International Journal of Medical and Pharmaceutical Case Reports

Volume 16, Issue 1, Page 1-5, 2023; Article no.IJMPCR.94818
ISSN: 2394-109X, NLM ID: 101648033

A Rare Incidence of Ethambutol Induced Toxic Optic Neuropathy

M. V. Mousigan [a*], L. Nissi [a] and V. Sreenivasan [b]

[a] C. L. Baid Metha College of Pharmacy, Chennai, India.
[b] Gleneagles Global Health City, Perumbakkam, Chennai, India.

Authors' contributions

This work was carried out in collaboration among all authors. Author MVM did the case collection and gathered the evidence from the previously published study. Author LN designed the case report and did the literature review data mining. Author VS completely reviewed the article and guided through out. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJMPCR/2023/v16i1322

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/94818

Case Study

Received: 20/10/2022
Accepted: 28/12/2022
Published: 02/01/2023

ABSTRACT

Ethambutol induces toxic optic neuropathy (EON), which most typically presents as bilateral symmetrical loss of vision and, due to a lack of early detection and adequate treatment, often causes serious irreversible visual impairment. EON is time and dose dependent. In this case report, we will discuss a 59-year-old female patient who came in with complaints of visual impairment, inclusive of a colour vision defect (dyschromatopsia) and blurred vision (scotoma). Her past medication history includes use of first-line anti-tubercular therapy (ATT) with four drugs: Rifampicin, Isoniazid, Ethambutol, and Pyrazinamide. Pyrazinamide was taken for two months, and other medications (Rifampicin, Isoniazid, and Ethambutol) were taken for a period of seven months. From this case report, we will get a clear picture necessitating continuous monitoring for ocular toxicity.

Keywords: Ethambutol-induced Optic Neuropathy (EON); Anti-Tubercular Therapy (ATT); reversible; Duration and dose dependent.

**Corresponding author: E-mail: mousiganmurugesan@gmail.com;*

ABBREVIATIONS

ATT : Anti-Tubercular Therapy
EON : Ethambutol- induced Optic Neuropathy
EPTB : Extrapulmonary Tuberculosis
GCIPL : Ganglionic Cell Inner Plexiform Layer
MTB : Mycobacterium Tuberculosis
RNFL : Retinal Nerve Fiber Layer
TB : Tuberculosis
TON : Toxic Optic Neuropathy

1. INTRODUCTION

India is a tropical country, and people are more susceptible to acquiring bacterial infections. *Mycobacterium tuberculosis* (MTB) causes tuberculosis (TB) infection [1]. More than 40% of the population in India is affected by TB. MTB that also affects other parts of the body other than the lungs is referred to as extrapulmonary tuberculosis (EPTB). In India, EPTB accounts for 20%. First-line drugs for treating MTB are Rifampicin, Isoniazid, Ethambutol, and Pyrazinamide [2]. Among these, ethambutol has a higher affinity to cause toxic optic neuropathy, which is dose and duration-dependent. This condition is usually reversible once the drug is discontinued [3]. Toxic optic neuropathy (TON) is a complex, multifactorial disease that can affect people of all ages, races, locations, and socioeconomic backgrounds. Nutritional, environmental, toxicologic, and genetic factors all play a role in etiology. Toxic optic neuropathy is characterised by bilateral, often symmetrical vision loss, papillomacular bundle damage, central and cecocentral scotomas, and diminished colour vision. Early identification and treatment can help to alleviate and possibly prevent serious vision impairment [4].

2. CASE PRESENTATION

A 59-year-old female patient came to the hospital with complaints of visual impairment, including a colour vision defect (dyschromatopsia) and blurred vision (scotoma). Her past medical history includes hypothyroidism, C7 body destruction with quadriparesis, and D12 left paravertebral collection. For this, she was scheduled for a C7 corpectomy, decompression, debridement, and stabilisation with C6C7D1 and biopsy. Her histopathology report showed C6-C7 soft tissue and bone tissue biopsy: necrotizing granulomatous inflammation, possibly of tubercular origin. Her expert report revealed Mycobacterium tuberculosis (MTB) detection was very low and rifampicin resistance was not detected. So, she was started on anti-tubercular therapy (ATT) that includes a combination capsule of Rifampicin and Isoniazid (600 mg and 300 mg, respectively), 800 mg of Tab. Ethambutol, 1500 mg of Tab. Pyrazinamide, and 40 mg of Tab. Pyridoxine for 9 months. Tab. Pyrazinamide (150 mg) was taken for 2 months, and Rifampicin, Isoniazid, and Ethambutol were to be taken for a period of 7 months.

