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A Case Study of Drug Resistance Extra Pulmonary TB and HIV: A Deadly Syndemic with Co morbidity of Diabetes and COVID-19

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Introduction

Tuberculosis (TB) remains the top infectious killer, ranking above HIV/AIDS, with 10.0 million cases and 1.4 million deaths in 2018[1]. Tuberculosis [TB] has been a major cause of suffering and death since times immemorial. Thought to be one of the oldest human diseases, the history of TB is at least as old as the mankind. Over the years, not only the medical implications but also the social and economic impact of TB has been enormous.[2]

1882 Sir Robert Koch announced the discovery of the tubercle bacillus during the monthly evening meeting of the Berlin Physiological Society. In 1905, he was awarded the Nobel Prize for his contributions in the field of TB research[3]. In 1982, a century after Dr Koch's announcement, the World Health Organization [WHO] and the International Union Against Tuberculosis and Lung Disease [IUATLD], now called The Union proposed the 24th March as the "World TB Day" as a part of a year-long centennial effort under the theme "Defeat TB: Now and Forever." Thereafter, since 1996, 24th March is celebrated as "World TB Day" every year[2].

Mycobacterium tuberculosis (MTB), the causative agent, usually affects the lungs (pulmonary TB/PTB). However, MTB may spread through lymphatic or hematogenous routes to virtually any organ in the body, resulting in extrapulmonary TB (EPTB). The most common sites of EPTB infection include peripheral lymph nodes, pleura, genitourinary sites, bones and joints, abdomen (peritoneum and gastrointestinal tract), and the central nervous system.[1]

Extrapulmonary drug-resistant tuberculosis (DR-EPTB) poses a formidable diagnostic and therapeutic challenge. Besides associated with high morbidity, it is a major financial burden for the patient and the health system. EPTB is often less contagious than PTB, and is therefore overlooked even though it constitutes about 15% of all forms of TB, amounting to nearly 1 million incident cases notified in 2018, as per the WHO Global TB report[4] The World Health Organization (WHO) has reported a 52% cure rate which is much lower than that for drug-sensitive

TB (DSTB).[5] Rifampicin-resistant TB (RR-TB) is defined as the cases of TB resistant to at least rifampicin. RR-TB consists of the major DR-TB cases and both the terminologies are used interchangeably. 78% of RR-TB is Multi Drug Resistant (MDR)

In the present era of HIV pandemic coupled with global emergence of multidrug-resistant TB(MDR TB) and extensively drug-resistant TB (XDRTB), drug-resistant EPTB (DR-EPTB) presents a real and new public health challenge that has yet to receive serious attention. While drug resistance in PTB has been extensively studied, DR-EPTB has been neglected.

Previous studies in four large states of India also reported poor overall treatment outcomes (40%– 56%) among DR-TB patients, with high rates of death and lost-to-follow-up (LTFU)[6]. India aims to eliminate TB by 2025; however, this goal will remain unachieved if EPTB, especially the drug-resistant cases, continues to be ignored[7].

In 2019, global diabetes (DM) prevalence was 463 million. Diabetes increases the risk of TB and adverse treatment outcomes including death and relapse. Diabetes also increases the risk of severe disease, multi-organ failure, coagulopathy and death in COVID-19. TB and COVID-19 share many features, suggesting opportunities to integrate prevention, diagnosis and care.[8] The risk of acquiring TB in a patient with DM is 4.8% compared to 0.8% in general population[9]

Bashar et al[10] have shown that multidrug-resistant TB was more common [36% vs 10%] in patients with DM compared with those without DM[10]. DM patients have also been found to have a higher baseline mycobacterial burden; longer time for sputum conversion and higher treatment failure and relapse rate[10-11]. Mortality is higher in DM patients with TB probably because of increased severity of TB or co-existing co-morbid conditions.

Patients with poorly controlled DM are more prone to be affected by TB. It has been shown in large studies[12] that DM is a moderate to strong risk for development of TB.

