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Bilateral Optic Neuropathy Secondary to Prolonged Linezolid Use in XDR-TB Patient

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Abstract: We report a case of bilateral painless progressive loss of vision associated with prolonged linezolid use. A 22 year old male patient with extensive drug resistant tuberculosis (XDR-TB), who was on treatment with multiple second line anti-tubercular drugs including linezolid for the past 3 months started developing progressive painless loss of vision in both the eyes over a period of 10days. Discontinuation of linezolid resulted in complete resolution of visual symptoms within a month. Our report emphasizes the need for monitoring of visual function in patients on long-term linezolid treatment.
Keywords: Linezolid, optic neuropathy, XDR- TB.

INTRODUCTION

Linezolid is an oxazolidinone, synthetic antimicrobial agent with activity against many important pathogens including drug-resistant tubercle bacillus, methicillin-resistant staphylococcus (MRSA) and streptococcus. It is normally given in the dose of 600 mg twice daily for a maximum of 14 days when used as an antibiotic. In case of infection with drug resistant tuberculosis i.e. multi-drug resistant tuberculosis (MDR-TB)/XDR-TB, it has to be used for prolonged periods (up to several months) as a group V agent. Rare but severe adverse effects are noted when the drug is used for a longer period of time and include myelosuppression, lactic acidosis, optic and peripheral neuropathy [1]. We report a case of toxic optic neuropathy occurring in a patient of XDR-TB who was on linezolid therapy for a period of 3 months.

CASE REPORT

A 22year old male patient with pulmonary Koch's, diagnosed on the basis of sputum analysis and chest radiograph, presented in January 2015, with no clinical, microbiological or radiographic improvement even after 9 months of anti-tubercular treatment (ATT). His sputum culture confirmed him to be infected with a resistant strain of mycobacteria with resistance to quinolones, amikacin, and kanamycinalong with all the first line anti tubercular drugs like isoniazid, rifampicin, ethambutol, pyrazinamide and streptomycin. He was only sensitive to injectable capreomycin. On the basis of the culture sensitivity report done at a microbiology laboratory, he was started on an anti tubercular drug regimen according to his body weight, from January 2015. He was prescribed capreomycin 500 mg once daily for five days a week, linezolid (600 mg/day), orally granules of para-aminosalicylic acid (PAS) mixed in water twice a day, Tab. clofazimine (100 mg/day) and Tab. Pyridoxine (100mg/day). The patient was responding clinically to this regimen. After 3months of treatment with these drugs, he developed progressive painless loss of vision in both eyes over a period of 10 days. On Ophthalmologic examination, visual acuity was 20/200in the left and right eye. Color vision was defective as noted by Ishihara's charts. Anterior segment examination was unremarkable and pupils were 3mm, round, regular and reactive to light in both eyes (Direct and Indirect). Fundus examination showed mild optic disc edema in both the eyes. His visual evoked potential (VEP) study showed delayed to absent VEP on both sides (Figure 1).The visual changes were attributed to linezolid and the drug was withdrawn from the treatment regimen and subsequently the patient's vision improved significantly within a month of discontinuing the drug. Color vision was restored to normal and visual acuity returned to stable values (20/20).Fundus examination revealed resolved optic disc edema. Patient is on regular follow up and no toxic effects have been noted. Our patient did not have any features of peripheral neuropathy.

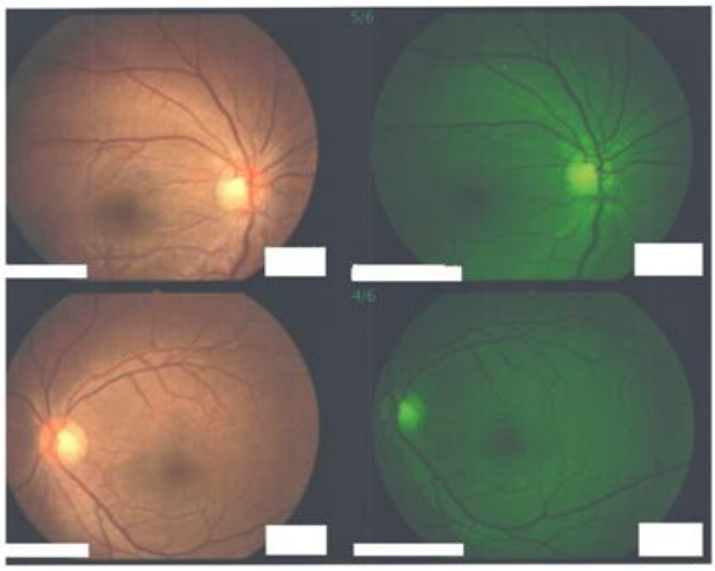

Fig-1: VEP study. Impression: 1. Absent VEP on both sides with 8' checks. 2. Delayed VEP response on both sides with LED goggies

DISCUSSION

Linezolid, a synthetic oxazolidinone inhibits bacterial protein synthesis by preventing the formation of the initiation complex composed of the 30Sand 50S subunits of the ribosome, tRNA and mRNA. It binds to the 23S portion of the 50S subunit (the center of peptidyl transferase activity), close to the binding sites of chloramphenicol, lincomycin and other antibiotics. Due to this unique mechanism of action, cross-resistance between linezolid and other protein synthesis inhibitors is highly infrequent or nonexistent 1. Hence, linezolid is being increasingly used for the treatment of infections caused by multidrug-resistant Gram-positive bacteria and also as a part of combination therapy for the treatment of drug resistant-TB. The safety of linezolid treatment has been established for use only up to 28 days and is usually well tolerated with few adverse effects when used on a short-term basis 2. Rare but serious adverse effects of the drug are commonly noted when the drug is used for a prolonged period of time. There are a few case reports of linezolid-induced optic or peripheral neuropathy in patients treated for a time period beyond 28 days. Only two cases of toxic optic neuropathy have been reported following short-term linezolid treatment of 16 days [4, 5 complete visual recovery has been reported in all cases except one.

In our patient, bilateral optic neuropathy occurred after linezolid had been used for 3 months at a dose of 600mg/day for the management of XDR-TB. The mechanism of linezolid induced optic neuropathy is unknown. Recent mechanisms propose that long-term linezolid interferes with bacterial ribosomes and also with mammalian ribosomes, thereby disrupting mitochondrial oxidative phosphorylation and protein synthesis. In all varied clinical conditions where this drug is used for more than 3-4 weeks, a regular ophthalmic check up should be done. Steroids have no proven role in the treatment of optic neuropathy. However, this toxicity is reversible soon after the drug is discontinued. In our patient, full visual recovery occurred within a month of discontinuing the offending drug.

Ophthalmologists and physicians must be aware that monitoring of visual function is important in patients on long-term linezolid therapy and that early recognition of toxicity and discontinuation of drug results in complete visual recovery. In this brief communication, we wish to emphasize that visual system affectation due to Linezolid need to be actively looked for, particularly when use of Linezolid beyond 28 days is deemed inevitable. Monthly check for visual acuity, field of vision, and color vision and fundus examination is important to avoid delay in diagnosis. Individual susceptibility towards rapid optic neuropathy also needs to be kept in mind.

CONCLUSION

The purpose of reporting this unique case is to emphasize the point that prolonged linezolid use can lead to optic neuropathy and blindness and that early recognition of toxicity and discontinuation of the drug results in complete visual recovery in majority of cases.

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