Case Report

Optic neuropathy induced by ethambutol: A rare case from Nepal

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\textbf{ABSTRACT}

\textbf{Introduction:} Ethambutol is a drug used against tuberculosis and causes side effects like problems with vision, which may lead to optic neuropathy. It has a low prevalence of 1% and typically develops after 4–12 months of its medications.

\textbf{Case presentation:} Here, we report a case of a 42-year-old male with ethambutol-induced optic neuropathy after six weeks of initiation of ethambutol.

\textbf{Discussion:} Nutritional and tobacco/alcohol, ischemia, compressive, demyelinating, and genetic optic neuropathies were all ruled out as differential diagnosis for toxic optic neuropathy. Because our patient did not have vasculopathy and his vision loss was progressive on follow up and bilateral, rather than acute and unilateral, as is more usual with an ischemic disease, ischemic optic neuropathy was ruled out. Finally, because hereditary optic neuropathy usually manifests at a younger age and is expressed in many generations which was not the case in our patient, it was effectively ruled out as the cause of optic neuropathy.

\textbf{Conclusion:} This case highlights that ethambutol toxicity is rare in cases of new onset pulmonary tuberculosis where ethambutol has been administered for only 2 months.

1. \textbf{Introduction}

Toxic optic neuropathy is an adverse effect of some medications like ethambutol and linezolid. Ethambutol is a bacteriostatic antimicrobial medication, used as a first-line drug against tuberculosis (TB). However, it may lead to side effects including problems with vision, liver problems, and allergies [1]. Central vision loss, centrocecal scotoma, acquired color vision defects are the commonest ocular findings of ethambutol induced optic neuropathy [2]. Ethambutol-induced toxic optic neuropathies have a low prevalence of 1% and typically develop after 4–12 months of its medications. Here, we report a case of a 42-year-old male with ethambutol-induced optic neuropathy just after six weeks of administration of ethambutol. This case has been reported in line with SCARE 2020 criteria [3].

2. \textbf{Case presentation}

A 42-year-old male presented to our center complaining of blurred vision in both eyes noticed since last 5 days. Vision loss was gradually progressive and painless without associated diplopia. He had no history of headache, recent trauma, or exposure to any toxic chemicals or heavy metals. He had no significant past ocular/family history of any eye-related anomalies. He had normal bowel and bladder habits. 45 days before this presentation, he was diagnosed with pulmonary tuberculosis for the first time and was started on anti-tuberculous therapy of isoniazid (H), rifampicin (R), pyrazinamide (Z), and ethambutol (E). He was on a daily dose of ethambutol of 18 mg/kg. He had been diagnosed with hypertension five years back and was non-diabetic and had a normal renal function. He was a non-smoker but had been occasionally consuming alcohol for the past 10 years.

His blood pressure at the time of presentation was 150/90 mm Hg and his body weight was 50 kg. His best-corrected visual acuity (BCVA) was 2/60 in the left eye and finger counting close to face (CFCF) in the right eye at the time of presentation. His intraocular pressure (IOP) was 14 mm Hg and 16 mm Hg in right and left eye respectively (Goldmann Applanation Tonometry). The slit-lamp microscope examination

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revealed normal anterior segments and anterior vitreous findings. On swinging flashlight test, the pupils were found reactive with grade II relative afferent pupillary defect (RAPD) in the right eye. Funduscopic examination showed normal macula and foveal reflex was present in both eyes along with bilateral temporal pallor in the optic nerve head of both eyes (Fig. 1). His cup-to-disc ratio was 0.2 in both eyes. His visual field, color vision, and contrast sensitivity examinations could not be assessed due to poor vision. Magnetic resonance imaging (MRI) of the brain and orbits was normal. The rest of the neurological examination was within normal limits.

The retinal nerve fiber layer (RNFL) thickness was measured using optical coherence tomography (OCT). The results showed that the bilateral RNFL thickness was within the normal range. He was then diagnosed with ethambutol-induced optic neuropathy and advised to stop taking ethambutol immediately; it was after 45 days that antitubercular drugs were started. Even after discontinuing ethambutol, our patient’s visual symptoms did not improve; in fact, they worsened. He continued the medications with isoniazid and rifampicin for the next four months. He was given methylcobalamin (1000 mcg).

He was re-assessed after a month following ethambutol cessation which revealed an improvement in the vision (3/60 in the right eye and 5/60 in the left eye). Color vision, contrast sensitivity, and visual field could not be accessed again because of poor vision.

The vision was 5/60 and 6/60 in right and left eye respectively after six months of withdrawal of ethambutol. Color vision was assessed with Farnsworth dichotomous panel D 15 and showed a tritant defect in the left eye while there was a non-specific color defect in the right eye. Also, contrast sensitivity was assessed with the Peli Robson chart which showed 1.45 and 1.50 log units in right and left eye respectively.

