Are weak health systems a brewing ground for multi-drug-resistant tuberculosis?

M O Akanbi and C O Ukoli

Abstract
Multidrug-resistant tuberculosis (MDR-TB) posses a huge threat to public health in Nigeria and most of sub-Saharan Africa where weak health systems exist. Diagnostic facilities and drug treatment of MDR-TB are largely unavailable in several countries in sub-Saharan Africa, and where treatment is available treatment outcome has been poor. This case report illustrates challenges in the implementation of basic Directly Observed Treatment (short-course) (DOTS) and its impact on the control of MDR-TB in sub-Saharan Africa. The case notes of a 48-year-old widow, who had been on treatment for smear-positive TB between 2004 and 2008 in Jos, Nigeria, were reviewed. Failure of basic DOTS and delayed diagnosis of MDR-TB were identified as potential challenges in control of the disease on the African continent. This case report illustrates weaknesses in the health system in sub-Saharan Africa in the area of TB control and how this could contribute to the development and spread of multidrug and possibly extensively drug resistant (XDR) TB.

Introduction

Multidrug-resistance (MDR) tuberculosis, defined as tuberculosis (TB) caused by strains of *Mycobacterium tuberculosis* resistant to at least rifampicin and isoniazid, has been recognised as a global epidemic.[1,2] Nigeria, with the fifth largest burden of TB among 22 high-burden countries, a high HIV seroprevalence and a weak health system, is an ideal milieu for the proliferation of MDR-TB.[1,3] The World Health Organization (WHO) estimates that the prevalence of MDR-TB in Nigeria is about 1.7% among new TB cases and 7.9% among retreatment cases.[1] Despite this high prevalence, facilities for diagnosis of MDR-TB are sparse and treatment largely unavailable. This case report illustrates some challenges encountered in the management of MDR-TB in Nigeria and a call for urgent action to stem an impending health crisis.

Case report

AL a 48-year old widow was first seen in May 2004 at the TB clinic of the Jos University Teaching Hospital in Nigeria, with a 6-month history of productive cough, weight

Dr Maxwell O Akanbi, Respiratory Physician, and Professor Christiana O Ukoli Professor of Respiratory Medicine, both at Jos University Teaching Hospital, Jos, Nigeria. Correspondence to: Dr Maxwell O Akanbi. Email: maxwell_akanbi@yahoo.com

loss, low-grade fever, and night sweats. She had been diagnosed with pulmonary tuberculosis (PTB) 2 years prior to this visit. She commenced anti-TB drugs after the initial diagnosis but defaulted after 2 months following improvement in symptoms. She subsequently procured anti-TB medications whenever the cough recurred. Significant investigation results during the review were an elevated erythrocyte sedimentation rate of 130 mm/hour and smear-positive sputum for acid-fast bacilli. Her HIV status was negative. An assessment of smear-positive TB was made with the possibility of MDR-TB. Facilities for sputum culture and drug susceptibility testing (DST) were unavailable so treatment was commenced on standard quadruple anti-TB drugs (WHO Category 1) with follow up at the TB clinic.

The cough persisted and after 5 months of treatment the patient was reassessed and remained sputum-smear positive. Based on this, a diagnosis of treatment failure was made and she was commenced on Category 2 treatment (rifampicin, isoniazid, ethambutol, pyrazinamide, and daily streptomycin injections for the first 2 months). There was no improvement in her condition and after a year of treatment a diagnosis of possible MDR-TB was made. Due to limited treatment options, the patient was recommenced on Category 2 treatment with the addition of a floroquinolone.

AL was referred to the pulmonology clinic in October 2008 on account of persistent cough and acid-fast bacilli (AFB) smear-positive sputum. Her treatment history showed that she had not received Directly Observed Treatment (short-course) (DOTS) because she could not afford daily transportation to the nearest DOTS facility 3 km away from her home. Her HIV status was still negative. An assessment of possible MDR-TB was made and sputum culture and DST were ordered. Through the assistance of a faith-based organisation she had sputum tests done in a private facility in Abuja (300 km away from Jos). The result showed *M Tuberculosis* resistant to all first-line drugs tested – isoniazid, streptomycin, rifampicin, and ethambutol. Unfortunately, efforts to get her second-line drugs have not been successful and she remains untreated living within the community with the resistant bacilli.

Discussion

MDR TB has been recognised globally as an emerging epidemic. Cases have been reported from all parts of the world with China, India, and the Russian Federation accounting for two-thirds of the world global incident

cases.[2,3] Poor management of MDR-TB cases has resulted in the development of extensively drug-resistant XDR-TB, which is defined as MDR-TB with additional resistance to a fluroquinolone antibiotic and at least one of one of the three injectable drugs used for treatment of MDR-TB (capreomycin, amikacin, or kanamycin).[4] The danger of XDR-TB is exemplified by the outbreak in KwaZulu-Natal in South Africa in which 52 of 53 HIV-infected patients died with a median survival of 16 days from the day of diagnosis.[5] MDR-TB results from the interplay of various factors, mainly inefficient TB treatment programmes and high HIV seroprevalence; factors which abound in most of sub-Saharan Africa.[3]

Although the National Tuberculosis and Leprosy Control Programme (NTBLCP) in Nigeria currently reports DOTS coverage of about 75%, these facilities are still not available to a large number of patients with TB.[6] Low stocks of anti-TB drugs and availability of these drugs over the counter remain challenges of TB control in Nigeria that may be contributing to the development of MDR-TB. A government commitment to sustain the DOTS programme is imperative for its proper functioning.

