Case Report

Rifampicin-Resistant Tuberculosis in a Toddler: A Report of a Rare Paediatric Case in Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria

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Abstract

The emergence of resistant strains of mycobacterium tuberculosis (TB) to antituberculous drugs has compounded the management of the chronic infection. More than 90% of rifampicin (RIF)-resistant isolates are also isoniazid resistant; hence, rifampicin resistance (RR) is a surrogate marker for multidrug resistant TB (MDR-TB). Although there are limited reports of pediatric RR/MDR-TB in Nigeria, there had not been similar report in our hospital until now. A 2-year-old girl was admitted with 2-month history of fever, cough with dyspnea, and progressive weight loss. There was no known contact with adult who had chronic cough; the toddler and her parents have not been treated for TB in the past. Her chest X-ray showed nodular opacities, while gastric washout for GeneXpert MTB/RIF confirmed RIF-resistant TB. The parents declined screening for TB despite counseling. The patient was subsequently referred to a specialized center for the management of drug-resistant TB, but the parents failed to go for the treatment. Young children are at risk of developing TB disease and MDR/RR-TB, which is more complex to manage than drug-susceptible TB due to longer treatment duration, increased toxicity, as well as poor parental compliance to the demand of treatment.

Keywords: Ile-Ife, Nigeria, rifampicin-resistant, toddler, tuberculosis

Introduction

Drug-resistant tuberculosis (DR-TB) is a major public health problem and a notifiable disease.[1] Resistance to rifampicin (RIF) implies any resistance to RIF in the form of either mono-resistance, poly-resistance, multi-DR TB (MDR-TB), or extensive-DR TB (XDR-TB). Globally, 3.5% of new TB cases and 20.5% of previously treated cases were estimated to have MDR-TB in 2014.[2] The first Nigerian DR-TB survey in 2012 reported a MDR-TB prevalence rate of 2.9% among new TB cases and 14.3% among retreatment cases, giving an overall crude prevalence rate of 4.8%.[3] According to a recent systemic review and meta-analysis in Nigeria, the prevalence rate of any drug resistance among new TB cases was 32.0% and while it was 53.0% among previously treated cases; in the same study, multidrug resistance among new and previously-treated cases was 6.0% and 32.0%, respectively.[4] As a proxy for MDR-TB in most cases, rifampicin-resistant TB (RR-TB) is treated like MDR-TB in line with the WHO recommendation. However, the treatment is more complex than drug-susceptible TB due to prolonged duration of treatment coupled with increased toxicity and treatment failure.[5,6]

There has been no previous report of pediatric case of RR/MDR-TB in our hospital, hence this single report.

Case Report

A 2-year-old girl was admitted on account of fever and fast breathing with cough of 2 months' duration. She had

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progressive weight loss of 1 month. The patient had incomplete vaccination although immunization card was not available. She was the only child of the mother, but the father had two other children for his first wife who is separated. There was no known contact with adult who had cough or weight loss, although her mother routinely takes her to a commercial market where she trades. None of the parents nor patient have been treated for TB in the past. The child and her parents live in a room apartment with a single window; there is no demonstrable evidence of overcrowding. At admission, she was febrile and dyspneic with Grade 2 digital clubbing and had evidence of chronic illness [Figure 1]; other findings were tachycardia and crepitation with tender hepatosplenomegaly. There was no Bacillus Calmette–Guerin scar. Investigation showed anemia, leukocytosis, and elevated erythrocyte sedimentation rate (ESR) of 97 mm/hr Westergren [Table 1], but rapid test for human immunodeficiency virus test was nonreactive for the child and her mother. Her oxygen saturation ranged from 91% to 97%, while her chest X-ray showed nodular opacities on lung zones [Figure 2]. GeneXpert was done using the sample obtained from gastric washout, which confirmed RIF-resistant TB. She was transfused following a packed cell volume (PVC) of 19% and had broad-spectrum antibiotics and antifailure drugs. Her posttransfusion PCV was 35%. Parents were adequately counseled on the line of treatment and the need for their screening for TB but they declined. The patient was subsequently referred to a specialized center for the management of DR TB; the parents were later contacted but failed to go to the treatment center.

Discussion

The problem of TB has been compounded in recent years by the emergence of resistant strains to RIF and other drugs.[6] More than 90% of RIF-resistant isolates are also isoniazid resistant; hence, rifampicin resistance (RR) is frequently used as a surrogate for MDR-TB, which is defined as resistance to at least the two major first-line anti-TB drugs, namely isoniazid (INH) and RIF.[7,8] Total DR-TB or super XDR, which is defined as resistance to all first-line and second-line anti-TB drugs, has also been described. A report from the WHO in 2016 indicated that the prevalence of MDR/RR-TB was 4.3% among new TB cases and 25% among previously treated TB cases in Nigeria.[9]

Although the prevalence reports of RR vary from center to center in Nigeria, it is commonly within the ranges of 4.2%–14.7%.[1,10-12] The prevalence rate in children is similar to the general population. In independent reports by Arega *et al.*[10] in Addis Ababa and Ide *et al.*[13] in Port Harcourt, they found the prevalence levels of 7.9% and 10.8%, respectively, in their studied children population. Drug-resistant TB is rarely reported among toddlers in Nigeria. Ide *et al.*[13] reported four cases of MDR-TB among children whose ages ranged from 3 months to 24 months; the authors observed positive history

