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RESEARCH ARTICLE

CASE REPORT: LINEZOLID INDUCED OPTIC NEUROPATHY

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ABSTRACT

We report a case of toxic optic neuropathy due to linezolid occurring in a patient who was on linezolid for Multi drug-resistant pulmonary tuberculosis (MDR-TB).

INTRODUCTION

Linezolid, a synthetic oxazolidinone antibiotic, has been shown to be efficacious in the treatment of mycobacterial infections, including multi-drug-resistant tuberculosis (MDR-TB, defined as tuberculosis resistant to rifampicin and isoniazid)[1].It belongs to Group 5 of anti-tuberculosis agents used as 2nd line in multi-drug resistant tuberculosis, caused by multi-drug resistant Mycobacterium tuberculosis (MDR-TB) and extensively-drug resistant Mycobacterium tuberculosis (XDR-TB)[2].Patients on linezolid should be under close monitoring for adverse events, particularly anaemia, peripheral and optic neuropathy and lactic acidosis as these can be severe and life threatening. Linezolid inhibits bacterial protein synthesis but it has no major effect on the protein synthesis in mammalian cells. However, intracellular mitochondria are affected by linezolid and long-term administration of the drug may affect protein synthesis. It has been hypothesized that optic and peripheral neuropathy may potentially be the result of this mitochondrial dysfunction.3,4 Toxic optic neuropathies are characterized by gradual, progressive, painless, bilaterally symmetric visual loss affecting central vision, and causing central or centrocecal scotoma.[5]

CASE REPORT

A 54 year old man presented to our outpatient department with painless progressive diminution of vision both eyes for the past 10 days.

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Medical history included MDR-TB on treatment with linezolid (600 mg/day), cycloserine (500 mg/day), ethionamide (500 mg/day), and kanamycin (750 mg/day) for the past 9 months. He was a non-smoker and non-alcoholic. On examination, his best corrected visual acuity was 1/60 (OD) and 6/60 (Os), not improving with pin hole. Color vision was defective in both eyes.Extraocular movements were normal .Intraocular pressure was 14 (OD) and 11 (OS). Anterior segment examination was unremarkable and pupils were 3 mm, round, regular, and reacting to light in both eyes (Direct and Indirect). There was no relative afferent pupillary defect (RAPD). Fundus examination revealed hyperemic disc with blurred margins (OU) (Figure 1 and 2). Visual field evaluation by Humphrey field analyzer showed peripheral constriction and quadrantanopia in the right eye (Figure 3) and central scotoma in the both eyes (Figure 4). He underwent a magnetic resonance imaging (MRI) of the brain and orbits with gadolinium contrast but it was normal in all respects. Preliminary diagnosis of linezolid was made and linezolid was discontinued.At day 38 follow-up, his visual acuity had improved to 6/36 bilaterally.

DISCUSSION

Linezolid inhibits protein synthesis by preventing formation of the ribosome complex that initiates protein synthesis. Its unique binding site located on 23S ribosomal RNA of the 50s subunit results in no cross resistance with other drug classes. Long-term linezolid interferes with bacterial ribosomes and also with mammalian ribosomes, thereby disrupting mitochondrial oxidative phosphorylation and protein

synthesis.[2] Mitochondrial dysfunction is the cause of Leber's hereditary optic neuropathy, chloramphenicol induced bone marrow suppression, and optic neuropathy due to ethambutol and a variety of antibiotics.

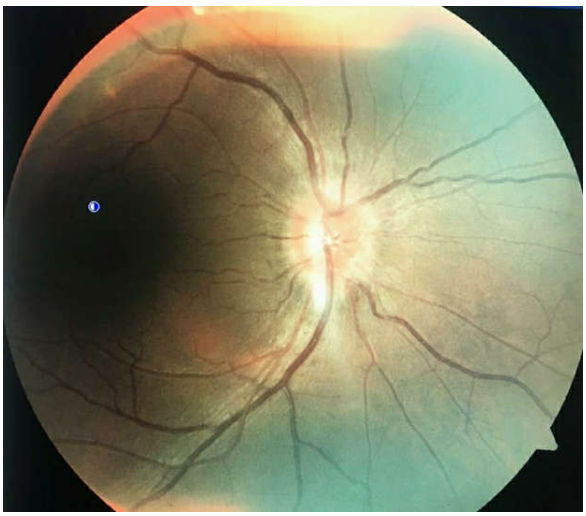

Figure 1. Fundus photograph of right eye showing hypermic disc, obliteration of cup and blurred margins

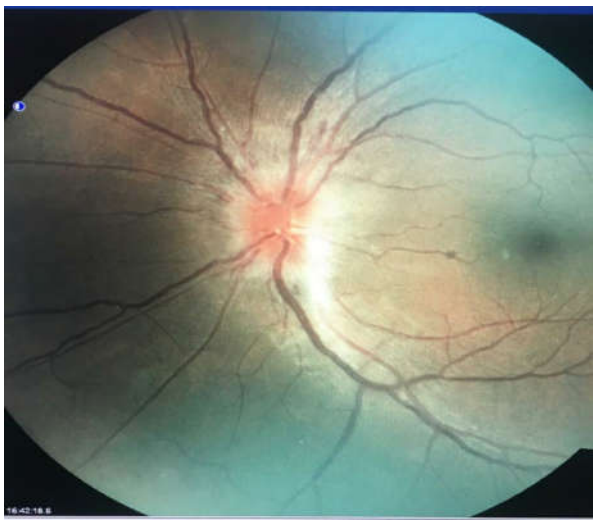

Figure 2. Fundus photograph of left eye showing hypermic disc with blurred margins

