

A rare case of cavernous sinus syndrome in a patient with tuberculous meningitis

Abstract

Cavernous sinus syndrome is a rare manifestation of Tuberculous (TB) meningitis. Initial MRI finding may be normal despite clinical manifestation of complex ophthalmoplegia. Early diagnosis and commencement of tuberculous treatment is crucial as it effects the rate of nerve recovery. A case of 33 year old Malay gentleman, presented with symptoms associated with elevated intracranial pressure and isolated left sixth nerve palsy which then evolved to complex ophthalmoplegia. Initial MRI brain done revealed no abnormality. Elevated CSF (Cerebrospinal Fluid) protein with raised ESR (Erythrocyte Sedimentation Rate) and repeated MRI (Magnetic Resonance Imaging) which showed inflammatory changes over bilateral cavernous sinus and surrounding structure raised high index suspicion of TB meningitis. He was empirically treated with anti TB medication and he responded well. Further review of repeated MRI orbit and patient revealed resolution left sixth nerve palsy and resolution of inflammation over both cavernous sinus.

Keywords: ophthalmoplegia, cavernous sinus syndrome, tuberculous meningitis

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Introduction

The incident of Tuberculosis (TB) in Malaysia is estimated 81.4 per 100,000 population.¹ In 2011, the number of extra pulmonary TB reported was 2888 cases.¹ Reported cases of extra pulmonary TB in Malaysia noted to be increasing in trend over the years based on statistic from 2005 to 2011.¹ Although the prevalence of TB meningitis is low, it has high mortality and morbidity if inadequately treated. Presentation of TB meningitis varies from chronic headache, neurological abnormalities to behavioural changes. As TB is endemic in Malaysia, TB meningitis is one of differentials in patient who presents with signs and symptoms of CSF infection. CSF in TB meningitis have the characteristic finding of elevated CSF protein with low CSF sugar. CSF direct smear for acid fast bacilli may not yield any findings. As CSF *Mycobacterium Tuberculosis* (MTB) has sensitivity of 40 to 60 percent² and newer method namely CSF for TB PCR has sensitivity of 44.5 percent and specificity of 92.0 percent,¹ the definitive diagnosis of TB meningitis could prove to be challenging at times. The diagnosis of TB meningitis highly relies on high index of suspicion based on presentation and clinical findings, aided with characteristic of CSF findings and radio imaging.³ Treatment needed to be commenced early despite pending CSF culture in order to reduce mortality and morbidity. We report a rare case of TB meningitis presenting with bilateral cavernous sinus syndrome.

Case report

A 33 year old Malay gentleman who presented with left sided headache for 11 days duration. The headache was throbbing and persistent in nature with a Wong and Baker pain score of 9 over 10. It was associated with vomiting of about 5 times a day. A day prior to admission, he experienced blurring of vision. Otherwise, there was no limb weakness or facial asymmetry. Examination revealed isolated left sixth nerve palsy. He was referred to the ophthalmology team and further eye examination revealed no papilledema. He was also referred to the ENT team which revealed normal ENT findings. CT brain plain done showed no abnormality. MRI brain done showed no evidence of tumour or infarct (Figure 1a,1b). Patient had refused lumbar puncture and had taken discharge at own risk to

seek alternative medicine. He was readmitted four days later with worsening of double vision. Examination revealed bilateral eye 3rd, 4th. and 6th nerve palsy. Otherwise there was no limb weakness and there was no pulmonary findings. Erythrocyte sedimentation rate was elevated at 100 mm/Hr. Further screening test such as sputum for acid fast bacilli (AFB), Chest X-ray and Mantoux test were negative. Additional tests such as FBC, Renal profile and liver function test was normal. He was tested negative for human immunodeficiency virus (HIV) (Table 2). Repeated MRI brain revealed inflammatory changes involving bilateral cavernous sinus and surrounding regions, which favour central nervous system (CNS) infection or granulomatous disease (Figure 1c-1d).