Table 1: Anthropometry and laboratory results of patient

Signs/tests	Findings
Anthropometry	
Weight (weight for age)	6.5 kg (< - 3 Z score)
Weight (weight for length)	6.5 kg (< - 3 Z score)
Length (length for age)	80 cm (- 2 Z score)
Mid arm circumference	10 cm (severe malnutrition)
Vital signs	
Respiratory rate	70 c/m (↑)
Heart rate	180 b/m (↑)
Temperature	38.8°C (↑)
Results	
Full blood count	Hematocrit - 19% (↓)
	Leukocytosis - 29 900/cmm (↑)
	Neutrophil - 88% (↑)
	Lymphocyte - 12% (↓)
	Platelet - 502 000/cmm (↑)
HIV	Nonreactive
ESR	97 mm/h (↑)
GeneXpert	Rifampicin- resistant TB

↓: Low; ↑: High. HIV – Human immunodeficiency virus, ESR – Erythrocyte sedimentation rate, TB – Tuberculosis

Figure 1: Picture of the toddler with evidence of marked wasting

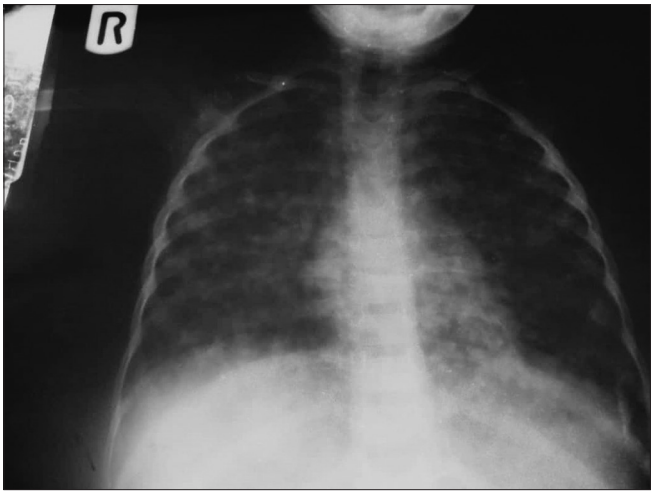

Figure 2: Patient's Chest X-ray showing multiple opacities on the lung zones and microcardia (consistent with cardiac muscular wasting)

of contact in all the patients who belong to low socioeconomic class. Previous treatment for TB is the strongest risk factor for the development of MDR-TB;[5,10,12-14] this is partly due to acquired drug resistance which emanates from poor compliance to dose and duration of treatment, substandard drugs, and the absence of infection control measures in hospitals. Resistance to anti-TB medications is due to mutations in the drug target genes of the bacterial chromosome before the strains are exposed to the drugs.[15] The mechanisms of chromosomal resistance vary; RR is associated with the alterations in the ß-subunit of RNA polymerase (rpo ß) gene. Isoniazid resistance is associated with deletion/mutation of catalase-peroxidase gene kat G and alterations in the INH A gene.[15]

Similar to drug-susceptible TB, common features of DR-TB include chronic cough, prolonged fever, weight loss, and enlarged lymph nodes.[13] Features of disseminated disease and severe malnutrition may also occur. Undernutrition, which manifests as severe wasting and stunting in this reported case, tends to impair innate and adaptive immune responses needed to fight Mycobacterium tuberculosis.[16] Inflammatory cytokines such as tumor necrosis factor-alpha, interleukin-1 (IL-1), and IL-2 are responsible for clinical and laboratory findings such as fever, leukocytosis, and thrombocytosis. TNF-alpha associated with IL-1 can also cause tissue necrosis and cachexia; elevated globulins (alpha, beta, and gamma-globulins) cause marked increase in ESR, a nonspecific test for inflammatory and infectious processes to evaluate activity and disease extent, response to treatment, as well as prognosis of chronic diseases such as TB.[17,18]

The GeneXpert MTB/RIF is a novel automated molecular assay endorsed by the WHO for early diagnosis of both MTB infection and RIF resistance;[19] it has a high sensitivity and specificity at 97.6% and 99.8%, respectively.[19] The resistance of Mycobacterium tuberculosis to RIF and other drugs makes treatment more exorbitant, prolonged with increased exposure to more toxic medications.[5] Measures to prevent refusal of treatment for RR/MDR-TB include health education on the gravity of the disease and its treatment modality, coupled with provision of readily accessible treatment centers in all states of the federation. In addition, provision of incentives to parents of TB-infected children may help to limit refusal of treatment.

Conclusion

Young children are at risk of developing TB disease and MDR/RR-TB. Malnourished toddlers should be screened for TB for early diagnosis and better prognosis. Source identification may sometimes be cryptic in childhood DR-TB, which is a more complex to manage than susceptible TB due to longer treatment time, increased toxicity, treatment failure, as well as poor parental compliance to the demand of treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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