It is likely that the development of linezolid associated optic neuropathy, manifest by the development of central scotomas and temporal optic nerve pathology, may be the result of a similar mechanism.[6,7]In the meta-analysis by Zhang et al., with 23 optic and 79 peripheral neuropathies, the duration of treatment with linezolid was greater than 5 months[8]. In other study on a retrospective cohort with five optic neuropathy cases, the time of linezolid administration was greater than 7 months in all cases, and the mean time of administration was 10 months[9]. According to the results mentioned by Brandariz Nunez et al[10], the mean treatment duration was 10 months.

The only known form of treatment for linezolid-associated optic neuropathy is cessation of the antibiotic.[11,12] The presented patient stopped taking the medication after our initial evaluation, once we received approval from his orthopedist. Literature review has shown that in similar cases, some level of visual recovery can be expected after weeks to months post-cessation of linezolid.[12-15] Due to apparent optic atrophy, visual prognosis is guarded; however, other cases have shown significant visual recovery after up to one year of extended use of linezolid.[11-15]

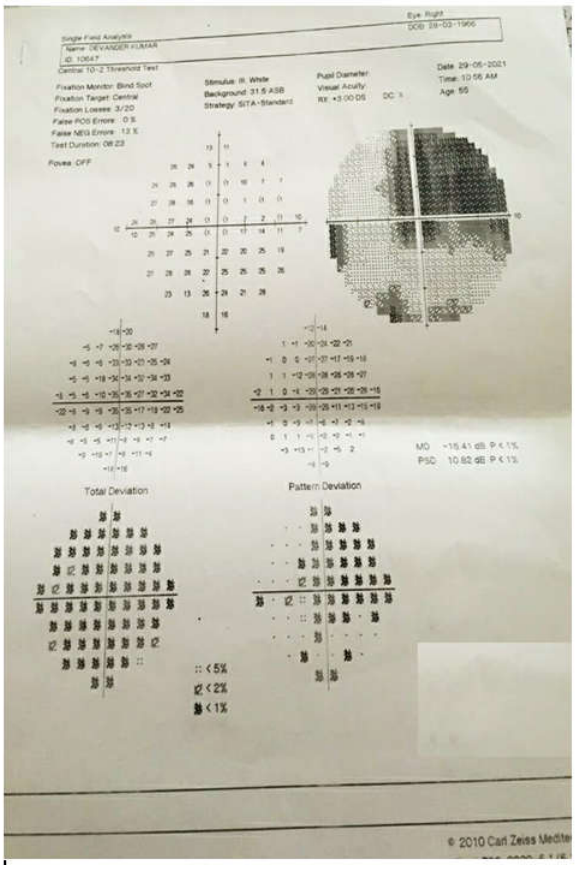

Figure 3. Visual field showing upper quadrantic

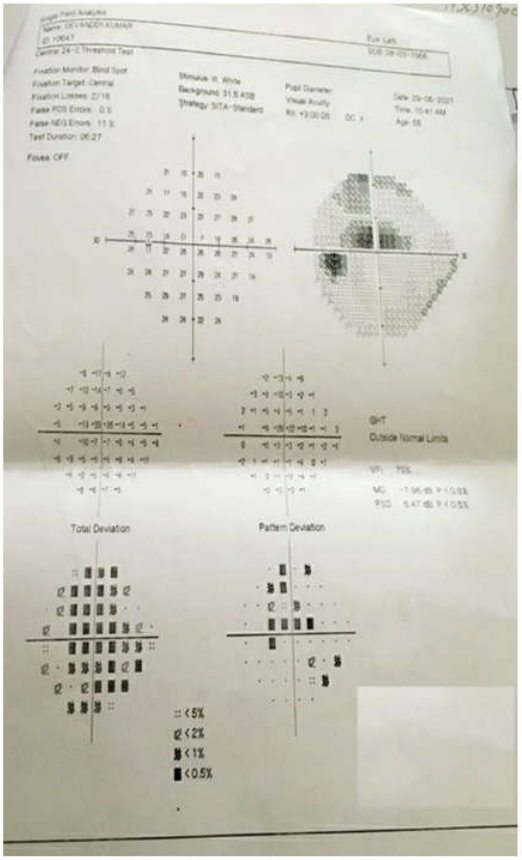

Figure 4. Visual field showing central defect and central scotomascotoma

CONCLUSION

Although ethambutol is the most common antitubercular drug implicated to cause toxic optic neuropathy, we should be aware that if withdrawal of one drug does not show recovery or there is further deterioration of vision, the possibility of toxicity due to linezolid should be kept. Ophthalmologists and physicians must be aware that monitoring of visual function is important in patients on anti tuberculardrugs and that early diagnosis and discontinuation of drug results in complete visual recovery.

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