IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 21, Issue 1 Ser.9 (January. 2022), PP 26-28
www.iosrjournals.org

Drug-induced Peripheral Neuropathy in MDR TB Patient

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Date of Submission: 03-01-2022 Date of Acceptance: 14-01-2022

I. Introduction

World Health Organization (WHO) estimated 1,24,000 Multi-drug resistant Tuberculosis (MDR TB) cases in India in the year 2020.[1]Treatment of MDR TB is more challenging than the drug-sensitive TB because of requirement to take more toxic multidrug regimens for longer duration of timeswith the higher rates of adverse drug reactions and lower cure rates.[2]Peripheral neuropathy (PN)has been reported in MDR TB patients with varying rates in different studies, ranging from 13% to29%.[3,4]PNis a condition wherethe peripheral nerves gets affected, compromising the relay of information. In TB, PN can occur because of the anti-tubercular drugs, the associated co-morbidities or the disease itself. This case report includes the difficulties faced in the management of amiddle-aged female with MDR TB complicated by PN.

II. Case Report

A 45-years old female patient was referred to our nodal TB center for initiation of treatment after being diagnosed to be MDR TB on geneXpert. She complained of cough, myalgia, anorexia and weight-loss for last one month. She did not give any previous history suggestive of TB, Hypertension, Diabetes or any other chronic disease. She underwent pre-treatment evaluation, including blood tests (**Table 1**), ECG, Audiogram and Ophthalmic examination; which were found normal. Her Line Probe Assay (LPA) report was awaited, but as she had no prior history of ATT intake, she was started on shorter drug regimen (Moxifloxacin, Kanamycin, Ethionamide, Clofazimine, Pyrazinamide, Isoniazid and Ethambutol along with Pyridoxine 100 mg daily). Except for mild nausea, she tolerated the medications well and took the same for around 20 days, when her LPA report was received that showed an additional resistance to second-line injectables. Now she was shifted to all oral longer regimen including Bedaquiline, Levofloxacin, Linezolid, Clofazimine and Cycloserinealongwith Pyridoxine. She was monitored for 2 weeks and discharged with these drugs after 14 days as she tolerated the medications well. In the follow-up visit after one month, she complained of mild numbness inbilateral feet.The severity was assessed using subjective PN scale,[5]**(Fig. 1)**and she was graded to have mild PN on the severity scale. The other follow-up tests were normal. Dose of Pyridoxine was increased to 200 mg daily and she was given Paracetamol on SOS basis. She was reviewed every week. Her symptoms remained persistent but did not worseneither for 5 to 6 visits. At the end of 5th month, PN worsened to moderate on the severity scale and she had to be admitted for close monitoring. Also, her 4thmonth culture was positive for TB bacilli. She was started on Pregabalin 150 mg daily with NSAIDS, Pyridoxineas well as the physical therapy. Progression of PN decreased but symptoms persisted and meanwhile amitryptiline had to be added. After two weeks of this therapy when the symptoms were not decreasing, the dosages of the linezolid and levofloxacin were reduced to half. Also the 5th month sputum culture came negative. After one week with reduced doses, linezolid was stopped and levofloxacin continued with half dose. Also, bedaquiline was continued beyond 6 months till 6th month sputum culture came negative. Patient alleviated of her symptoms gradually over 2 months. Levofloxacin was gradually increased to full dose; and amitryptiline, pregabalin and NSAIDs were stopped sequentially; linezolid was not restarted. Patient is clinic-radiologically and microbiologically improved and will complete her treatment in 2 months.

Table 1. Blood Investigations of the patient

Parameter	***Baseline***	***At 3rd Month***	***At 9th Month***
Hemoglobin (g/dL)	11.6	8.2	10.8
Platelet counts (cells/µL)	395000	187000	357000
Total leucocyte counts (µL)	7680	3810	8550
Blood urea nitrogen (mg/dL)	18.5	12.0	15.0
Serum creatinine (mg/dL)	0.6	1.03	0.5
Total bilirubin (mg/dL)	0.40	0.45	0.60
ALT (U/L)	18	13	24
AST (U/L)	24	28	36
ALP (U/L)	55	66	58

Figure. 1: Subjective Peripheral Neuropathy Scale

ALWAYS BEEN NORMAL	CURRENTLY ABSENT	MILD ←→ SEVERE
11	00	01-10

Symptoms	R	L
a. Pain, aching, or burning in feet, legs		
b. "Pins and needles" in feet, legs		
c. Numbness (lack of feeling) in feet, legs		

Use the single highest severity score from Question 1 above to obtain a subjective sensory neuropathy score. If all severity scores are "00" or "11," the subjective sensory neuropathy score will equal "0."

