



## **A Case Report on Reversible Toxic Optic Neuropathy on Long Term Treatment of Linezolid in Extensively Drug-Resistant Tuberculosis Patient**

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### **Authors' contributions**

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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### **Case Report**

### **ABSTRACT**

We describe a case of Linezolid-induced severe toxic optic neuropathy in a patient with drug-resistant tuberculosis. Linezolid produced severe toxic optic neuropathy in some who used it for a long time. To the best of our knowledge, the optic neuropathy was completely reversed after omitting Linezolid which is one of the effective drug regimens in his prescription, with significant improvements in eye vision.

**Keywords:** Extensive drug resistance tuberculosis; drug-induced optic neuropathy; linezolid induced severe toxic optic neuropathy.

### **1. INTRODUCTION**

Toxic optic neuropathy has been reported as an uncommon side effect of Linezolid treatment for a longer duration with the majority of cases

occurring in adults. [1-5] various cases have been documented in people of varying ages. Here we are reporting a case of a twenty-eight-year-old patient who experienced this complication after more than six months of

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Linezolid treatment for extensively drug-resistant tuberculosis (XDR-TB). Linezolid, a synthetic Oxazolidinone group drug, has gained favor in recent years and is now used to treat *Staphylococcus aureus* skin and soft tissue infections caused by *Staphylococcus aureus* (MRSA) in place of Vancomycin. [1] *Staphylococcus aureus* bacteria are the most common pathogen isolated in all types and stages of Osteomyelitis, and these strains are not treated by Methicillin now a day. MRSA-induced Osteomyelitis is managed with Linezolid, which is active on nearly all MRSA strains. [2] It has been successfully utilized as a long-term treatment for persistent *Staphylococcus aureus* Osteomyelitis despite its less than ideal safety profile. One research found an 80% clinical outcome, with one-third of the patients experiencing treatment-limiting side effects. [3] Acute toxic optic neuropathy is a condition in which the optic nerve is damaged. [3-5] the reported neuropathy resulted in blindness with one case also found. [5] We present a case of reversible optic neuropathy in a patient with XDR-TB who experienced it after long-term treatment (TB). The reversibility of optic nerve involvement has been proven in the visual examination after treatment has ended.

## 2. CASE DESCRIPTION

A 28-year-old man who has been receiving XDR-TB treatment for many years was referred to the ophthalmology clinic due to spontaneous vision loss. The patient received oral Linezolid Tab. (600mg ODS) with other Anti-Tubercular drugs like Cycloserine (100mg ODS), Neurobian Forte (ODS), and PAS Granules (sodium para-

aminosalicylate) (200mg/kg BDS), Tab. Moxifloxacin (400mg ODS), Tab. Clarithromycin (400mg ODS), Cap. Becosule (ODS). At the time of the examination, it has clearly shown vision problem. His pupils are responding very slowly to light. Anterior segment of both eyes was found normal. Amsler's Charting (Fig. 1) perform for Central scotoma and early evidence of drug toxicity specially AKT4 but no significant abnormality was found in favor of drug toxicity except Linezolid. Bjerrum's Central Visual Fields examination (Fig. 2) shows no Pre, Intra, Post chiasmal neurological field defect noticed and also no significant enlargement of blind spots or Centro paracentral scotoma noticed. On the measurement of blood pressure found normal suggests that possible side effect is not supposed to happen due to elevated blood pressure which is also a possible cause due to malignant hypertension. Therefore, the identification of drug-induced toxic optic neuropathy side effects was occurred due to Linezolid, After Linezolid was discontinued, the patient also started taking Tab. Prednisolone 10 mg and Ketoflox eye drop 5 ml, twice a day and Tab. Neurokind for one week, showing almost immediate improvement in Vision. After the one-week follow-up, his vision improved a little more. Discontinuing Linezolid without changing other drugs confirmed the diagnosis of toxic optic neuropathy occurs due to long-term use of Linezolid in XDR-TB. During the next follow-up his vision and perception of colors improved, three months after stopping the drug, his binocular vision was noted maximum and his color vision was also normal. This was confirmed by visual field tests; however, these results were found unbelievable as the person is very young.

