Successful Novel drug regimen for pre-xtensively drug resistant (pre-XDR) pulmonary tuberculosis- A Case report

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Abstract— Multidrug-resistant tuberculosis (MDR-TB) and xtensively drug resistant pulmonary tuberculosis (XDR-TB) both are difficult to treat and have become a significant public health problems. We report a twenty two year old girl with pre xtensively drug resistant pulmonary tuberculosis diagnosed by phenotypic drug susceptibility testing with MGIT culture method. We started treatment with kanamycin, linezolid,co- amoxiclav, high dose isoniazid, terezidone, ethambutol& Q-pas for 24 months in which kanamycin was given for first six months .Her subsequently sputum smear for acid fast bacilli and cultures were negative .We describe the first case of successful treatment of pre-xDR-TB with this novel regimen

Index Terms— Drug resistant, PreXDR , MDR, XDR, Tuberculosis, MGIT culture, Drug susceptibilty

1 INTRODUCTION

The World Health Organization estimates a Multi-Drug Resistant (MDR)-TB prevalence rate of 3.3% and 20% among New and Retreatment TB patients respectively in the country.(1) Multi-drug resistance (MDR) TB is defined as tuberculosis disease caused by a strain of M. tuberculosis that was resistant to at least isoniazid and rifampin.(2) Extensively resistant drug resistant (XDR) is defined as TB with resistance to at least isoniazid and rifampin plus a fluoroquinolone (e.g. moxifloxacin, ofloxacin, levofloxacin, sparfloxacin, gatifloxacin, ciprofloxacin) and one of three injectable second-line drugs (capreomycin, kanamycin, and amikacin).(3)Pre- extensively resistant drug resistant (Pre- XDR) is defined as disease caused by a TB strain resistant to isoniazid and rifampin and either a fluoroquinolone or a second-line injectable drug, but not both (World Health Organization 2008).(4) In absence of a standardized regimen, treatment need to be individualized.

2 CASE HISTORY

A twenty two year old Asian female presented to outpatient department with chief complaints of intermittent fever for last four years which was low grade with evening rise of temperature.

There was also history of cough with expectoration for last one year but no history of hemoptysis. Significant weight loss was also present for last four years. There was no history of contact with tuberculosis and neither was family history significant. But she was being treated empirically with first line antitubercular therapy intermittently for last 2years.Her vitals were stable without any significant lymphadenopathy .Her look was cachexic. On auscultation, crepitations were evident in left infrascapular region. Radiology of Lung was suggestive of left lower zone consolidation (Figure 1). Bacteriological examination sputum for AFB direct smear for three days were negative. However drugs, the phenotypic culture in Liquid media (MGIT-90) was positive for M.tuberculosis. Subsequent drug susceptibility revealed resistance to first line agents - isoniazid, rifampicin, pyrazinamide, ethambutol as well as second line drugs- ethionamide & ofloxacin. Since the patient was susceptible to kanamycin , amikacin ,streptomycin & PAS (para-amino salicylic acid) – a diagnosis of pre-XDR TB was entertained instead of XDR-TB. We commenced her on a novel 7 drug regimen as per weight for 24 month with an intensive

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phase of six months.(Table1)

Her initial sputum culture at 3rd month was negative for M.Tuberculosis. Following, the initial positive results we decided to continue the therapy as planned. 6th & 9th month sputum results were also favorable. Patient had improvement in her clinical symptoms like fever ,cough, and her weight also recovered in continuation phase .Her subsequent cultures at 15th,18th & 22th month were negative (Table 2). So, finally treatment was stopped at 24 months. During the course of treatment radiological improvement was also evident (Figure 2).

3 DISCUSSION

This case highlights the potential gray zone between MDR-TB and XDR-TB defined as pre-XDR-TB. Progression from MDR TB to XDR TB is facilitated by difficulties in prompt diagnosis and effectively treatment of cases due to lack of early availability of rapid susceptibility testing information.

Pre XDR TB terminology is not well defined and no universal treatment regimen exists for it. Fluoroquinolone resistant is very common in India because of widespread & irrational use of the drug for treatment of pyrexia of unknown origin and respiratory tract infections. MDR-TB and XDR-TB are of global concern due to associated high morbidity and mortality.(5)

Rapid identification of drug susceptibilities is vitally important in cases of MDR-TB and XDR-TB.(6) Expanding access to culture and DST services for all smear-positive previously treated patients could be an efficient strategy to detect MDR-TB, initiate early treatment and prevent further transmission.(7) So baseline culture and drug sensitivity testing is required in all previously treated symptomatic cases and should be treated accordingly drug susceptibility profile.

