Case Report

Poly-resistant Tuberculosis in an HIV-infected Child

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Abstract

Drug-resistant tuberculosis (DR-TB) has been reported in India, but has been rarely documented in children. HIV co-infection has led to resurgence of tuberculosis (TB), making treatment even more difficult due to complex drug interactions. Poly-resistant TB is rare in children, especially in HIV-infected children. We report an HIV-infected child who developed poly-resistant TB (resistance to Streptomycin and Isoniazid) after 3 years of completion of anti-tuberculosis treatment (ATT). His mother had also received ATT 3 years back. We conclude that DR-TB in HIV-infected children should be considered if the child had been treated with ATT in the past or there is contact with adults on second-line ATT therapy.

Keywords: Children, HIV, poly-resistant TB

Introduction

India has the world's highest burden of tuberculosis (TB). In India, the multidrug-resistant TB (MDR-TB) prevalence among all patients with TB combined is estimated to be 4.1%. A crude estimate derived from these data is that 4500 – 6000 HIV-infected persons develop MDR-TB annually in India.[1] Diagnosis of any form of TB, including drug-resistant (DR) TB, is more challenging in the presence of HIV disease and together they result in higher case fatality rates.[2]

Poly-drug resistant TB indicates resistance to two or more anti-TB drugs but not to both Isoniazid (INH) and Rifampicin (R) simultaneously.[3] Treatment of DR-TB in patients on antiretroviral therapy (ART) is complex due to the drug interactions.[1] DR-TB in HIV-infected children is difficult to diagnose and rarely reported. We report an HIV-infected child who developed poly-resistant TB.

Case Report

A 3-year-old HIV-infected boy was referred for further management in January 2005. Mother was diagnosed as tuberculous pleural effusion with HIV infection with acid fast bacillus (AFB) seen on sputum examination and was on Ofloxacin (O), INH (H), and Rifampicin (R) for the same. (Details of mother's investigations are not available.) The child was currently asymptomatic. He had oral thrush and herpes simpler in the past. He had been immunized till date. On examination, his weight was 12 kg and height was 86.5 cm. He had cervical adenopathy (non-tender, non-matted) and other systems were normal. Investigations showed positive Mantoux test (20 × 22 mm) and chest X-ray was suggestive of primary complex. His venereal disease research laboratory (VDRL) test, HBsAg, and anti-hepatitis C were negative. He was started on anti-tuberculous therapy (ATT) consisting of 2 HRZE + 10 HR (Z = Pyrazinamide, E = Ethambutol). His serial CD_4 counts are depicted in Table 1. ATT was stopped in January 2006. He was asymptomatic till June 2007, when we had mild molluscum contagiosum. In February 2009, at the age of 7 years, he was hospitalized with right lower zone pneumonia and his sputum was positive for AFB. He was restarted on ATT in category 2 regime as per WHO. His sputum culture grew *Mycobacterium tuberculous* (MTB) complex after 6 weeks and sensitivity after another 2 weeks showed resistance to Streptomycin (S) and H. He was then shifted to REZO in May 2009 and ART was started in the same period in view of decreasing CD_4 count, consisting of Zidovudine (AZT), Lamivudine (3TC), and Nevirapine (NVP at 400 mg/m^2/day). He was alright and chest X-ray normalized in August 2009. Ofloxacin was stopped in August 2009 and he was advised REZ for another 6 months.

Discussion

In India, MDR-TB is estimated to account for 2.3% [95% Confidence Intervals (CI): 1.8 – 2.8] of new cases and 17.2% (95%

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Quick Response Code:

Website: www.jfmpc.com

DOI: 10.4103/2249-4863.104989

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Table 1: Serial CD_4 counts

CD4 Counts	August 2005	February 2006	May 2006	August 2006	December 2006	March 2007	July 2007	October 2007	April 2008	August 2008	December 2008	May 2009	August 2009
CD_4 (%)	519 (24.3)	666 (17)	371 (23.4)	383 (26.2)	483 (25.2)	435 (26.2)	363 (22)	438 (23.2)	225 (15)	342 (12.6)	308 (12.5)	229 (13.9)	392 (21.3)
CD_8 (%)	1069 (50.1)	-	1164 (73.6)	1030 (70.5)	1441 (75.2)	1221 (73.5)	1147 (70)	1341 (71)	857 (58)	2135 (79)	2066 (80.9)	1275 (84.1)	1329 (73.39)
CD_4 CD_8	0.49	0.31	0.32	0.37	0.34	0.35	0.32	0.33	0.26	0.16	0.15	0.17	0.29
Viral load	-	-	-	-	2480	-	-	-	-	-	-	-	-

CI: 14.9 − 19.5) of previously treated TB cases.[4] Those at highest risk of DR-TB are in whom prior treatment had failed, cases of relapse, defaulters, and contacts of MDR-TB.[1] Drug resistance is rarely acquired in the pediatric population due to the paucibacillary nature of the disease and originates mainly in the adults who are treatment failures or defaulters. Thus, the main method of resistance in children is primary transmission of the resistant bacilli.[5] Our patient had been treated for pulmonary TB in 2005 for 1 year but again developed TB in 2009, which is suggestive of a relapse.

HIV co-infection is considered important in the development of DR-TB by increasing the rates of malabsorption of anti-TB drugs, thus causing treatment failures. Also, HIV increases the rate of DR-TB transmission.[1]

The diagnosis of DR-TB is established by laboratory methods (drug susceptibility tests or DST) which, however, are not available in most resource-limited settings and are difficult to do in children. Treatment of poly-resistant TB varies as per drug resistance pattern and consists of three to four sensitive drugs for six to eighteen months duration.[6] For H and S resistance, as in our patient, the suggested regimen is RZE for 6–9 months, and fluoroquinolone can be added in patients with extensive disease to strengthen the regimen.[6]

Thus, children who had been treated for TB in the past should be screened for drug resistance by DST. This case report emphasizes this fact. This has also been reiterated in our series of children with MDR-TB and partial over extensively drug-resistant (XDR) TB in whom we found that over 50% of patients had been treated for TB in the past.[7,8]

Conclusion

DR-TB in HIV-infected children should be considered if the child has been treated with ATT in the past or there is contact with adults on second-line ATT therapy. Poly-resistant TB is rare in children, especially in HIV-infected children.

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How to cite this article: Shah I, Bansal N. Poly-resistant tuberculosis in an HIV-infected child. J Fam Med Primary Care 2012;1:153-4.

Source of Support: Nil. **Conflict of Interest:** None declared.