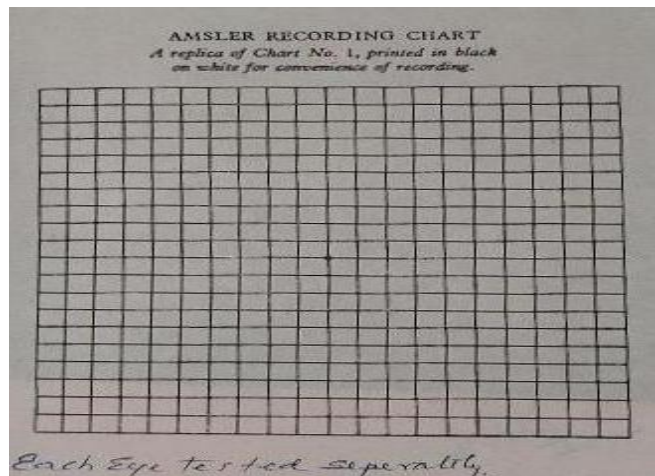


Fig. 1. Amsler recording chart

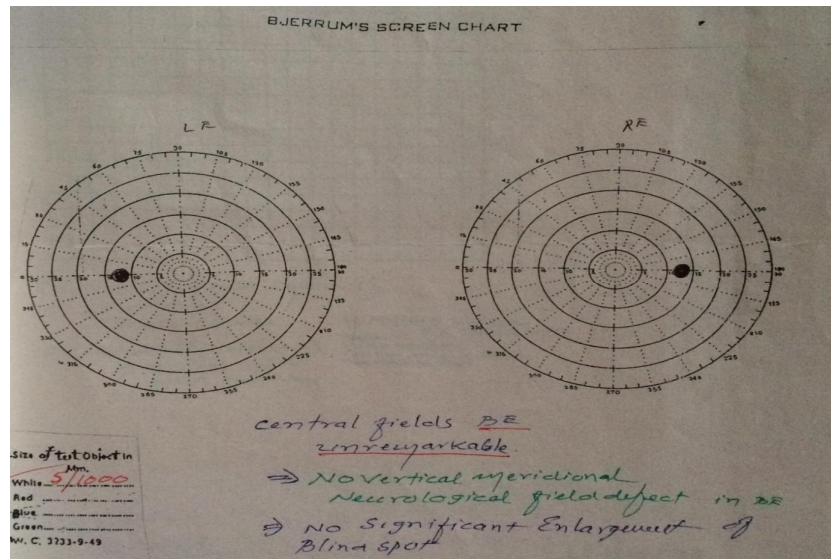


Fig. 2. Bjerrum's screen chart

### 3. DISCUSSION

Linezolid, an Oxidazolidine group drug has been widely used for many years; it has treated methicillin-resistant *Staphylococcus aureus* (MRSA) infections, penicillin-resistant streptococcal infections, vancomycin-resistant enterococcal infections, and mycobacterium infections. [6] Use of Linezolid caused optic neuropathy and peripheral neuropathy if treated for more than 1 month. [7] If the Linezolid prescription lasts longer, side effects such as lactic acidosis, bone marrow suppression, and serotonin syndrome will also be reported, but special attention is also required in drug-resistant infections. Linezolid acts primarily on bacterial ribosomal subunits and inhibits protein synthesis by binding to ribosomal RNA. The toxicity caused by Linezolid is assumed to be drug-related mitochondrial optic neuropathy (MON) because bacterial ribosomes are similar to protein synthesis and mitochondrial ribosomes are destroyed. [8] Linezolid causes optic nerve damage by interfering with mitochondrial oxidative Phosphorylation. It is required for papillary macular fibers associated with drug-related mitochondrial optic neuropathy. Here energy produces during conduction by oxidative Phosphorylation in Mitochondria. This leads to reversal of the damage when functional impairment occurs without loss of axons. Most of the patients with optic nerve damage can significantly improve when the Linezolid is withdrawn. Azamfieri et al. [9] reported one patient who suffered from muscular dystrophy

have reported complete blindness by taking Linezolid for 16 days in MRSA. Joshi et al. [10] have also reported optic neuropathy in acute lymphocytic leukemia patients who starting Linezolid Treatment for 16 days. Jahaveri et al. [11] also reported a 6-year-old child suffering from MRSA Osteomyelitis to whom Linezolid prescribed for one year has shown toxic optic neuropathy. which was similar to our patient. Similarly, A 7-year-old boy who took Linezolid for 7 months observed the side effects of optic neuropathy on cervical lymphadenitis. [12] The patient was infected with *Mycobacterium nonchromogenicum* and developed vision problems due to bilateral disc edema. After Linezolid was discontinued, the visibility of the patient's right eye improved, but the patient's left eye developed a pale optic disc and suffered permanent visual impairment. [13] Han et al. [14] it was reported that an adult patient had no clinically significant disc edema, but found optic neuropathy in MDR-TB patient Visual acuity and improvement in color vision drastically by omitting Linezolid. Karuppanasamy et al reported one male patient of 45 age cause optic neuropathy who taking Linezolid along with Ethambutol in the treatment of XDR-TB similar to our patient, but our patient is resistant to Ethambutol and has therefore not taken Ethambutol. [15] Withdrawal from Ethambutol showed no improvement in vision. However, after stopping the Linezolid, the disc edema was completely treated and vision improved completely after a month, while our patient's vision took a slight improvement within 15 days,

for his vision to completely improve. Our case is the report of a middle-aged case in therapy for XDR-TB, which had such severe side effects, Dose- and duration-dependent toxic effects of Linezolid induce optic Neuropathy in prolonged treatment and complete inversion on drug discontinuation confirmed drug-induced optic neuropathy in our patient.

#### 4. CONCLUSION

XDR-TB is a very serious disease with high mortality and morbidity in India and Asian countries. There are very few drugs that are effective XDR-TB. A serious side effect that occurs in therapy with one of the most important effective drugs such as Linezolid jeopardizes the entire treatment regimen, as in our case, therefore close observation of the patient being treated with Linezolid is necessary because of its side effects, especially in diseases such as Multi-Drug-Resistant (MDR) and XDR-TB, which are constantly increasing in our country. A routine ophthalmological examination is strongly recommended for all patients taking Linezolid for more than 3 months for the safety of the patient.

#### CONSENT

As per international standard or university standard, patient's consent has been collected and preserved by the authors.

#### ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

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#### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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