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**Case Report**

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# Bilateral optic nerve infiltration in tuberculous meningitis: A diagnostic dilemma

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## ABSTRACT

**Rationale:** Tuberculous meningitis (TBM) is severe extrapulmonary tuberculosis that can cause poor outcomes without timely treatment. We report a case of presumed TBM that presented solely ocular complaints without other neurological features.

**Patient's concerns:** A 71-year-old man presented with a sudden central visual defect in both eyes for 10 days. Fundoscopy showed bilateral hyperaemic swelling disc with infiltrates.

**Diagnosis:** A diagnosis of presumptive TBM was made with Mantoux test reading 15 mm, elevated erythrocyte sedimentation rate, subdural effusion on CT scan, and high opening pressure.

**Intervention:** Anti-tuberculous treatment.

**Outcomes:** Bilateral vision improved and optic discs swelling resolved.

**Lessons:** Early recognition of TBM with optic nerve infiltration is crucial for prompt treatment that may lead to a good prognosis. Neuroimaging will facilitate the diagnosis when other investigations show a borderline result.

**KEYWORDS:** Tuberculous meningitis; Infiltrative optic neuropathy; Tuberculoma

## 1. Introduction

Tuberculous meningitis (TBM) is relatively uncommon, but it is the most severe form of extrapulmonary tuberculosis with high mortality and morbidity[1,2]. The incidence rate of tuberculosis in 2018 was 92 persons per 100 000 people in Malaysia[3]. TBM comprises about 5%-15% of all extrapulmonary tuberculosis and is more prevalent among population from developing countries[1]. A high suspicious index is required for early recognition to avoid treatment delay that may result in poor outcomes and death[1-5]. We report a case of presumed TBM that presented the solely ocular complaint without other neurological features.

## 2. Case report

This case report was approved by the Human Research Ethics Committee of Universiti Sains Malaysia, and informed consent was obtained from the patient.

A 71-year-old male with underlying diabetes, hypertension, and stage 4 chronic kidney disease complained of a sudden central visual defect in both eyes for 10 d. The patient described the scotoma as a black spot obscuring the central vision. The scotoma was worse when he stood up from the sitting position and resolved slowly after a while. It was associated with mild frontal headache but no nausea and vomiting. Besides, no neck stiffness was noted. He had a history of cough with minimal whitish sputum for 2-week but without constitutional symptom and neurological symptom. He had no history of recent contact with tuberculosis or traveling abroad.

Visual acuity in the right eye was 6/9 and the left eye was 6/30 improved to 6/18 with pinhole. There was no relative afferent pupil defect, and the pupillary reflex was normal. Both anterior segments

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were unremarkable. Fundoscopy revealed hyperaemic swollen discs and infiltrates with the normal macula bilaterally (Figure 1). Both eyes' confrontation visual field test with the aid of red pin mapping showed enlarged blind spot. Extraocular movements were normal. Blood pressure was 182/95. Systemic examination was unremarkable with no neurological deficit.

Laboratory investigations showed high erythrocyte sedimentation of 69 mm/h (upper limit of age-adjusted ESR: 35.5 mm/h). Full blood picture, infective screenings, autoimmune markers, and tumour markers were unremarkable. The Mantoux test was 15 mm. The chest X-ray showed normal. Computed tomography (CT) scan of the brain and orbits showed thickened bilateral optic nerve. There was a presence of subdural effusion with left cavernous sinus enlargement suggestive of cavernous tuberculoma (Figure 2). The left cavernous sinus was avidly enhanced compared to the right side and slightly extends to anterior part of left tentorium cerebellum. Magnetic resonance imaging could not proceed because of high risk of contrast-induced nephrogenic systemic fibrosis. CT venography revealed bilateral subdural effusion with no cavernous sinus thrombosis.

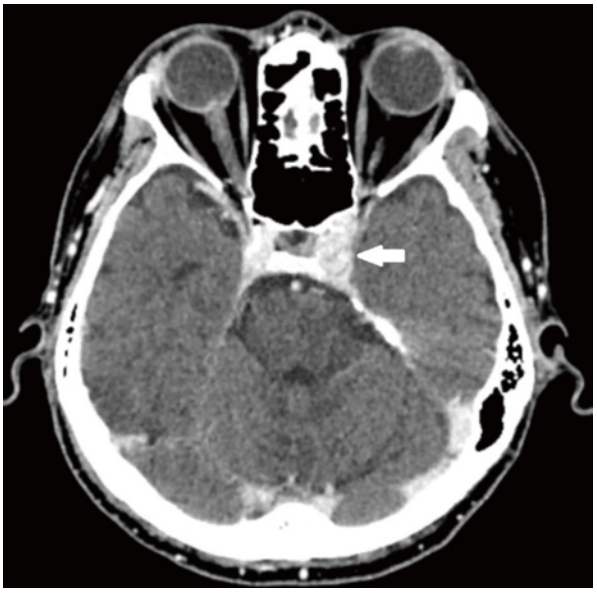

**Figure 2.** Computed tomography scan of the brain and orbits shows thickened bilateral optic nerve and left cavernous sinus enlargement suggestive of tuberculoma (white arrow).