She was adherent to the ATT, and by the end of the seventh month, she developed complaints of visual impairment, inclusive of a colour vision defect (dyschromatopsia) and blurred vision (scotoma). So she was referred to an ophthalmologist, and the ophthalmologist advised Optical Coherence Tomography (OCT) (Fig. 1). From her OCT report, we found that she has mild cataracts and cecocentral scotomas.

As a result, Tab. Ethambutol (800 mg) was removed from the therapy. Her condition gradually improved during the subsequent hospital visit.

3. DISCUSSION

While prescribing ATT drugs, all physicians explain to the patient and attender about the treatment course and the possible side effects of the drugs. In subsequent visits, the doctor always asks the patient about the potential side effects that they may experience after starting the therapy, and the patient is monitored by performing liver function tests (LFT), renal function tests (RFT), and a complete blood count (CBC), which helps to recognise the events at an earlier stage. This early detection helps to prevent the worsening of the condition and allows for the withdrawal of the drug as early as possible.

In recent studies, it has been reported that 1-2% of patients receiving ethambutol may develop EON. Although the precise pathophysiological mechanism behind EON is still unknown, it may be owing to reduced lysosomal activation as a result of zinc chelation or to impaired oxidative phosphorylation subsequent to decreased available copper in human mitochondria. Studies have shown that the adverse effect of EON is dose- and time-dependent [5].

