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Case Report

A Challenging Case of Ethambutol-Induced Optic Neuritis Manifesting with Perioptic Cystic Changes Diagnosed by Optic MRI

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Abstract

A 51-year-old female with a diagnosed case of Pott's spine has been on regular antitubercular treatment for the last 9 months and presented with complaints of progressive blurring of vision for the past 3 months. Ophthalmological examination revealed decreased visual acuity and bilateral retro-orbital pain on gentle compression of the eyeballs. This case highlights the role of MRI in the early detection of optic neuritis and demonstrates that early discontinuation of ethambutol can lead to favourable outcomes by preventing irreversible optic nerve damage

Keywords: Tuberculosis, Optic neuritis, Ethambutol, Pott's Spine, Adverse drug reaction.

Introduction

Ethambutol is a bacteriostatic antimicrobial medication used as a first-line antitubercular drug and is known to have a few adverse effects, of which optic neuropathy, though rare, is a significant one. Incidence ranging from 1 to 2% of patients administered ethambutol may experience ethambutol-induced optic neuritis[1]. Every year, around 9.2 million new cases of tuberculosis are reported worldwide, and nearly 100,000 patients develop toxic optic neuropathy due to ethambutol treatment[1]. Usually, ethambutol-induced optic neuropathy starts 4 to 12 months after therapy begins, but it might also happen soon after the onset of treatment. The present case report is unique in terms of optic neuritis manifested due to cystic changes in the optic nerve revealed by optic MRI in the course of a thorough workup.

Case Report

A 51-year-old female presented to us with complaints of progressive blurring of vision for 3 months. She was diagnosed with Pott's spine 9 months back and has been on regular antitubercular treatment since then. The patient has no other comorbidities. On examination, bilateral retro-orbital pain on gentle compression of the eyeballs. Color vision on the Ishihara chart: red-green color blindness. Visual acuity in the right eye is finger counting at 1 meter, and in the left eye, it is finger counting at 1.5 meters. Intraocular pressure in the right eye is 20 mmHg and in the left eye is 19 mmHg by Goldman applanation tonometry. Fundus examination (Figure 2) is normal in both eyes. Optical coherence tomography was normal in both eyes (Figure 3). MRI orbit (Figure 1a-Left eye sagittal, 1b-Right eye sagittal, 1c-Both eyes axial) revealing a mild vertical tortuous course of bilateral optic nerves with a mild sleeve of cystic intensity in bilateral perioptic spaces, suggestive of bilateral optic neuritis. Nutritional, tobacco/alcohol, ischemic, compressive, demyelinating, and genetic optic neuropathies were all ruled out as differential diagnoses for toxic optic neuropathy. Ethambutol was stopped, and therapy was continued with vitamin B complex and zinc being started along with antitubercular treatment. In follow-up visits, the patient's vision improved significantly after discontinuation of ethambutol.

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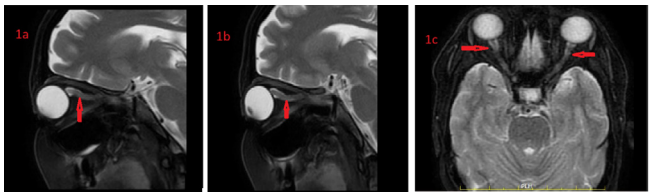

