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Cycloserine-Induced Psychosis in Multidrug-Resistant Tuberculosis (MDR-TB) in Young Male Patient: A Case Report

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Abstract: ***The genre of tuberculosis (TB) dubbed multidrug-resistant tuberculosis (MDR-TB) is resistant to at least two of the most potent first-line anti-TB medications, isoniazid (H) and rifampicin (R). Cycloserine is placed by the World Health Organization as a group four second line anti-tubercular medication for the treatment of MDR-TB. Psychosis, depression, and neuropathy have been linked to neuropsychiatric toxicity, which is caused by cycloserine or its structural equivalent terizidone. After receiving an MDR-TB diagnosis, a 32-year-old male patient received customized treatment regimens including bedaquiline, linezolid, levofloxacin, and Cs. The patient experienced psychosis with agitated behaviour, excessive talking, yelling episodes, fearfulness, photophobia, drowsiness, paranoid thoughts, and headaches multiple times after taking anti-TB medications for 54 days. He was prescribed clonazepam, olanzapine, and lorazepam. Over time, the patient recovered progressively. When giving cycloserine, extreme caution should be used along with frequent and close monitoring, as mental adverse medication reactions may increase the risk of poor drug adherence in patients with drug-resistant tuberculosis.***
Keywords: Drug Resistance Tuberculosis, Cycloserine, Psychosis, Adverse Drug Reaction, Fluroquinolones, Photophobia.

I. INTRODUCTION

Mycobacterium tuberculosis is the causative agent of tuberculosis, which is mainly spread by airborne droplets from an infected individual (1). Although extra pulmonary tuberculosis can also damage the spine and brain, tuberculosis primarily affects the lung (2). The cornerstone of tuberculosis treatment is ant tuberculosis medication, specifically isoniazid, rifampicin, ethambutol, and pyrazinamide as first-line therapies (3). Anti-TB medication side effects can be broken down into two different kinds: severe and mild (4). TB that is resistant to at least isoniazid (H) and rifampicin (R), the two most potent medications, is known as multidrug-resistant tuberculosis (MDR-TB) (5). The outcomes of a sensitivity test, which attempts to figure out if Mycobacterium tuberculosis (M. tb) has or has not been resistant to anti-TB medications, are used to confirm the diagnosis of multidrug-resistant tuberculosis (MDR-TB). The course of MDR-TB treatment consists of 18 to 24 months of minimum medication use (6).

For extended multidrug-resistant tuberculosis (MDR-TB) treatment regimens, the World Health Organization (WHO) listed terizidone or cycloserine as a group B medication (WHO, 2019) (7). The compound known as cycloserine, or D-4-amino-3-isoxazolidinone, first emerged and fabricated by Hidy et al. (8)(Hidy et al., 1955). Treatment of tuberculosis-resistant patients: Evidence-based guidelines and international medical societies have considered several treatment alternatives (9), such as the use of robustly effective extended-spectrum antibiotics such cycloserine (10). By competitively inhibiting two crucial enzymes involved in the formation of Mycobacterium tuberculosis's cell wall, CS demonstrates its antibiotic properties (11). But because cycloserine (CS) may cross the blood–brain barrier, inhibit GABA-transferase, and interact with N-methyl-d-aspartate (NMDA) receptors in the central nervous system, it also appears to be correlated with the onset of psychotic symptoms (12).

Cycloserine, or its structural analogue terizidone, has been associated with neuropsychiatric toxicity (psychosis, depression, and neuropathy) (13). Studies reporting the effect of cycloserine concentrations on both microbial kill and resistance suppression have recently been published, including penetration of the drug into TB cavities and resistance arising therein (14, 15)(Deshpande et al., 2018; Dheda et al.,2018). This case report is noteworthy because it illustrates the psychological adverse effects from various anti tuberculosis medications.

II. CASE PRESENTATION

A 32-year-old male patient presented to Pulmonary medicine ward with chief complaints of acute fever for 1 week, patient experienced productive non-blood-stained cough but not able to expectorate for 4 days, vertigo, Psychosis with the symptoms of agitated behaviour, overtalktiveness, shouting spells, fearfulness, photophobia, drowsiness, paranoid ideas and headache.

