CASE REPORT

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Acute Onset Blindness in a Tubercular Meningitis Patient on Antitubercular Treatment: A Rare Case

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Abstract

Ethambutol is a widely used antitubercular drug but has been known to cause optic neuritis, more specifically retrobulbar neuritis causing blurred vision, decreased visual acuity, central scotomas and loss of red-green colour vision[1,2,3]. This type of visual defect is termed as toxic optic neuropathy caused by ethambutol. Ethambutol, however, causes this side-effect 2 - 8 months after being started[4,5,6]. We present a case of a rare side-effect of complete but reversible blindness noted within 4 days of starting antituberculosis treatment with ethambutol in standard dosage.

Key words: Antitubercular treatment, ethambutol toxicity, occular ethambutol toxicity.

Introduction

Tuberculosis is widely prevalent in the Indian subcontinent and manifests as pulmonary and extra-pulmonary forms. Ethambutol is used as one of the first-line antitubercular therapy. However, ethambutol is associated with serious complication of toxic optic neuropathy which is generally seen 2 - 8 months after starting it.

Hereby we present a rare case report of a young female suffering from tubercular meningitis who presented to us within 4 days of starting antitubercular therapy with sudden onset, painless, complete loss of vision in both eyes.

Case report

A 23-year-old female presented to a private hospital with complaints of fever, headache for 15 days, and altered sensorium since 7 days. Therefore she was suspected of meningitis and on subsequent evaluation her CSF examination was done (CSF cells 4 - 5/mm^3 all mononuclear; CSF proteins 73 mg/dl; CSF sugar 40 mg/dl; CSF ADA-7; CSF CBNAAT- Mtb detected without resistance), suggestive of tubercular meningitis. Non contrast MRI spine was also done there and showed D10-11 discitis with erosion of end plates with small right-sided psoas abscess (Fig. 2). She was started on all four 1st-line antitubercular medication.

She presented in our hospital in emergency with complaints of blurring of vision on the 3rd day and complete loss of vision on the 4th day after starting fixed-dose antitubercular therapy without any other symptoms of focal nerological deficit. On clinical examination, she was completely blind with no light perception in either eye; her bilateral pupils were dilated and light reflexes (both direct and consensual) were absent with preservation of accomodation reflexes (other cranial nerve examinations were normal).

She was evaluated further and subjected to contrast MRI-brain which showed multiple tuberculomas with mild hydrocephalus not involving the optic nerve or tract with

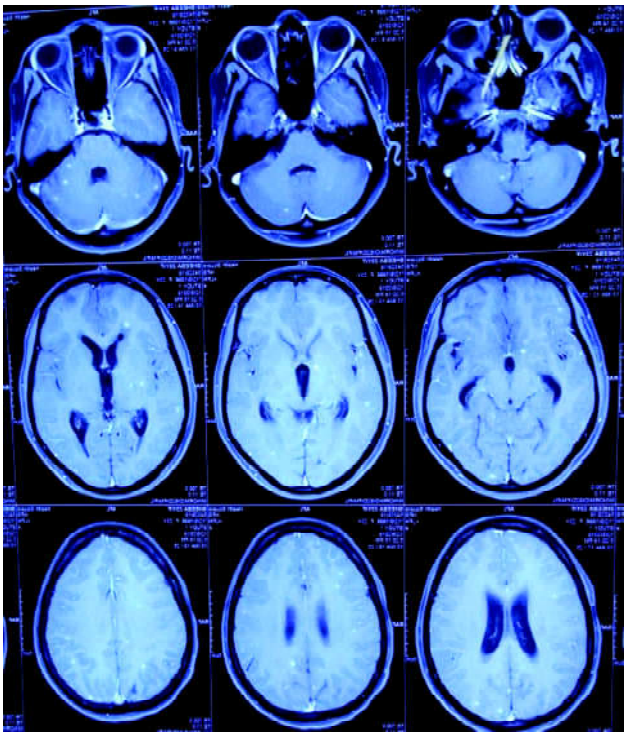

Fig. 1: *Multiple tuberculomas in bilateral cerebral and cerebellar hemispheres.*

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no evidence of infarct or abcess (Fig. 1). Ophthalmic examination was done which revealed normal bilateral fundus, and visual evoked potentials (VEP) showed p values of 105 and108 (Fig. 3) and macular Optical coherence tomography (OCT) suggestive of CMT 224 um and 190 um.