Figure 1

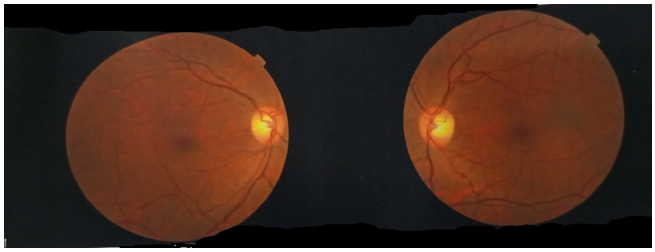

Figure 2

Discussion

Ethambutol inhibits the enzyme arabinosyl transferase, which is important for synthesizing the mycobacterial cell wall[5]. Adverse effects associated with ethambutol are rash, pruritus, joint pain, optic neuritis, gastrointestinal (GI) upset, malaise, headache, dizziness, mental confusion, disorientation, vision loss, and visual field defect.[2] Optic neuropathy is one of the most serious adverse effects of ethambutol. Differential diagnoses include Leber's hereditary optic neuropathy, dominantly inherited optic neuropathy, compressive or infiltrative lesion of optic chiasm, bilateral inflammatory or demyelinating optic neuropathy, and maculopathies/ macular dystrophy. Higher dose, prolonged duration, diabetes mellitus, hypertension, older age, tobacco smoking, alcohol consumption, and poor renal function are risk factors for ethambutol-induced optic neuropathy[6]. Patients are usually presented with a gradual, painless loss of vision. Initially, it can be noticed as reading-related blurring but may indicate central field abnormalities. There is bilateral involvement seen simultaneously, but the onset might also be unilateral. Affected central fibers hamper the visual acuity on usual presentation, but peripheral fibers can also be affected, rarely with peripheral field constriction. In turn, it may progress to optic atrophy, which appears as temporal disc pallor when a fundoscopic examination is performed[3]. Fundus examination in the initial stages is normal, but in the later stages, as optic atrophy progresses, disc pallor is noted more specifically temporal pallor. Considering the severity of the visual loss caused by ethambutol-induced optic neuropathy, it is imperative to detect it at an early and subclinical stage to prevent permanent visual loss. The screening modalities used are visual field examination, Fundus examination, optical coherence tomography (OCT) and visual evoked potential(VEP). Visual field examination reveals central, centrocecal scotoma or bitemporal hemianopia.[10] Ethambutol-induced optic neuritis can result in loss of red-green color discrimination.[1] OCT provides an objective and quantitative measure of retinal damage. Studies have shown a gradual

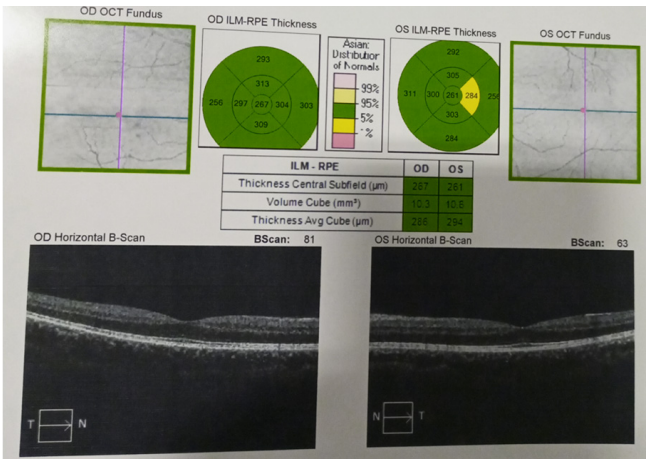

Figure 3

thinning of the retinal nerve fiber layer (RNFL), more significantly in the temporal quadrant of the peripapillary RNFL and loss of ganglion cell inner plexiform layer (GCIPL) thickness, indicating early neuronal loss (earlier than RNFL).[7] Subclinical toxicity in the form of increased latency of the P100 wave of pattern VEP was associated with consumption of a higher daily dose of ethambutol.[8] Studies have indicated that ethambutol-induced optic neuropathy (EON) is an adverse effect that depends on both the dosage and duration of treatment.[1] The probability of this reaction is higher with greater doses and longer use of ethambutol. This happens in 15% of patients who take 50 mg/kg daily, 5% who administer 25 mg/kg daily, and below 1% of patients on a daily dose of 15 mg/kg[2]. Since ocular toxicity can occur at any dose of ethambutol, there is no predetermined safe dose. Also, the onset time of optic neuritis cannot be anticipated. It is unknown how ethambutol causes optic neuritis, although theories have been put forward. One such theory is based on the fact that ethambutol and its metabolites can chelate zinc, causing a disturbance in retinal homeostasis[3]. In addition, ethambutol is believed to interrupt oxidative phosphorylation by acting on iron-containing complex I and copper-containing complex IV, leading to reactive oxygen species production, which may cause injury to the retinal ganglion cells[3]. It might result from decreased levels of copper in the mitochondria or from the accumulation of zinc in the lysosomes of the retinal ganglion cells[9]. Similarly, deficiencies in vitamins such as E, B1, B9, and B12 may worsen optic neuritis.[4] Optic neuritis caused by ethambutol is usually reversible after discontinuation of medication, but recovery is time-consuming.[2] Toxic optic neuritis may be of early or late-onset, reversible or irreversible and axial or periaxial. Ethambutol can cause visual impairment as a result of retrobulbar neuritis, which is related to the dose and duration of treatment.

Conclusion

Ethambutol-induced optic neuropathy is a dose-dependent toxicity, and hence the variability in initial dosing plays a major role in its development. Regular screening, early

diagnosis, and timely discontinuation of the drug in symptomatic patients are the keys. As in this case, the patient has been showing significant improvement in visual acuity. Conventional ophthalmic examinations, including visual acuity, color vision, and visual field, can determine reversibility of toxicity. Though visual evoked potentials and optical coherence tomography are the usual modalities of screening, the role of MRI should not be undermined. This case emphasizes the role of MRI, an advanced diagnostic modality, in the early detection of optic neuritis and structural changes to avoid irreversible loss or impairment of vision, where fundus examination and optical coherence tomography were normal. In literature, most of the cases were diagnosed by clinical history and ophthalmological examinations, whereas this is a unique case with MRI-confirmed optic neuritis with cystic changes in the peripapilled space.

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