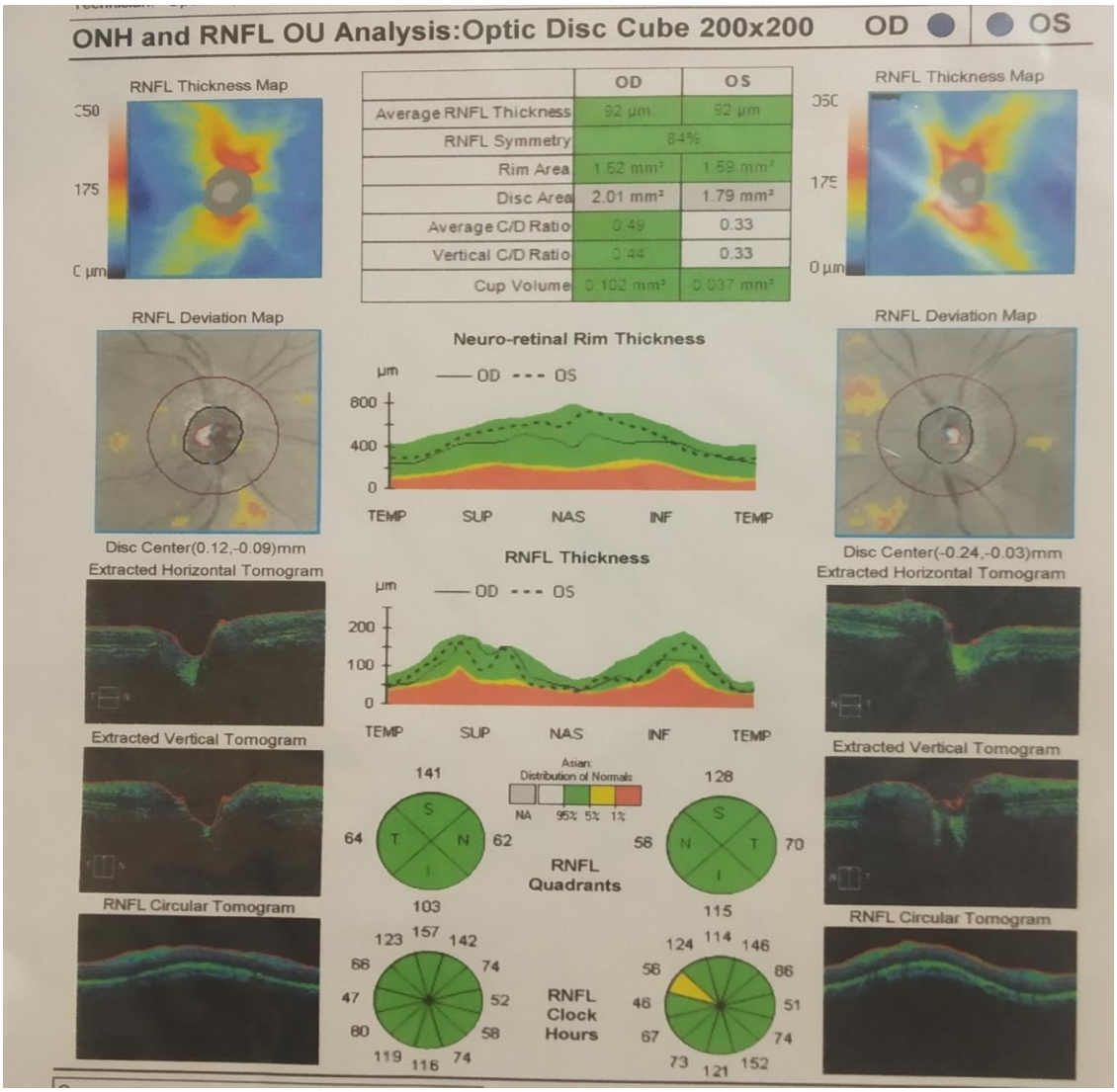

Fig. 1. Optical Coherence Tomography

As a matter of evidence, the same findings were reported in the following case reports:

According to Monika et al., EON does not have a predictable onset time. This can occur from a few days to two years after the start of drug-producing ocular symptoms. The majority of the patients shared the usual cecocentral scotomas seen by this patient. In the initial period of presentation, the disc will enlarge and become hyperemic during fundus examination. Because of the early diagnosis, it was possible to prevent the complications [6].

Wen-Yan Sheng et al.Ocular examination indicates impaired colour vision and a bilateral, painless, often symmetric loss of visual acuity in more than 60% of EON patients. It begins with one eye and progresses to affect both eyes.Green and red are frequently the colours for which colour vision loss is recorded, while blue-yellow colour alterations can also happen. The optic disc may initially seem normal, but as the condition worsens, it finally turns into a pale disc. OCT analyses revealed decreased thickness of the ganglionic cell inner plexiform layer (GCIPL) and the retinal nerve fibre layer (RNFL) as well [7].

Sagnik Sen et al. OCT is used to measure the thickness of the retinal fibre and ganglion cell layers in order to search for early signs of degeneration and alterations [8].

Sangam shah et.al Ethambutol is a medicine used to treat tuberculosis, but it also has adverse

effects like vision problems, which can result in optic neuropathy. It is uncommon (1% frequency) and often appears 4–12 months after starting treatment.The most prevalent ocular symptoms of ethambutol-induced optic neuropathy include central vision loss, centrocaecal scotoma, and acquired colour vision defect [9].

Depending on the dose and length of the antitubercular treatment, ethambutol-induced toxic optic neuropathy has been recorded in 1%–18% of patients, both in the adult and paediatric age groups, who are receiving the medication. The need for early detection of ethambutol toxicity, even in a preclinical state, and for corrective measures, such as dosing reduction or more frequently drug discontinuation, has been indicated as a way to lessen this effect [10].

Ethambuol toxicity to retinal ganglion cells via the excitotoxic pathway, which results in the loss of small-diameter axons, makes it a risk factor for optic neuropathy and chiasmopathy. The physiology of axon transport and axon-myelin interactions is altered by the Ethambutol, which also damages the mitochondria, in the optic nerve [11].

An ocular consequence of ethambutol use is ethambutol-induced optic neuropathy (EON), which is characterised by vision blurring, dyschromatopsia, and central or cecocentral scotoma [12].

4. CONCLUSION

Ethambutol induced toxic optic neuropathy is rare but not unusual. It is reversible when the drug is withdrawn. The patient should not neglect even the small changes that occurs after the treatment is initiated. The process of improving the quality of life is always a two-way between the patient and the medical practitioner. From this case report we conclude that early detection of an adverse effect after taking ATT drugs (Ethambutol) is reversible, if patient is properly counselled at every hospital visit.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

ACKNOWLEDGEMENTS

The authors would like to thank the institution's principal, Dr. Grace Rathnam, for her ongoing support, as well as fellow staff and students for their encouragement.