The patient was referred to the neuro-medical team. Lumbar puncture showed a high opening pressure of 41 cm$H_2O$ (normal range: 10-25). Cerebrospinal fluid (CSF) analysis revealed normal biochemical markers with a slightly low ratio of CSF to plasma glucose (0.47) (normal range: 0.50-0.80). CSF culture and sensitivity, tuberculosis polymerase chain reaction, and *Mycobacterium*

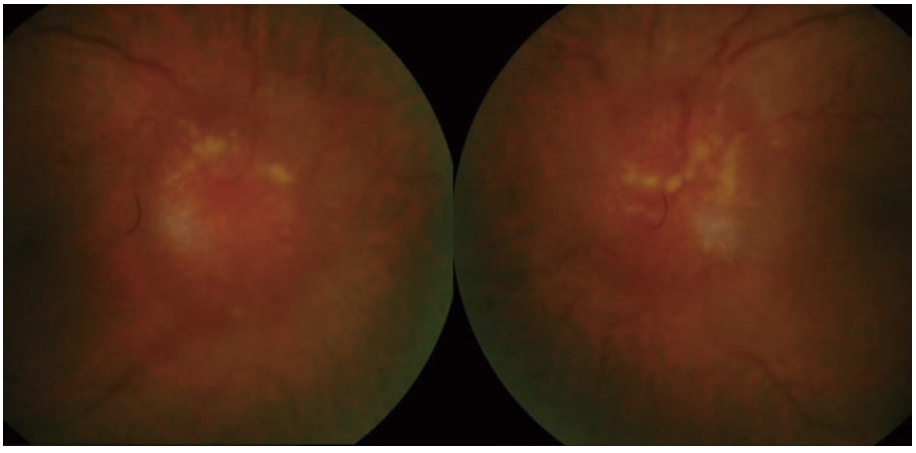

**Figure 1.** Bilateral fundi on admission show a hyperemic swollen disc with exudations.

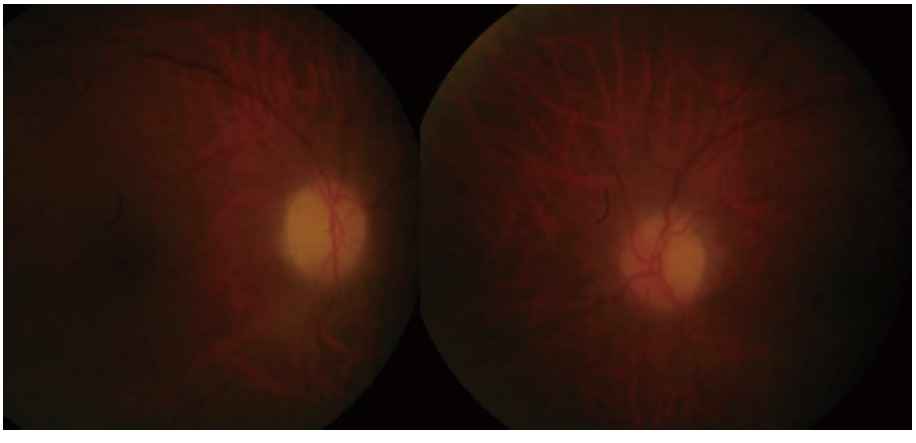

**Figure 3.** Bilateral fundi after treatment show optic atrophy with resolved exudation.

*tuberculosis* culture and sensitivity were negative. The patient was diagnosed as presumed tuberculous meningitis and started with anti-tuberculous regimes (isoniazid, rifampicin, pyrazinamide, and ethambutol and adjunctive corticosteroid) for 2 months. It was followed by isoniazid and rifampicin treatment for another 7 months. After completed treatment, the visual acuity of the patient was improved to 6/7.5 in the right eye and 6/15 in the left eye with a subjectively reducing area of enlarged blind spot. Both optic discs appeared pale (Figure 3). There was no other neurological deficit.

## 3. Discussion

*Mycobacterium tuberculosis* can spread to meninges through blood stream and remains dormant as Rich focus for years. It later forms an inflammatory exudate after releasing the bacteria and granuloma into subarachnoid space[5]. The meningeal exudates can affect optic nerves anteriorly as demonstrable in our case.