TB/COVID -Tuberculosis deaths rise for the first time in more than a decade due to the COVID-19 pandemic. The COVID-19 pandemic has reversed years of global progress in tackling tuberculosis and for the first time in over a decade, TB deaths have increased, according to the World Health Organization's 2021 Global TB report. In 2020, more people died from TB, with far fewer people being diagnosed and treated or provided with TB preventive treatment compared with 2019, and overall spending on essential TB services falling.[13]

Case Study

52 years male patients staying in Mumbai, unmarried, unemployed. Patient was on Anti-TB treatment Cat-1, diagnosed on chest x-ray showing infiltration in both apices. Patient was found to be having distended Abdomen, and Ascitic fluid was removed under CT guidance, and found to be Rifampicin Resistance in Cartridge based Nucleic Acid Amplification test (CBNAAT) dated 29/02/2020 as the patient is a case of Extra Pulmonary Tuberculosis (EPTB). also, CT KUB shows right hydronephrosis with hydroureter with staghorn calculus. Patient had a history of Human Immuno- deficiency virus (HIV) positive for 6 years and he is on Anti-Retrovirus treatment (ART), also patient is a known case of Diabetes and Hypertension since 3 and 2 year respectively and he is on its medication. Patient is not having history of addiction like smoking tobacco and alcohol consumption.

Patient was referred from health post to OPD-BDQ in the first week of March, 2020. Pretreatment evaluation was done and found eligible for all oral longer regime with new drug Bedquilin. It contains CBC- Hb 12gm%, WBC-7700, Platelet-3L, dt 27/02/2020. RFT 27/02/2020 Sr.Creatinine 0.85, LFT- SGOT 63, SGPT 33, dt 29/02/2020. Thyroid Stimulating Hormone (TSH) 2.6, Urine – NAD (Nothing Abnormal Detected), Electrolyte Na-131, K- 3.6 Cl-95 with Calcium-8.9 and Magnesium 1.67. Ophthalmologist

examination was NAD to rule out optic neuritis. ECG -NAD with QTcF -395ms, Informed consent was taken and psychiatric evaluation was nil. X-ray chest PA view shows bilateral patchy infiltration in lower zone without cavitation. HIV status Reactive with CD4 count 149 (cells/ul). Patient was referred to ART center to modify the drug, which causes drug – drug interaction and it was modified.

Patient was started on all oral longer regimen with new anti-TB drug Bedaquilin with Levoflox, Linozolid, Cycloserine and Clofazamine with Pyridoxine as per Programmatic Management ofDrug Resistant TB in India (PMDT)on OPD basis with daily ECG monitoring of QTcF prolongation using Fridericia method on 18/03/2020 for 14 days with two Sunday bedaquilin was given at home without ECG monitoring, his 12 days QTcF was in the range of 395 to 437ms, Patient was sent to continue the regimen for 18 months in health post with follow up in Drug resistance Center as per guidelines.

Patient was admitted in COVID isolation ward on 4/6/2020. His RTPCR 19/6/2020 was positive for Covid 19 and repeat RTPCR was negative on 24/6/2020. Patient was discharged from isolation ward on 26/6/2020. 24/7/2020 Tingling numbness both extremities. Linozolid withhold pregabalin was started. During his regular follow-up, he was clinically examined with weight monitored and sputum culture was done, as patient was not having fluid in abdomen, so in EPTB monitoring is done clinically. Sputum for culture AFB was negative for 12th 15th 18th and 21st month. Patient was clinically stable and his vital parameters were within normal limit, Patients' Anti TB treatment was stopped.

Discussion

Extrapulmonary drug-resistant tuberculosis (DR-EPTB) poses a formidable diagnostic and therapeutic challenge. Besides associated with high morbidity and mortality, it is a major financial burden for the patient and the health system.

Drug resistance TB is a health crisis, it has hampered the path of global TB control. As compared to drug sensitive TB, morbidity and mortality is more DRTB patients. Drugs used in DRTB are more toxic, leads to more adverse drug reaction. Which results in discontinuation of drugs and increases default rate and patient losses faith in medicine. Sputum conversion is very slow, as compared to DSTB patients so the drug regimen is longer. DRTB drugs are costlier than DSTB, so it results in less affordable. Since above all condition results in increase in default rate, repeated hospitalization due to ADR, financial crunch results in economic crisis. TB stigma is still common in society and patient faces discrimination in community and at workplace, also leads to unemployment and social isolation resulting in psychological trauma and driven in poverty.

