Multidrug Resistance Tuberculosis (MDR-TB) And Pre-Extensively Resistant Tuberculosis (Pre-XDR TB) In A 27 Year Old TB/HIV Co-Infected Patient In Ibadan, Oyo State, Nigeria A Case Report

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Introduction

Nigeria currently ranks 10th among the High Burden Countries (Countries which account for 80% of the World's tuberculosis burden) in the world.[1] However, the emergence of drug resistance has severely threatened tuberculosis (TB) control in the country, and has raised the concern of a return to an era in which drugs are no longer effective.

The World Health Organization estimates the country has Multi-Drug Resistant Tuberculosis (MDR-TB) prevalence rate of 1.9% and 9.3% among New and Retreatment TB patients respectively. Some isolated hospital based studies have documented the presence of MDR-TB in the country.

The MDR-TB prevalence rate ranged from 4% - 76.3%.[3,4]

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MDR-TB is defined as infection with a strain of M. tuberculosis that is resistant to at least Isoniazid and Rifampin.

Pre-extensively Drug Resistant Tuberculosis (Pre-XDR TB) is defined as disease caused by a strain of M.tuberculosis that is resistant to Isoniazid and Rifampin and either a Fluoroquinolone or a second-line injectable drug, but not both.[5]

The interaction between MDR-TB and Human Immunodeficiency Virus (HIV) has been described in the literatures. HIV infection has been described as a major risk factor for the development of resistance to second line drugs. HIV infection has also been described as a risk factor for the development of acquired resistance to Fluoroquinolones and second line anti-TB drugs.[6] Studies have also shown that there is a high rate of drug toxicity in MDR-TB/HIV co-infected patients.[7] Also, increased mortality has been reported in MDR-TB/HIV patients who are not on antiretroviral therapy.[7] The increased interaction between MDR-TB and HIV need to be borne in mind while managing the co-morbidity. This case report is presented to show the challenges in the diagnosis and management of patients co-infected with Pre-XDR TB and HIV.

Case Report

A.S was a 27 year old woman who presented at the Chest clinic, Iwo Local Government Area of Ibadan, Oyo State, South-West Nigeria in February 2010.

Her presenting complaints were cough, weight loss, fever and loss of appetite.

Her past history suggested that she had been receiving anti-TB medications for four months in a private hospital within the Ibadan metropolis. She had been on Rimactazid, Streptomycin and other drugs which she could not identify. She had not been taking the medications regularly because she could not afford the cost of the medications in the private hospital. She later absconded from the private hospital after three months of treatment due to inability to pay, coupled with the fact that she felt much better. The patient lived with her mother and her 5 years old daughter; both of whom were not symptomatic at the time.

On examination, she was ill looking, afebrile, anicteric, mildly pale; there was no generalized lymphadenopathy and she weighed 40kg.

The patient was counseled and referred to the laboratory for sputum examination for Acid Fast Bacilli (AFB) and microscopy; and retroviral test. The sputum AFB result was positive (2+). The retroviral test was also positive for HIV 1 and 2. A diagnosis of pulmonary TB in a HIV positive patient was made.

The patient was commenced on treatment regimen for Category II, in line with the National TB guidelines on the management of tuberculosis.

The drugs administered were a fixed dose combination of Rifampicin, Isoniazid, Ethambutol, Pyrazinamide (RHZE) for 3 months, in addition to 0.75g of Streptomycin daily for 2 months during the intensive phase of treatment. The patient was placed on 3 drugs, namely Rifampicin, Isoniazid and Ethambutol in a fixed dose combination during the continuation phase which lasted 5 months. The total duration of treatment was thus 8 months. The patient was also commenced on prophylactic Co-trimoxazole, 960mg daily, for the entire duration of treatment. She was referred to the University College Hospital (UCH) Ibadan for antiretroviral therapy (ART). During her work up at UCH, she was found to be positive to the Hepatitis B Virus (HBV) surface antigen test. She received ART at UCH as well as treatment for the HBV co-infection. While receiving her ART, she also continued her anti-TB medications at the Chest clinic.

During her treatment, her weight increased from 40 kg to 50kg. The sputum examination for AFB at 2months, 5months and 7months after commencement of treatment were all negative.