HIV infection is another important factor that may contribute to the burden of MDR-TB. Although the evidence of HIV infection as a specific risk factor for MDR-TB is variable, it has been associated with acquired rifamycin resistance.[7,8] Some factors contributing to this are: a poor adherence to TB treatment; co treatment with antiretroviral medication; and gastrointestinal malabsorption of antituberculous medications.[3,9] While our index case is HIV seronegative, there is a paucity of data on the burden of MDR-TB among this vulnerable population in Nigeria.

This case highlights the lack of diagnostic facilities for MDR-TB in developing nations. TB diagnosis is still largely rudimentary, relying mainly on sputum-smear microscopy. Even when MDR-TB is suspected the inability to make a bacteriological diagnosis stalls further patient management. Where diagnostic facilities are available, they are often unaffordable.[10] In line with WHO and Stop TB Partnership's call for significant expansion of mycobacterial culture and DST testing capacity, the Nigerian government is striving to make diagnostic facilities available in six zonal laboratories in the country.[6] There is, however, an urgent need to role out more diagnostic facilities to meet the needs of the population, and this will require the cooperation and assistance of private and corporate organisations. The recent introduction of liquid culture and most recently rapid molecular diagnostic tools into the country is a welcome development.

While we are tackling the challenges of diagnosis, a more formidable foe along the pathway of MDR-TB management is the unavailability of second-line antituberculous medications. The NTBLCP last year provided a guideline for the management of MDR-TB in Nigeria using the DOTS–Plus approach. Recommended second-line drugs are: kanamycin, cycloserine, prothionamide, ofloxacin, and pyrazinamide. Unfortunately, kanamycin, cycloserine, and prothionamide are not readily available within the country. A recent report on the treatment of 20 cases of MDR-TB in Nigeria, however, showed a 95% cure rate with a combination of amikacin, ethinonamide, pyrazinamide, ethambutol, and ofloxacin – with a treatment duration of 24 months.[10]

With increasing diagnosis, there is a growing pool of MDR-TB patients within the country awaiting treatment – there are an estimated 8000 cases of MDR-TB in Nigeria.[2,11] This group portends a potential public health hazard. Patients are more likely to be exposed to some second-line antituberculous medications which could potentially lead to resistance to these drugs, the most likely being the fluoroquinolones, to which the index case has been exposed. The use and abuse of fluoroquinolones for treatment of various infections in Nigeria underscores the need for a study on its resistance pattern. Another area of concern is the potential increases risk of acquiring primary MDR-TB.

Conclusion

This case report typifies how weaknesses in TB control programmes could contribute to the development of MDR-TB. Although these challenges are huge, some countries on the African continent are recording successes in their battle against TB and MDR-TB. We need to draw on their wealth of experience and wage an integrated war to achieve our set goals. There is an urgent need to strengthen the health systems and increase capacity to bring DOTS facilities closer to the people. While activities should be coordinated by the government, there is a need for collaboration with developmental partners-both within and outside the country. The clock is ticking and the time to act is now.

Rerences
1. WHO/IUATLD. Anti-tuberculosis drug resistance in the world: report 3. WHO/HTM/TB/2004.343. Geneva: WHO,2004.
2. Zignol M, Hosseini M, Wright A ,et al. Global Incidence of Multidrug Resistant Tuberculosis. *J Infect Dis* 2006; 194: 479–85.
3. Wells CD, Cegielski J, Nelson LJ, et al. HIV infection and multidrug-resistant tuberculosis - the perfect storm. *J Infect Dis.* 2007; 196: s86–s106.
4. Centers for Disease Control and Prevention. Emergence of mycobacterium tuberculosis with extensive resistance to second-line drugs worldwide, 2000–2004. *MMWR Morb Mortal Wkly Rep.* 2006; 55: 301–5.
5. Gandhi N, Moll A, Sturm A, et al. Extensively drug-resistant tuberculosis as a cause of death in patients co-infected with tuberculosis and HIV in a rural area of South Africa. *Lancet.* 2006; 368: 1575–80.
6. World Health Organization. Global tuberculosis control: surveillance, planing and financing. WHO Report 2007. Geneva: World Health Organization, 2007.
7. Jenny-Avital ER. Acquired rifampin resistance in AIDS related TB. *Clin Care* 1997; 14: 72–3.
8. Munsiff SS, Joseph S, Ebrahimzadeh A, Frieden TR. Rifamycin-monoresistant tuberculosis in New York City, 1993–1994. *Clin Infect Dis.* 1997; 25: 1465–7.
9. Burman WJ, Gallicano K, Peloquin C. Comparative pharmacokinetics and pharmacodynamics of the rifamycin antibacterials. *Clin Pharmacokinet* 2001; 40: 27–41.
10. Dosumu EA, Osagie KO, Shuaib A Multidrug-resistant tuberculosis at the National Hospital, Abuja, Nigeria. *AJRM* 2008; 4: 22–3.
11. World Health Organization. The global MDR-TB and XDR-TB response plan. Geneva: World Health Organization, 2007.