Subjective Sensory Neuropathy Score (based on highest severity rating)

01 - 03 = grade of 1
04 - 06 = grade of 2
07 - 10 = grade of 3
11 or 00 = grade of 4

R	L

III. Discussion and Conclusion

Community-based anti-tubercular treatment is an attractive and a feasible approach for resource-constrained countries,[6] but adverse drug reactions are the major obstacle for the same.

Although, PN is one of the most common adverse reactions faced in the TB patients, little is known about its exact prevalence, etiology and management protocol in the TB patients, which warrants large-scale studies in future. During the management of PN, all possible etiologies should be targeted altogether, that includes treating the co-morbidities, modification of drug doses or the regimen and addition of therapy for neuropathy.Other studies have reported improvement in PN after discontinuing offending agent, but this have been mostly reported with first-line TB drugs.[7, 8]Stopping or modifying the drugs in MDR TB case remains a difficult decision, especially when there are additional resistances making it Pre-XDR or XDR, like in our patient. We stopped the Linezolid only when one sputum culture report was negative and extended bedaquiline duration till the time second negative culture report was received. Also, expected clinic-radiological improvement was seen in our case. Replacement of the drug can be done if a patient shows severe adverse reaction with a drug at a time when there is no significant clinic-radiological or microbiological improvement of the primary disease of TB.

A previous study,[4] showed no significance of dose (Linezolid ≥600mg vs ≤600mg) among TB patients with severe PN. When linezolid is used for longer durations, it can affect mitochondrial DNA, affecting protein synthesis, leading to respiratory chain dysfunction. PN mostly starts from lower limbs, with symptoms of pain, tingling or burning sensation, numbness and allodynia. Also, linezolid is known to cause hematologic

abnormalities and optic neuritis. In this case, only asymptomatic transient pancytopenia was present that did not require any treatment. The discordance of neurologic and hematolgic adverse effects have been reported previously.[9, 10]

Addition of drugs for neuropathy can interact with the MDRTB drugs and pose a risk of other adverse reactions. Adding drugs like amitryptiline with bedaquiline and linezolid warrants hospitalization and close monitoring. In our case, patient did not show any additional complication due to drug-interactions.

In conclusion, close monitoring should be done for adverse drug reactions while treating MDR TB patients. The aim should be to avoid the potential adverse reactions and when present, should be treated at the earliest without compromising with the treatment part and cure-rate of MDR TB. In this case, patient was improved of PN after discontinuing linezolid and it did not affect the overall improvement in TB also.

References

[1]. WHO. Global Tuberculosis Report 2020

[2]. Farmer P E, Furin J J, Shin S S. The clinical management of multidrug-resistant tuberculosis. J Respir Dis 2000; 21: 53–56

[3]. FurinJJ,MitnickCD,ShinSS,BayonaJ,BecerraMC,SinglerJM,AlcantaraF,CastaniedaC,SanchezE,AchaJ,FarmerPE,KimJY.Occurrenceofseriousadverseeffectsinpatientsreceivingcommunity-basedtherapyformultidrug-resistanttuberculosis.IntJTuberculLungDisease2001;**5**(7):648–55.

[4]. Agyeman AA, Ofori-Asenso R. Efficacy and safety profile of linezolid in multidrug-resistant and extensively drug-resistant tuberculosis: a systematicreview and meta analysis. Ann ClinMicobiolAntimicrob. 2016;15:41.

[5]. SimpsonDM,KitchD,EvansSR,McArthurJC,AsmuthDM,CohenB,GoodkinK,GerschensonM,SoY,MarraCM,Diaz-ArrastiaR,ShriverS,MillarL,CliffordDB.HIVneuropathynaturalhistorycohortstudy:assessmentmeasuresandrisk factors.Neurology2006;**66**:1679–87.

[6]. Farmer P E, Bayona J, Shin S, et al. Preliminary results of community-based MDR-TB treatment in Lima, Peru. Int J TubercLung Dis 1998; 2 (Suppl 2): S371.

[7]. Gohel D, Oza J J, Panicker M G. Pyridoxine and isonex. J AssocPhysicians India 1993; 41: 229.

[8]. Aoun M, Jacquy C, Debusscher L, et al. Peripheral neuropathyassociated with fluoroquinolones. Lancet 1992; 340:

[9]. Nambiar S, Rellosa N et al. Linezolid induced peripheral and optic neuropathy in children. Pediatrics. 2011 Jun; 127 (6): e: 1528–32

[10]. Park IN, Hong SB, et al. Efficacy and tolerability of daily half dose linezolid in patients with intractable multidrug-resistant tuberculosis. J AntimicrobChemother. 2006;58:701–4. 14.

Bardhan M, et. al. "Drug induced peripheral neuropathy in MDR TB patient." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), 21(01), 2022, pp. 26-28.