TBM classically presents with a subacute prodrome of malaise, weight loss, low-grade fever, and headache over 1-2 weeks. The characteristic clinical signs of meningism include a variable degree of neck stiffness, cranial nerve palsies, limb weakness, and seizure. If untreated, the patient may develop confusion, coma and, death[2,5,6]. However, our patient came with ocular complaints of bilateral visual field loss and papilloedema with infiltrative optic neuropathy but without characteristic features of meningism.

A high suspicious index for tuberculosis is needed when dealing with patients with optic neuropathy in an endemic area. Davis *et al.* reported that tuberculous optic neuropathy most commonly presented as papillitis (more than 50%) followed by neuroretinitis and optic nerve tubercle. More than one-third of tuberculous optic neuropathy patients are associated with extraocular tuberculosis, especially pulmonary and meningeal[7]. Thus, despite the absence of neurological features, our patient with infiltrative optic neuropathy needs to be further investigated for TBM.

Lumbar puncture is mandatory for confirmation of TBM. Our patient had high opening pressure (>25 $cmH_2O$) which is present in 50% of TBM[5]. However, his CSF analysis did not show common TBM features such as raised white cells number ($0.05\times10^9$-$1.00\times10^9$/L); raised protein (0.5-2.5g/L) except for ratio of CSF to plasma glucose <0.5[4,5]. We also met other diagnostic challenges due to low sensitivity (5%-30%) of detection of *Mycobacterium tuberculous* bacilli in smear microscopy and long waiting time for culture result which results, although both results showed negative[1-4]. The United States Preventive Services Task Force claimed induration more than 10 mm should not be attributed to previous Bacillus Calmette-Guerin vaccination, but our diagnosis still unable to be strongly supported by the positive Mantoux result due to low sensitivity and specificity of the test[8].

Neuroimaging helps manage TBM for demonstrating features of tuberculous meningitis such as meningeal enhancement, basal exudates, hydrocephalus, infracts, and tuberculoma[2,9]. In our case, CT of brain and orbits showed thickened bilateral optic nerve, which may indicate inflamed optic nerve secondary to mycobacterial invasion and subdural effusion with left cavernous sinus enlargement suggesting tuberculoma. Tuberculosis tuberculoma does not have a pathognomonic radiological finding, although magnetic resonance spectroscopy can demonstrate a lipid peak. A biopsy is required to confirm the diagnosis histologically[9]. Given making a diagnosis of TBM in such a challenging case, various diagnostic criteria were applied for early recognition of TBM (Table 1)[10].

Concerning the treatment, a 2-month intensive phase treatment should be promptly initiated in highly suspicious cases, and long-term anti-tuberculous treatment is essential (9-12 months) to prevent disease relapse as recommended in most of the observational studies and clinical practice guidelines. Adjunctive corticosteroids also are recommended to reduce mortality and

**Table 1.** Clinical criteria and scoring of the patient based on various diagnostic criteria.

| Vietnam rule for the diagnosis of TBM on admission[a] | Scores/diagnostic index |
|---|---|
| Age≥36 | 2 |
| Blood WCC<15000 ($10^3$/mL) | 0 |
| History of illness≥6 days | −5 |
| CSF total WCC<750 ($10^3$/mL) | 0 |
| CSF % neutrophils<90 | 0 |
| The Marais criteria for the diagnosis of TBM on admission[b] | |
| Symptoms more than 5 days | 4 |
| Systemic symptoms suggestive of TB: persistent cough for more than 2 weeks | 2 |
| Clear appearance CSF | 1 |
| CSF to plasma glucose ratio <0.5 | 1 |
| Tuberculoma | 2 |
| Diagnostic formula for discrimination of TBM & bacterial meningitis[c][10] | |
| Duration of illness>5.5 days | 4 |
| Duration of coughing≥2 weeks | 4 |
| Blood sodium≤137.5 mmol/L | 0 |
| CSF % neutrophils≤72.5 | 0 |

TBM: Tuberculous meningitis; WCC: White cell count; CSF: Cerebrospinal fluid; [a]: Our patient was diagnosed to have TBM with scoring -3 (≤4); [b]: Our patient was defined as possible TBM with a scoring of 10 (6-11) after excluding the alternative diagnosis; [c]: Our patient was considered as TBM with a total diagnostic index of 8 (≥0).

morbidity by about 30%[2,5].

Early treatment is important to avoid severe complications as observed in our case. TBM can be complicated with hydrocephalus and causes multiple cranial nerves palsies as sequelae. The mortality is higher if requires surgical intervention[1,5]. TBM brings poor outcomes if manifest as stroke. Tuberculoma mostly is silent but can cause focal neurological deficits and increase intracranial pressure[5].

## Conflict of interest statement

The authors report no conflict of interest.

## Authors' contributions

Writing, revision and figures: L.T.H., W.H.W.H; Review: L.T.H., I.M., W.H.W.H, S.A.H.

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