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Patient also experienced shortness of breath for 4 days was admitted in MDR department. Past medical history of patient was diagnosed to have multidrug resistance tuberculosis (MDR-TB), patient resistance too both rifampicin and Isoniazid.
Patient was advised for CX-R, ABG, ECG, CBC, LFT, KFT, PT/INR, D-dimer. Urine analysis R/E Followed by serum sodium, potassium and magnesium levels. Patient was primarily stabilized with antipsychotics, antidepressants and benzodiazepines for psychosis. His blood test at presentation illustrated as:

Table1: Complete blood count and comprehensive metabolic panel.

Complete blood count	Comprehensive metabolic panel
Haemoglobin: 13gm/dl (13-17)	Sodium: 136mmol/L (137-145)
Platelets: 259000/uL (150000-400000)	Potassium: 3.9mmol/L (3.5-5.1)
Differential leucocyte count (DLC) Neutrophils: 71.9% (44-68) Lymphocytes:19.9% (25-48) Eosinophil:0.9% (1-0.6)	Magnesium: 2.0 mmol/L (1.6-2.3)
PCV: 37.7% (40-50)	Serum Bilirubin direct: 0.5mg/dl (0-0)
	Serum globulin: 3.70gm/dl (2.30-3.59)
	Serum Creatinine: 0.5mg/dl (0.8-1.5)
	Serum Uric acid: 3.2mg/dl (3.5-8.5)

Anti HCV, HBsAg test was negative, prothrombin time, and international normalized ratio and urine examination(R/E) were normal.

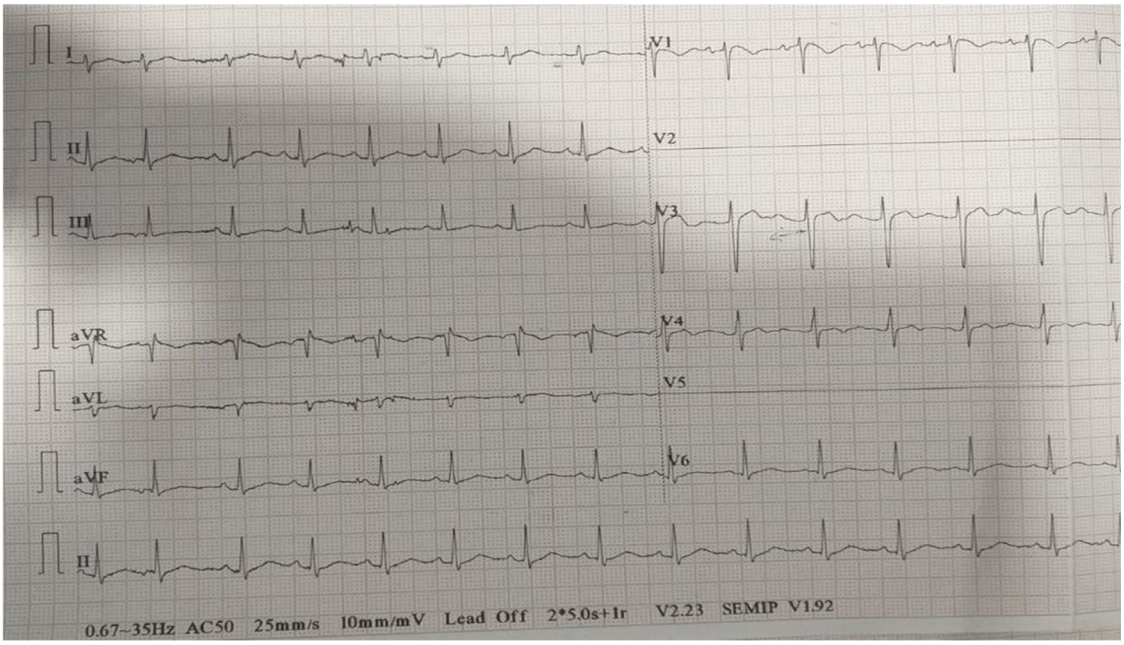


Figure 1: - ECG illustrates prolonged QT Intervals.