3. Discussion

Toxic optic neuropathy is the result of toxins damaging the optic nerve. Drugs, metals, organic solvents, ethanol and methanol, tobacco, and carbon dioxide are among the toxins. The medications that may cause toxic optic neuropathy are antituberculosis (ethambutol and isoniazid), antimicrobials (linezolid and ciprofloxacin), antiepileptic (vigabatrin), phosphodiesterase type 5 inhibitors (sildenafil, tadalafil, vardenafil), anti-Y-tumor necrosis factor agents, amiodarone, and tamoxifen [4]. Nutritional deficiency, particularly in the B complex vitamins and folic acid, can cause or worsen toxic optic neuropathy. There is no evidence of a racial or gender bias in either toxic or nutritional ocular neuropathy [4].

Nutritional and tobacco/alcohol, ischemia, demyelinating, and genetic optic neuropathies were all ruled out as differential diagnosis for toxic optic neuropathy. Nutritional optic neuropathy could be ruled out because the patient consumed a healthy diet, had normal serum B12 and red blood cell folate levels, and showed no improvement in his symptoms despite initiating vitamin B12 and coenzyme Q10 supplements. Tobacco and alcohol are also thought to cause optic neuropathy synergistically [4]. However, tobacco as the cause of optic neuropathy was ruled out in his case because he was a non-smoker. Also, the fact that he only consumed alcohol occasionally ruled out alcohol induced optic neuropathy. Because our patient did not have vasculopathy and his vision loss was progressive on follow up and bilateral, rather than acute and unilateral, as is more usual with an ischemic disease, ischemic optic neuropathy was ruled out. Because of the unremarkable magnetic resonance imaging of the brain and orbits, demyelinating and compressive optic neuropathies were ruled out. Finally, because hereditary optic neuropathy usually manifests at a younger age and is expressed in many generations which was not the case in our patient, it was effectively ruled out as the cause of optic neuropathy [5].

Ethambutol was the only remaining likely cause of toxic neuropathy. Tuberculosis and Mycobacterium infections are treated with ethambutol. Ethambutol has been used to treat tuberculosis since the 1960s, and cases of ethambutol-induced optic neuropathy have been documented since then [3]. Optic neuropathy is one of the most serious adverse effects of ethambutol, which affects 1–6% of patients [4]. Peripheral neuropathy, cutaneous responses such as rashes, pruritus, and urticaria, thrombocytopenia, and hepatitis are among the rare adverse effects. Visual difficulties usually appear 4–12 months after starting the medicine; however, renal failure can shorten this time by lowering ethambutol excretion and increasing serum levels. Furthermore, an increased risk of toxicity has been linked to the elderly, hypertension, and a high daily dose of ethambutol medication [4]. A few uncommon cases of ethambutol optic neuropathy have been documented several days after the medicine was started; however, few cases of ethambutol optic neuropathy have also been reported after the drug was stopped [6]. Patient education about potential side effects is critical for early detection of drug-related toxic optic neuropathies and withdrawal of the causative agent to improve vision recovery. Even after discontinuing ethambutol, our patient’s symptoms did not improve; in fact, they worsened. Even though a dose of 15 mg/kg per day is deemed safe and effective, occurrences of optic neuropathy have been observed at this dose, with an incidence of about 1% [7]. Our patient was on a daily dose of 18 mg/kg and developed optic neuropathy rather early at 45 days even though there were no other risk factors. There was a slight improvement in vision after 6 months of cessation of ethambutol.

Although the specific mechanism of EON is unknown, it is thought to be caused by disturbed oxidative phosphorylation as a result of decreased accessible copper in human mitochondria [8] or restricted lysosomal activation due to zinc chelation [9,10].

![Fig. 1. Funduscopy examination of (a) right eye (b) left eye showing bilateral temporal pallor in optic nerve head of both eyes.](image-url)
4. Conclusion

Ethambutol use has been linked to permanent vision loss; thus, it should be avoided if at all feasible, or used with caution and thorough ophthalmological monitoring in patients being treated with ethambutol. Eye care providers and other medical experts should inform their patients about the potential adverse effects of these medications and encourage them to seek help as soon as any visual abnormalities occur.

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Ethical approval

None.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Authors’ contribution

SS conceptualized the study, reviewed, edited the manuscript, and was in charge of the case; SS, YRA and SP wrote the original, reviewed and edited the manuscript; SS, YRA, SP, SS, BK, SA, YP, and RK were in charge of the case, and reviewed the manuscript. SS supervised the research.

Data availability statement

All the required data are available in the manuscript itself.

Research registration

None.

Registration of research studies

Name of the registry: None
Unique Identifying number or registration ID: None
Hyperlink to your specific registration (must be publicly accessible and will be checked):

Guarantor

Sangam Shah.

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Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Declaration of competing interest

None.

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Appendix A. Supplementary data

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