Table 1 CSF culture

Cerebrospinal Fluid (CSF) Investigation	Result
CSF culture	No growth after 48 hours
CSF AFB direct smear	No AFB seen
CSF for MTB culture (BACTEC)	<i>M. tuberculosis</i> not grown (after 8 weeks)
CSF for Cryptococcal Antigen	Negative

Table 2 Infective screen

Additional Tests	
VDRL/TPHA*	Non-reactive
Hepatitis B surface Antigen	Not detected
Anti HCV	Non-reactive
HIV1/ HIV2	Negative

*VDRL/TPHA abbreviation: Venereal Disease Research Laboratory/ Treponema Pallidum Hemagglutination.

Lumbar puncture was done with opening pressure of cerebrospinal fluid (CSF) elevated at 37cmH2O with turbid appearance of CSF. The CSF protein was 2.4g/L with cell count of 110, predominantly polymorphs. CSF glucose was 2.1mmol/L and plasma glucose level was 4.5 mmol/L. CSF test was negative for bacteria and Cryptococcus (Table 1).

He was empirically treated as Tuberculous Meningitis (TB meningitis) and was started on SHRZ regime (IM Streptomycin 1g

OD, Isoniazid 300mg OD, Rifampicin 600mg OD, and Pyrazinamide 1 g OD) with intravenous dexamethasone 8mg TDS. There was a remarkable improvement in terms of headache and eye movement by day 3 of treatment, whereby there was a complete resolution of restricted extraocular movement of the right eye with persistent isolated sixth nerve palsy of left eye.

He had repeated MRI scan 2 months after anti TB treatment which revealed complete resolution of previous inflammatory changes (Figure 1e,f). Patient was reviewed after 2 months of starting anti TB and currently the isolated sixth nerve palsy has resolved. Also, there was no more headache. He will be reviewed again in sixth month time (eight month of anti TB). He is planned for standard of 12 months anti TB treatment as per TB meningitis protocol.⁴

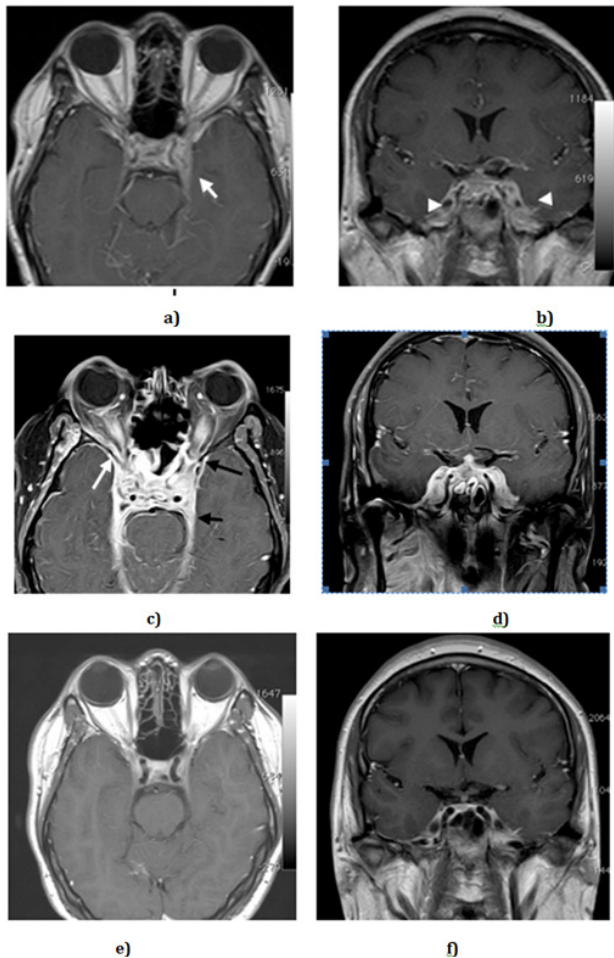


Figure 1 Axial and Coronal post-contrast T1-weighted images at initial presentation (a-b), at one week (c-d) and at 2 months (e-f) interval.