Also thanking the patient who is very cooperative and helpful to make this happen.

And also thanking for the support of pulmo team from Gleneagles Global Health City.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. More than 40% of the population in India carry Tuberculosis infection in their body but only 10% get TB disease: Chief Medical Officer, National Tuberculosis Institute [Internet]. Gov.in. [cited 2022 Nov 18]. Available:https://pib.gov.in/PressReleasePage.aspx?PRID=1808092
2. Shamseeda, Jayasree. Epidemiological profile of extrapulmonary tuberculosis and its association with diabetes in tertiary care center in Northern Kerala. Int J Community Med Public Health [Internet]. 2022 [cited 2022 Nov 18];9(6):2590. Available:https://www.ijcmph.com/index.php/ijcmph/article/view/9762/6005
3. Song W, Si S. The rare ethambutol-induced optic neuropathy: A case-report and literature review. Medicine (Baltimore) [Internet]. 2017 [cited 2022 Nov 18];96(2):e5889. Available:http://dx.doi.org/10.1097/md.0000000000005889
4. Kesler A, Pianka P. Toxic optic neuropathy. Curr Neurol Neurosci Rep [Internet]. 2003 [cited 2022 Nov 18];3(5):410–4. Available:https://pubmed.ncbi.nlm.nih.gov/12914684/
5. Sheng W-Y, Wu S-Q, Su L-Y, Zhu L-W. Ethambutol-induced optic neuropathy with rare bilateral asymmetry onset: A case report. World J Clin Cases [Internet]. 2022 [cited 2022 Nov 18];10(2):663–70. Available:http://dx.doi.org/10.12998/wjcc.v10.i2.663
6. Monika, Kumar J, Rathi M et.al. Ethambutol induced optic neuropathy: a rare case report. International Journal of Research and Review. 2020;7(2):13-17.
7. Sheng WY, Wu SQ, Su LY, Zhu LW. Ethambutol-induced optic neuropathy

with rare bilateral asymmetry onset: A case report. World J Clin Cases 2022;10(2):663-670 [PMID: 35097092
DOI: 10.12998/wjcc.v10.i2.663]

8. Sen S, Mandal S, Banerjee M, Gk R, Saxena A, Aalok SP, et al. Ethambutol-induced optic neuropathy: Functional and structural changes in the retina and optic nerve. Semin Ophthalmol [Internet]. 2022;37(6):730–9.
Available:http://dx.doi.org/10.1080/08820538.2022.2085517
9. Shah S, Adhikari YR, Paudel S, Sitaula S, Koirala B, Aryal S, et al. Optic neuropathy induced by ethambutol: A rare case from Nepal. Ann Med Surg (Lond) [Internet]. 2022;77(103637):103637.
Available:https://www.sciencedirect.com/science/article/pii/S2049080122003971
10. Saxena R, Singh D, Phuljhele S, Kalaiselvan V, Karna S, Gandhi R, et al. Ethambutol toxicity: Expert panel consensus for the primary prevention, diagnosis and management of ethambutol-induced optic neuropathy. Indian J Ophthalmol [Internet]. 2021 [cited 2023 Jan 13];69(12):3734–9.
Available:http://dx.doi.org/10.4103/ijo.IJO_3746_20
11. Islam IC, Umar BT, Minhajat R, Bukhari A, Sari DK, Kaelan C. Ethambutol effect on retinal and optic nerve structural changes in toxic optic neuropathy case: A literature review. Ophthalmol Res Int J [Internet]. 2022 [cited 2023 Jan 13];16(3):26–36.
Available:http://eurolibpress.uk/id/eprint/764/
12. Zhang X-H, Xie Y, Xu Q-G, Cao K, Xu K, Jin Z-B, et al. Mitochondrial mutations in ethambutol-induced optic neuropathy. Front Cell Dev Biol [Internet]. 2021;9:754676.
Available:http://dx.doi.org/10.3389/fcell.2021.754676

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/94818