Table 2: - Patient Arterial Blood Gas analysis

Components	11/09/2024	12/09/2024	Normal Range
pH	7.40	7.40	7.35-7.45
PCo_2	33	31	35-45 mmHg
PO_2	88	100	60-100 mmHg
HCO_3^-	20.4	20.1	22-26 mmol/L
Hct	41	53	40-54%
SO_2c	97	98	95-100%

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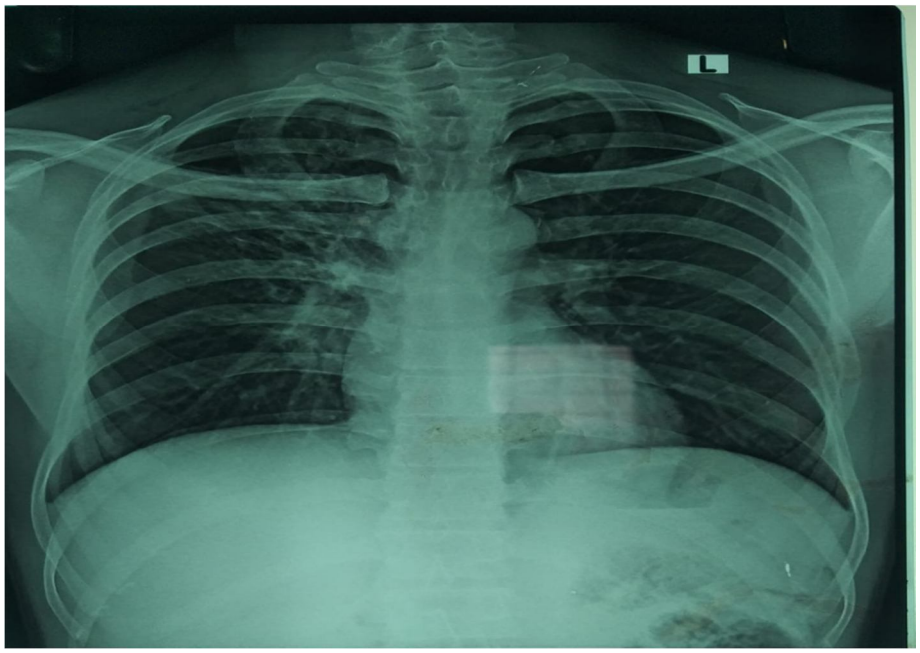


Figure 2: - Chest X-ray of patient (Bilateral prominent markings with hyper inflated lungs)

Patient was treated with suitable medications as mentioned below. The care taker were counselled about the MDR-TB therapy side effects, patient diet and patients was discharge.

Table 3: Medication Treatment Chart

Medication	Dose	Route	Frequency
Tab. VMS MAX	1 tab.	Oral	OD
Tab. BEDAQUILLINE	2x100 MG	Oral	On alternate days
Tab. CYCLOSERINE	3x250 MG	Oral	OD
Tab. LINEZOLID	600 MG	Oral	OD
Tab. LCIN	750 MG	Oral	OD
Tab. DELAMANID	2x500 MG	Oral	BD
Tab. PYRIDOXINE	100 MG	Oral	HS
Tab. ACILOC	300 MG	Oral	OD
Ensure protein	2 TSF	Oral	TDS with half glass of water
Tab. OLIMELT	5 MG	Oral	BD
Inj. LOPEZ	2 MG	IM	SOS
Tab. CLONOTRIL	0.25 MG	Oral	BD

III. DISCUSSION AND CONCLUSION

MDR-TB management might occasionally be challenging. While therapy for MDR-TB with an individual regimen requires at least five medications and lasts 18 to 24 months, treatment for sensitive TB only requires four drugs and takes six to nine months. Many medications have serious negative effects when used. Streptococcus orchidaceous produces the broad-spectrum antibiotic cyclorine. In 1995, it was initially extracted from a fermentation brew and then synthesised. Currently, when main medicines fail to cure pulmonary or extra pulmonary TB, cycloserine is used in combination with other tuberclostatic medications. The patient was started on cycloserine due to resistance. Although our patient was on multiple potentially psychotic ant tubercular medications, he had no family or personal history of mental health issues. When antipsychotic medications were stopped and CS was stopped, the majority of documented individuals showed improvement in their ability to treat CS-induced psychosis. This feature varies based on accounts in the literature because a retrospective study demonstrates that most patients' psychosis improves when the dosage of CS is decreased or temporarily stopped. Nonetheless, the findings of both trials concur that lowering CS exposure and giving antipsychotics lessens the likelihood that CS-induced psychotic symptoms will manifest.