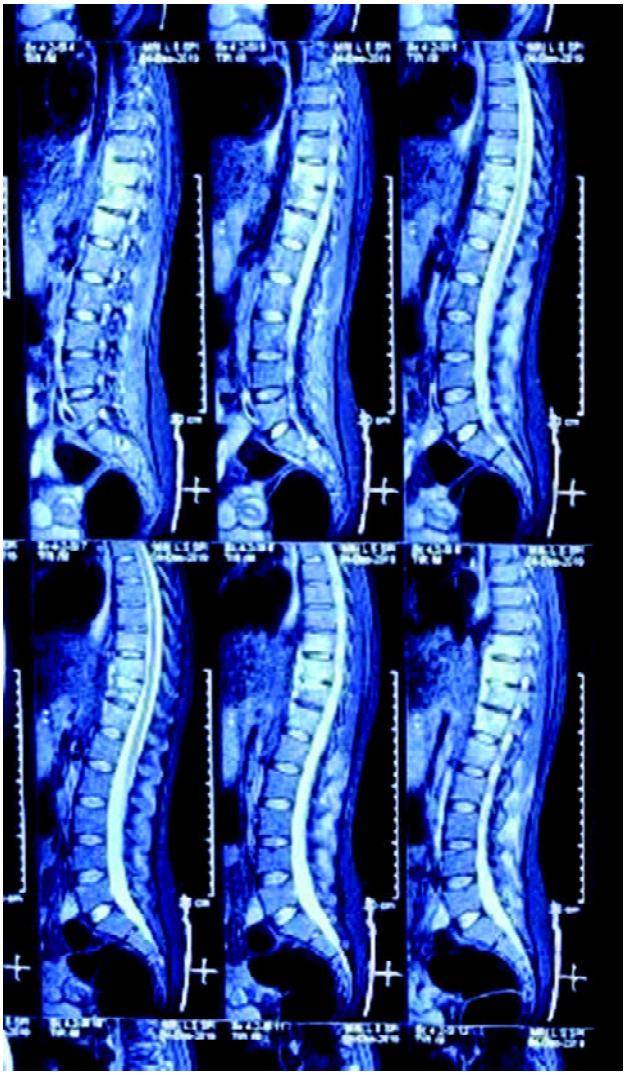

Fig. 2: *D10-11 discitis with erosion of end-plates.*

On evidence of this, ethambutol-induced optic neuropathy was suspected, and ethambutol was withdrawn. Further, the patient was managed symptomatically along with other 1st-line group of ATT.

On withdrawal of ethambutol, her vision improved gradually with projection of rays to 6/60 by the 10th day[10,11].

Discussion

Tuberculosis is a widespread disease in India and a major killer among infectious diseases. Various antitubercular drugs have been used which encompasses isoniazid, rifampin, pyrazinamide, and ethambutol as 'first-line'. These drugs have been attributed to various adverse effects during the treatment short course.

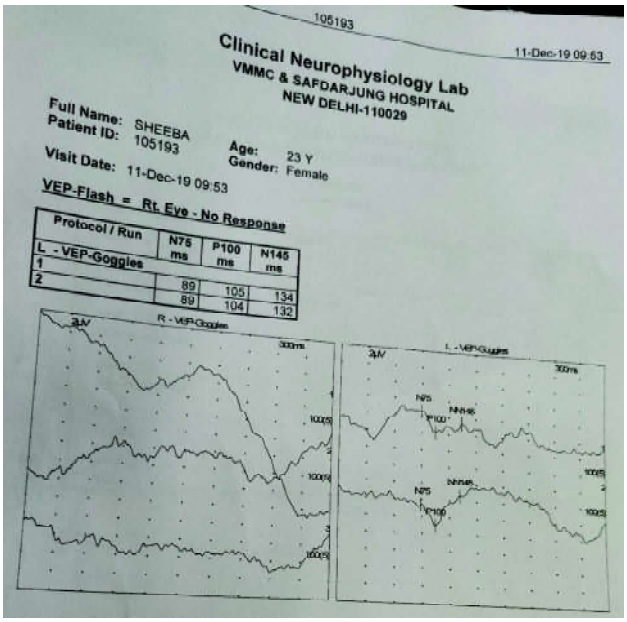

Fig. 3: *Visual evoked potential showing increase p wave latentcies.*

Ethambutol is a bacteriostatic agent active against slow growing mycobacteria. It acts on the bacterial cell wall by inhibiting the formation of mycolyl-arabinogalactan-peptidoglycan complex and increasing the permeability of the cell wall[7,8].