First row (a-b): Initial MR Brain images show evidence of inflammatory change largely confined to the cavernous sinus (short white arrowhead); the left cavernous sinus is enlarged (white arrow).

Second row (c-d): The MRI images show increasing inflammatory change with extensive enhancement and enlargement of both cavernous sinus extending to the orbital apex (small black arrow) and temporal regions (white arrow) anteriorly, and Meckel's cave (black arrowhead) posteriorly.

Third row (e-f): MRI images 2 months later shows significant resolution of the inflammatory change.

Discussion

Our patient presented headache and vomiting for 11 days duration with isolated left sixth nerve palsy. Initial radiological imaging were

normal and he had refused lumbar puncture at first presentation which caused diagnostic dilemma. Referrals made to ENT and ophthalmology team did not revealed any abnormalities to aid the diagnosis. On second presentation 4 days later he has developed worsening of vision characterized by diplopia and physical examination revealed bilateral 3rd, 4th and 6th nerve palsy (bilateral cavernous sinus syndrome). Lumbar puncture done revealed high opening pressure of 37 cmH₂O with significantly raised in CSF protein with low CSF sugar. Also the ESR was elevated at 100mm/Hr. Repeated MRI brain showed inflamed bilateral cavernous sinus and surrounding area. He was treated as TB meningitis as TB is endemic in Malaysia and also the characteristic of CSF findings which highly suggestive of TB meningitis. He had responded well to tuberculous treatment and repeated MRI scan and reassessment of patient 2 months after starting treatment showed resolution of inflammatory changes surrounding both cavernous sinus and complete resolution of eye symptoms.

TB is worldwide problem with estimated prevalence in 2014 reported at 9.6 million with 1.5 million mortality. South East Asia and Western Pacific accounts for 58% of cases reported.⁵ In Malaysia the prevalence of TB is reported at 81.4 per 100, 000 population. Extra pulmonary TB accounts for 15.0 percent of reported TB cases in Malaysia in year 2011.¹

The challenges faced in diagnosis TB meningitis is due to variable CNS presentation which ranges from headache, neurological deficits, and behavioural changes to as serious to stupor. Although TB meningitis is highly associated with immunocompromised patient, report shows that immunocompetent person is also at risk as in case studied. This case is to report the spectrum presentation of TB meningitis in previously healthy adult, where in this case patient presented with bilateral cavernous sinus syndrome. TB meningitis presenting with cavernous sinus syndrome is rare with only 13 literature reported worldwide.^{6,7} Although rare, TB infection need to be considered in patient with cavernous sinus syndrome as there are cases reported worldwide. Early diagnosis and treatment is important to ensure complete nerve recovery.

The biochemistry findings which favours TB meningitis include elevated white cell count with predominant lymphocytosis, elevated CSF protein of more than 1.0 g/L and low glucose of less than 2.2 mmol/L with CSF to serum glucose ratio of less than 0.5.⁸

The confirmatory test in TB meningitis is identification of TB in CSF. The yield of culture relies on the TB load and could be negative in paucibacillary.² The sensitivity and specificity of CSF for TB PCR is varied; this is due to the complex nature of the mycobacterium cell wall resulting in low yield of nucleic acid.⁵ Another new test available in detecting TB is called GeneXpert. It is used in pulmonary TB to detect rifampicin susceptibility. However, this test is reported to have moderate sensitivity at detecting TB in CSF.⁹

In conclusion although rare, the possibility of TB meningitis need to be sought in patient presenting with cavernous sinus syndrome especially in TB endemic area in order for prompt commencement of TB medication as TB meningitis carries high mortality and morbidity if not treated early.^{10,11} Diagnosis of TB meningitis is challenging due to variable CNS presentation. Therefore, the aid of CSF sampling and also advanced radio imaging is required to support the diagnosis. In cases where high index of suspicion with characteristic CSF biochemistry finding, treatment need to be commenced in the absence of CSF microbiological evidence of AFB in view of low to moderate rate of detection of AFB in CSF based on culture or PCR method.⁹

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Conflicts of interest

None.

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