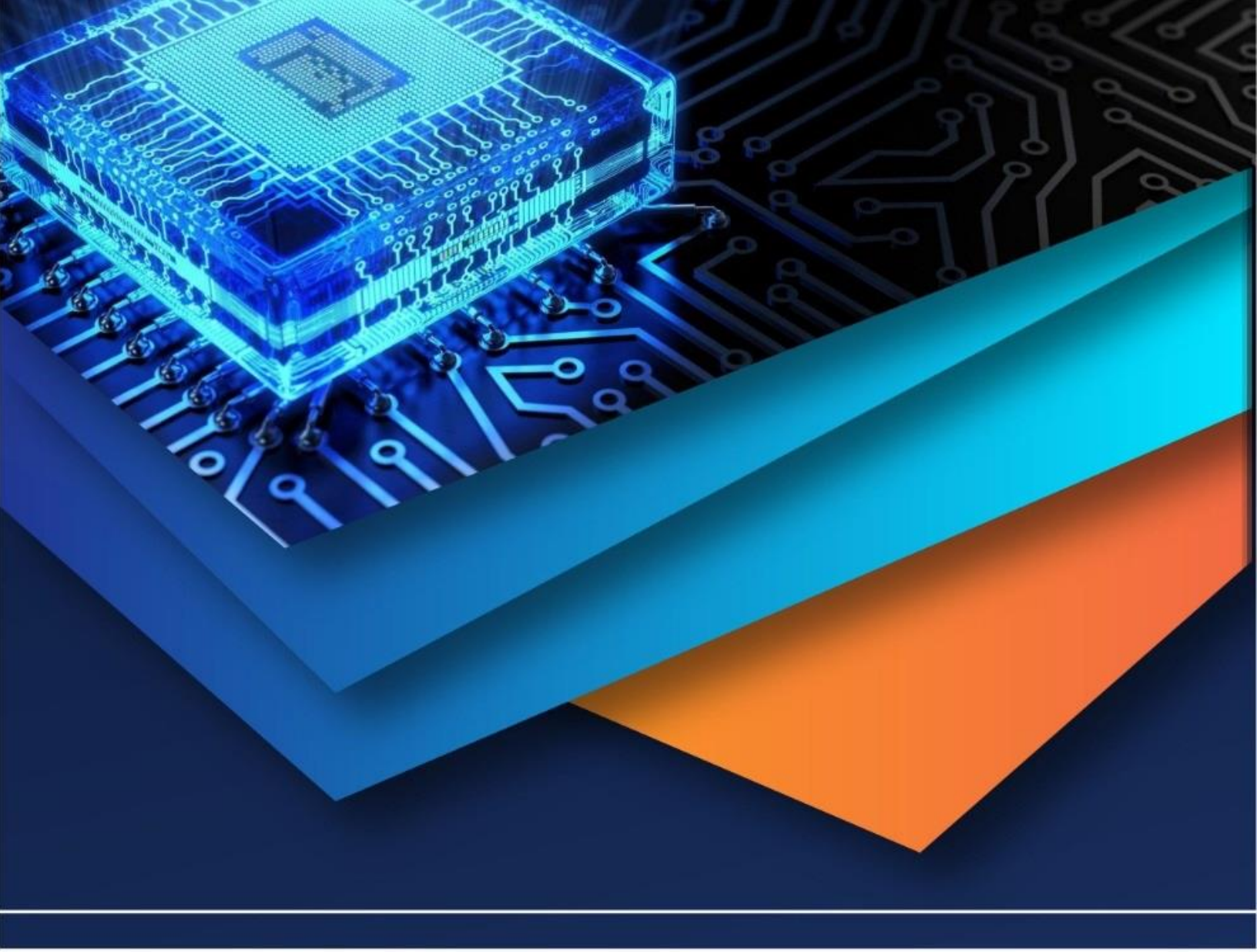
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Initially, 250mg 12hrly for the first 2 weeks, followed by 500-1000mg daily in equally divided doses. Adjust dose based on blood concentration and response. Max. 1000mg daily. There were some contraindication with CS: Hypersensitivity, Epilepsy, mental depression, severe anxiety, psychosis, alcohol abuse or alcoholism and some sever renal impairment. There was some special precaution taken with CS, patient with porphyria, history of chronic alcoholism, potential vit. B_{12} or folate deficiency. Patient receiving >500mg daily dose have mild to moderate renal impairment. Monitoring parameters initial to CS therapy: perform culture and susceptibility tests, renal, hepatic and haematological functions periodically. Evaluate neuropsychiatric status every month or more frequently if symptoms occur (Disorientated with loss of memory, paraesthesia, dizziness, coma, personality changes, hyperirritability, aggression).[1]

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