4 CONCLUSION

Pre XDR is emerging as a challenge in management of tuberculosis .In absence of clearcut guidelines indivisualised treatment regimens may be needed. Sputum microbial Culture and drug susceptibility testing are remain integral part for management of such cases.

ACKNOWLEDGMENT

The authors wish to thank Dr. A.K.Pradhan, MD, Department of Cardiology, King George's Medical University for persistent support and encouragenment.

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Figure 1. Chest x-ray at diagnosis showing Left lower zone consolidation.

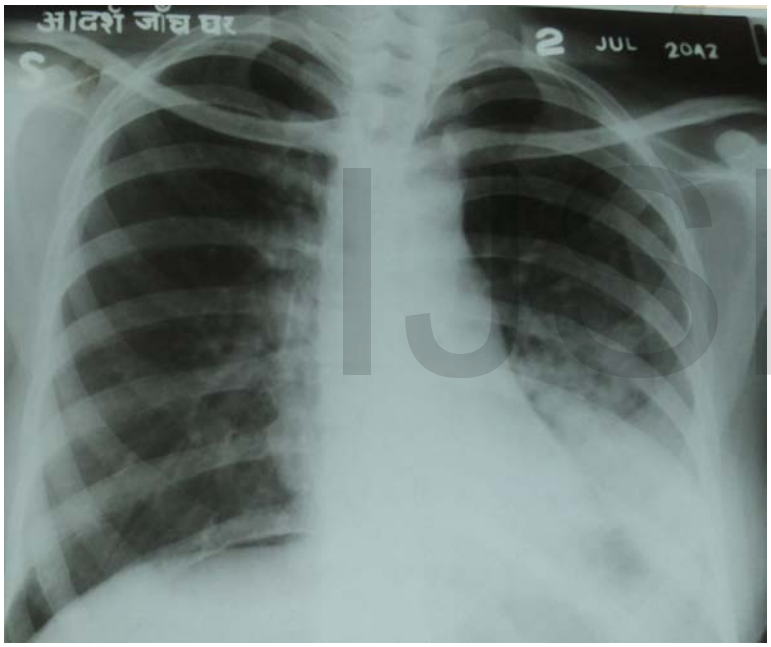

Figure 2. Chest x-ray at 24 months showing radiological improvement

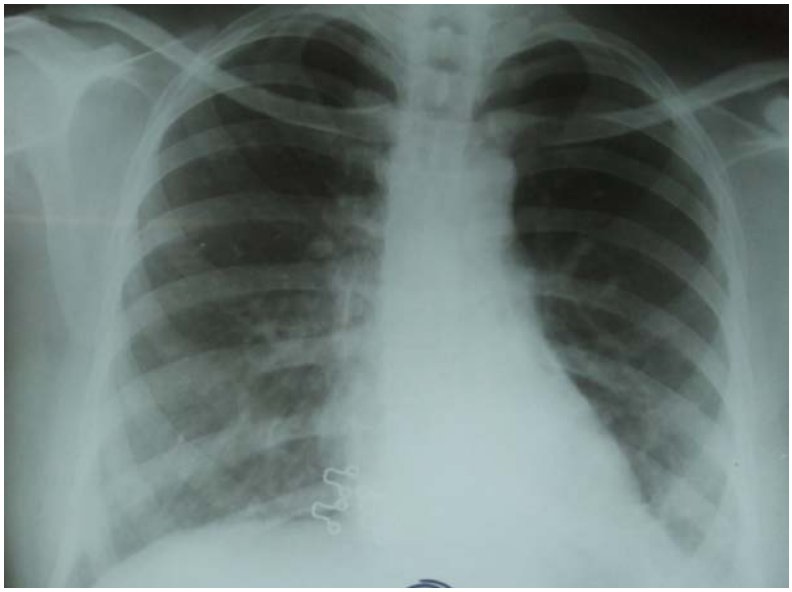

Table 1. Drug dosing and schedule of the Novel regimen used

	Drug	**Dose**	**Duration**
1.	Kanamycin	0.75 gm, I/M ,once daily	6 months
2.	Linezolid	600 mg , per oral once daily	24 months
3.	Co amoxyclav	1gm , per oral, once daily	24 months
4.	Isoniazide High Dose	600mg , once daily	24 months
5.	Terizidone	250 mg , 2 tablets once daily	24 months
6.	Q-PAS	8gm once daily	24 months
7.	ethambutol	600 mg daily	24 months

Table 2. Sequential Bacteriological Examination Results

Serial no	Month	Sputum smear	Culture
1	3rd month	negative	negative
2	6th month	negative	negative
3	9th month	negative	negative
4	15thmonth	negative	negative
5	18thmonth	negative	negative
6	22ndmonth	negative	negative
7	24thmonth	negative	negative