Patient is a case of HIV+, it also carries stigma like TB, as HIV is a risk factor for TB and it help for disease progression from latent to mild, and from mild to severe disease, which is 18 times more than HIV neg or general population and which can result into death also. HIV causes multiple opportunistic infection (OI) or disease, which also results severe morbidity to patient. And required treatment for OI.

The association between diabetes mellitus [DM] and TB has been recognized for centuries. The risk of getting TB in DM is 3 to 5 times more than general population. TB Co-morbid conditions like DM further complicate the outcome of disease.

Conclusion

Patient is a HIV+ with extra pulmonary DR TB, there is diagnostic and therapeutic challenge to manage such patient. Patient is also a case of Diabetes and during treatment he also suffers from COVID-19, which has killed more than 6 million people within two and half year worldwide. Every third DR-EPTB patient has unfavorable treatment outcomes, with high rates of LTFU that needs to be tackled if we want to eliminate TB, as our goal of ending TB in2025. The use of oral regimen

with new drug like Bedaquilin and Delanamid with close monitoring of the ADR and treating them, tracking of patient and closely monitoring for compliance of treatment and preventing them from LTFU and also infection control measures and Tuberculosis Preventive Treatment (TPT) will help us to achieve our goal.

Keywords: TB/HIV, EPTB, TB/DM, DRTB/EPTB/HIV, COVID/EPTB/HIV.

References

1. World Health Organization. Global Tuberculosis Report 2019 [Internet]. [Cited 8 March 2020]. Available online: https://www.who.int/tb/global-report-2019 (accessed on 28 May 2020).
2. Sharma. Text book of Tuberculosis Ed 3, History
3. Daniel TM. The history of tuberculosis. Respir Med 2006;100: 1862-70.
4. WHO. Tuberculosis Country Profile-India. [Last accessed on 2017 Dec 24]. Available from:
   https://www.extranet.who.int/sree/Reports?op=Replet&name=%2FWHO_HQ_Reports%2FG2%2FPROD%2FEXT%2FTBCountryProfile&ISO2=IN&LAN=EN&outtype=html .
5. WHO. Multi-Drug Resistant Tuberculosis (MDR-TB) 2016 Update. [Last accessed on 2017 Apr 07]. Available from: http://www.who.int/tb/challenges/mdr/mdr_tb_factsheet.pdf?ua=1 .
6. Nair, D.; Velayutham, B.; Kannan, T.; Tripathy, J.P.; Harries, A.D.; Natrajan, M.; Swaminathan, S. Predictors of unfavourable treatment outcome in patients with multidrug-resistant tuberculosis in India. Public Health Action 2017, 7, 32–38.
7. Singh, P.K.; Jain, A. Epidemiological perspective of drug resistant extrapulmonary tuberculosis. World J. Clin. Infect. Dis. 2015, 5, 77.
8. TB and COVID-19: paying attention to diabetes mellitus. Anthony D Harries 1 2, Ajay M V Kumar 1 3 4, Srinath Satyanarayana 1 3, Yan Lin 1, Riitta A Dlodlo 1, Mohammed Khogali 5, Rony Zachariah 5, Anil Kapur 6.
9. Patel JC. Complications in 8793 cases of diabetes mellitus 14 years study in Bombay Hospital, Bombay, India. Indian J Med Sci 1989;43:177-83.
10. Bashar M, Alcabes P, Rom WN, Condos R. Increased incidence of multidrug-resistant tuberculosis in diabetic patients on the Bellevue Chest Service, 1987 to 1997. Chest 2001;120:1514-9.
11. Singla R, Khan N. Does diabetes predispose to the development of multidrug-resistant tuberculosis? Chest 2003;123:308-9.
12. Dooley KE, Tang T, Golub JE, Dorman SE, Cronin W. Impact of diabetes mellitus on treatment outcomes of patients with active tuberculosis. Am J Trop Med Hyg 2009;80:634-9.
13. Global TB report 2021.