of tuberculous meningitis. A detailed workup leading to an appropriate diagnosis paved way for early management and significant improvement in the patient's condition.

CASE REPORT

A 24 year old male patient presented with fever, headache and projectile vomiting for 2 weeks and altered sensorium for 2 days with associated history of weight loss and loss of appetite. On examination patient was drowsy, not oriented to time, place or person with GCS-E3V2M5 10/15. His left pupil was 4mm and sluggishly reactive to clear and the right pupil was 2.5 mm and reactive to light. He also had bilateral lateral rectus muscle palsy, left Upper Motor neuron facial palsy, left oculomotor nerve palsy. He could move all 4 limbs but had hypotonia of all 4 limbs. Reflexes - 2+ and bilateral plantar reflexes were mute. Initial investigations showed ESR -100mm, Hemoglobin -10 g/dL and total count - 13,100/mm^3. Peripheral smear showed microcytic hypochromic anemia with leucocytosis. Prothrombotic profile was done and was normal. Electrolytes were within normal limits. Chest X-ray showed normal lung parenchyma. Computed tomography (CT) of the brain revealed hypo-density with attenuation of 11 HU in the genu of left internal capsule with diffuse cerebral edema. Cerebrospinal fluid (CSF) showed elevated proteins with lymphocytic predominance and CSF adenosine deaminase (ADA) was found to be 10U/L. Cartridge Based Nucleic Acid Amplification Test was positive. MRI brain showed multiple acute non hemorrhagic infarcts in the right high frontal, left capsulo-ganglionic, left thalamus and left medial temporal lobes (Figure 1). MRA showed normal course and caliber of all vessels. Multiple infarcts were in the tubercular zone. On contrast administration, minimal abnormal enhancement of the meninges were seen in the basal cistern and Sylvian fissure on the left side showed subtle enhancement of the capsulo-ganglionic region infarct and hence possibility of TBM causing vasculitis was considered. Fundus showed no evidence of papilledema. Electroencephalogram (EEG) showed diffuse cerebral dysfunction. Patient was then initiated on anti-tubercular therapy. Since the patient was found to have deranged liver function tests, Rifampicin and Isoniazid were withheld and Inj. Streptomycin 750 mg, Tab. Ethambutol 800mg OD and Tab. Levofloxacin 1g OD were continued. Patient was initiated on intravenous Dexamethasone initially at dose of 0.4mg/kg IV and then tapered each week by 0.1mg/kg and was switched to oral after 4 weeks of dexamethasone therapy. Patient improved symptomatically with a power of 3/5 in the right upper and lower limb and was discharged with advice regarding limb physiotherapy.

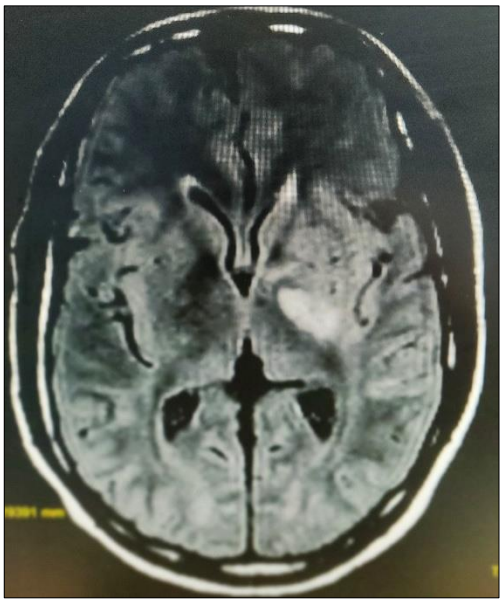

Figure 1: MRI - T2 hyper intensities noted in the right high frontal, left capsule-ganglionic, left thalamus left hippocampal and left medial temporal.

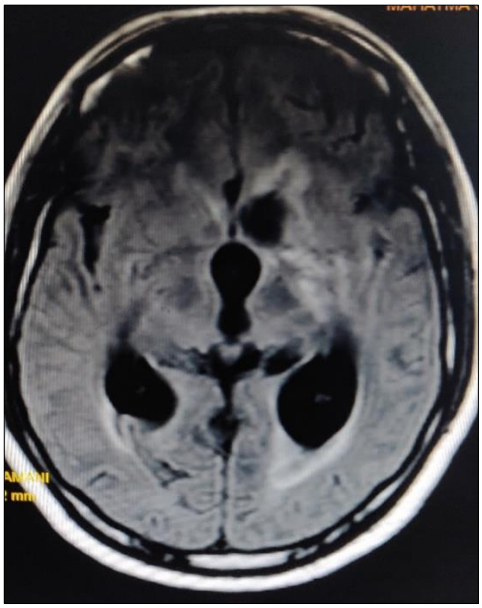

Figure 2: MRI - T2w flair hyper intensities in the left capsulo-ganglionic and left thalamus.