Ocular toxicity of ethambutol manifests as optic neuritis (retro-bulbar). The sign and symptoms manifest as visual field defects, red-green colour blindness. Unlike other more commonly known visual toxicity agents (e.g., hydroxychloroquine), where long durations of therapy are required for toxicity, ethambutol optic neuritis may begin rapidly between 1 month and 36 months after beginning the therapy. In general, however, most patients experience visual symptoms within the first 9 months of treatment. In more than 60% of patients, physical examination reveals bilateral, painless, and typically symmetric loss of visual acuity as well as abnormal colour vision. Colour vision loss is typically of indistinguishing green and red, though blue-yellow colour changes may also occur. Initially, the optic nerve is normal, but eventually optic disc pallor develops. If optic atrophy is present at the onset, it is generally considered to be a poor prognostic sign. Visual field testing most often reveals central or ceco-central scotoma, though bitemporal breakout of the visual field defect with optic chiasma involvement has also been reported.

This reaction is proportional to the dose of ethambutol and is observed in 15% of patients receiving 50 mg/kg/day, in 5 - 6% of patients receiving 25 mg/kg/day and in < 1% of patients receiving daily doses of 15 mg/kg[4,5,9]. In one study, 13 patients developed optic neuritis between 1 and 6 (mean = 2.9) months after receiving ethambutol at a dose ranging from 13 to 20 mg/kg/day (mean = 17 mg/kg/day) for pulmonary tuberculosis or of the lymph nodes. However, in our case, the patient developed severe ocular toxicity with a daily dose of 15 mg/kg and that too within 4 days of starting the drug. The possibility of such toxicity according to literature is < 1%[4,5,19]. A rare case report of idiosyncratic reaction with ethambutol has been described by Karnik *et al*[13]. Rapid development of optic neuritis in our patients could possibly be due to idiosyncratic reaction to the drug.

Factors which may predispose to toxicity include altered renal function. Furthermore, history of ethanol and tobacco consumption may predispose to ocular toxicity[6,14]. In our case, the patient had no history of ethanol and tobacco consumption, and renal functions were normal.

The exact mechanism of this ocular neurotoxic effect has not been identified. Animal studies have demonstrated ethambutol toxicity in the retinal ganglion neurons of rodents. One of the principal theories for its toxicity has been the zinc-chelating effect of ethambutol and its metabolite[15,16,17]. Postulated biochemical pathways that mediate the toxic damage include downstream effector caspase-3 and caspase-6,815 and an excitotoxic pathway[18].

Karnik *et al*, in their article reported rapidly progressive deterioration of vision after only 3 days of treatment with ethambutol[13]. In conclusion, ethambutol could cause an optic neuritis after even a few doses. The mechanism of injury is probably different from the common optic neuritis secondary to ethambutol. Early detection of these cases and withdrawal of ethambutol along with initiation of hydroxycobalamin may be associated with good prognosis in such cases[13].

In many studies, treatment of sudden severe acute toxicity caused by ethambutol includes withdrawal of the drugs. It is recommended to stop isoniazid also in severe cases, as the drug itself has been implicated in probable ocular toxicity. Isoniazid should also be stopped if less severe optic neuritis does not improve within 6 weeks after stopping ethambutol[6,19].

Conclusion

Anti-tubercular drugs like ethambutol can cause potentially dangerous adverse effects. Measures to ensure a high level of awareness of these potential adverse effects appear to be the best current preventive method. Although rare, ethambutol induced acute vision loss is an alarming complication, which needs timely withdrawal of anti-tubercular drugs (both isoniazid and ethambutol in severe cases), and initiation of hydroxycobalamin.

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