Though her treatment was interrupted for 3 weeks, she completed her anti-TB treatment and was discharged from the the Chest clinic in November 2010. She however continued her visit to UCH for the ART.

In February 2011, she presented again with cough, fever and weight losss. The Sputum AFB showed scanty AFB bacilli while her weight was 44kg.

She was recommenced on the 8 months regimen as above. After 55 days into the daily supervised treatment, the patient requested to be transferred to Ondo State (South-West Nigeria) in order to continue her education. Her treament was transferred to a Primary Health Centre (PHC) in Ondo State, where she never attended, proven by a phone call made to the PHC days after her referral.

On the 29th of December 2011, 7 months after defaulting from treatment, the patient returned to the Chest Clinic, Iwo road, Ibadan with symptoms similar to those present at her initial presentation. At presentation, the patient was very ill-looking, she weighed 44kg and her sputum AFB result was negative. She was recommenced on anti-TB drugs for two months, at the end of which her sputum examination showed scanty AFB. The sputum specimen was then transported to the Institute of Tropical Medicine, Antwerp Belgium for culture and Drug Susceptibility Test (DST) for both first and second line drugs. The culture and DST results were received three months after. The isolate from her sputum sample was resistant to all the first line anti TB drugs i.e. Rifampicin, Isoniazid, Ethambutol, Streptomycin and second line anti-TB drugs like Cycloserine, Ofloxacin, Prothionamide and Ethionamide.

The culture isolate was only sensitive to Kanamycin. A diagnosis of MDR-TB was made. The patient was traced to her residence; only to be informed she had died two months after the sputum sample was collected.

Discussion

This case report demonstrates a pre-XDR-TB patient co-infected with HIV and HBV and the challenges of treating tuberculosis in a resource limited setting.

Secondly, this case highlights the challenges patients face in the treatment of TB in a private hospital setting. In many studies relating to the health-seeking behaviour of TB patients, the patients were more likely to patronize private hospitals or clinics at first when they develop symptoms. However, it has been observed that many private hospitals do not adhere to the regimen (in terms of drugs, dose and duration) prescribed by the National TB treatment guidelines.[8] In addition, many of the patients are of the low socioeconomic status and cannot afford the cost of treating a chronic illness like TB, especially in a private hospital setting. Thus, the likelihood of default is very high, especially when patients feel better on completing the intensive phase of treatment. Studies have shown that default from TB treatment is more common during the continuation phase of treatment.[9]

In order to prevent default, especially in private hospitals, the national TB programme needs to engage more private hospitals in the delivery of TB treatment services through the public-private mix-DOTS initiative. This initiative is now identified world over as a proven strategy[10] to improve case finding, as well as the institution of appropriate treatment. Through training and support in terms of provision of drugs and other consumables; the cost of care will be drastically reduced for patients who seek care in private hospitals.

The need to strengthen laboratory diagnosis and management of TB in the country cannot be overemphasized. If the patient had access to culture and DST earlier at the first presentation, she could have commenced treatment for drug resistant TB early, which could have resulted in a better outcome. There is need to deploy newer technologies with faster lead-time to forestall delay of access to treatment. The resistance pattern of the isolate from the patient to second line drugs such as Cycloserine, Prothionamise, Ethionamide and Ofloxacin was observed in this study. Whether this patient was exposed to these drugs earlier could not be immediately ascertained. However, cross resistance between Isoniazid and Ethionamide has been documented. It is possible that the patient was exposed to Fluoroquinolones at some point during her treatment, since Ofloxacin is readily available in the open market. Though this patient did not receive treatment for MDR-TB, achieving a positive response to treatment would have been more difficult in her case, compared to patients who have no resistance to second line drugs.

In addition, there is the likelihood of the progression of Pre-Extensively Resistant Tuberculosis (Pre-XDR TB) to Extensively Drug Resistant Tuberculosis (XDR- TB), which has a higher morbidity and mortality. It is important to note that clinicians need to be sensitized on the need for rational drug use when managing MDR-TB suspects to prevent amplification of resistance when new drugs are introduced to a failing or failed regimen.

In conclusion, early diagnosis of MDR-TB is important for proper case management with second line anti-TB drugs. HIV counseling and testing should be offered to all TB patients for early diagnosis of HIV co-infection. Adequate management of co-infected patients and counseling on adherence to treatment is necessary to reduce morbidity and mortality.

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