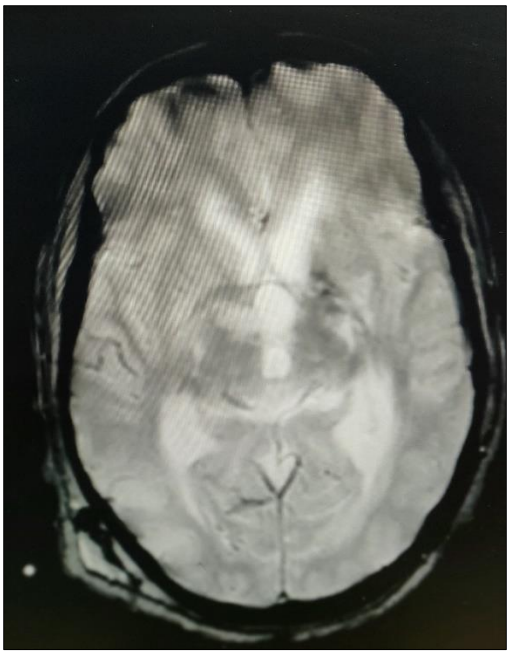

Figure 3: MRI - T1 hyper-intensity seen in the left capsulo-ganglionic region which show subtle blooming on FFE sequence, suggests possibility of hemorrhagic transformation.

Patient presented to the emergency room after 1 month with 1 episode of generalized tonic clonic seizures and fall in sensorium. All the metabolic parameters were within the normal range. Patient was intubated and was on mechanical ventilator in view of poor GCS. MRI brain showed T2 flair hyperintensities noted in the left capsule-ganglionic region and left thalamus with no diffusion restriction (Figure 2). T1 hyperintensity was seen in the left capsule-ganglionic region with subtle blooming on fast field ECHO (FFE) sequence, which suggested the possibility of haemorrhagic transformation in a previously known case of infarction (Figure 3). Moderate communicating hydrocephalus-with Evans index of 0.38, with periventricular seepage which is suggestive of TB meningitis sequelae. External ventricular drain was placed in view of hydrocephalus. Patients GCS improved to 11/15 and following which patient was extubated. Patient had multiple fever spikes and hence all sentinel cultures were sent. Urine culture showed growth of extended spectrum beta lactamase *Escherichia coli* 105 CFU. Patient was initiated on IV *Pipercillin tazobactum* 4.5g/QID according to sensitivity. Patient developed status epilepticus, and hence put on mechanical ventilation. The patient was started on Tab. Levatiracetam 1g TDS, Tab. Lacosamide 100mg BD and Tab. Clobazam 10mg OD opinion. Following this ventriculo-peritoneal (VP) shunting was done. Repeat CT showed VP shunt in situ with its tip in the right lateral ventricle. Mild ventriculomegaly with Evans index -0.33 with multiple small hypodensities in the thalamo-capsular region were observed which was a sequelae of previous insult Also detected were ill defined white matter hypodensities in bilateral high frontal parietal lobe and right occipital lobe. EEG showed diffuse cerebral dysfunction. Patient was continued on ATT, antiepileptics and DVT prophylaxis. Patient underwent elective tracheostomy in view of prolonged intubation. Endotracheal tube culture showed growth of Klebsiella oxytoca sensitive to Colistin and hence IV Colistin 45MU BD was initiated. Patient was bedridden with a fluctuating GCS and developed decerebrate posturing. Our patient had a poor clinical outcome, due to delay in presentation and hence the delay in initiating anti-tubercular therapy and steroids and also due to concomitant infections.

DISCUSSION

Tubercular meningitis usually presents with preceding constitutional symptoms like low grade fever, loss of appetite, malaise, fatigue and weight loss. The prevalence ranges from 65%-76%.[8,9]

The cerebrospinal fluid ADA ranging between 1-4 U/L have high sensitivity and specificity.[10] Real time PCR also known as Gene Xpert detects mycobacterium tuberculosis and gives information regarding its resistance to Rifampicin and hence this test is highly sensitive in ruling out the diagnosis of tubercular meningitis.[11] Gene Xpert is used as an adjunctive in the diagnosis of TBM. CSF interferon gamma assay, Zeil Neilson staining and Chest X-ray are the other diagnostic modalities used to rule out TBM.

Imaging modality commonly used for diagnosis is MRI with MRA depicting the arterial territory with the narrowing of the vessels suggestive of vasculitis.[12] Multiple infarcts are seen in tubercular zone which is supplied by the branches of thalamo-striate and the medial striate arteries. They also present as cortical stroke involving the major arterial territories.[13] Diagnosis can be confirmed by vessel walls appearing beaded and infiltration of the media and adventitia with fibrinoid necrosis. Usually the artery and the vein are equally involved in histopathology samples obtained postmortem. Tuberculoma in the vessel wall is a rare entity.

WHO guidelines advice intensive phase therapy for 2 months with ethambutol, isoniazid, pyrazinamide and rifampicin or streptomycin followed by continuation phase therapy with rifampicin and isoniazid for 10 months. But there are various regimens which differ in dose and duration varying from 6 -24 months.[7]

CONCLUSION

Many cases of tubercular meningitis have been reported but with presentation as stroke in young due to vasculitis is a rare entity. Young patients presenting with stroke need to be evaluated for TBM causing vasculitis. Early initiation of treatment with anti-tubercular therapy with steroids may improve the outcome, without which the patient has a poor clinical prognosis.

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