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Multi-Drug Resistant Tuberculosis and HIV Infection about 06 Cases

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ABSTRACT

Multi-drug-resistant tuberculosis remains a significant threat in people living with HIV and promotes increased mortality rates. It is often a combination of pulmonary tuberculosis forms and extra-pulmonary forms. We report 6 cases of patients with HIV and multi-drug-resistant tuberculosis collected over a two-year period from 01/01/2018 to 31/12/2019 hospitalized for multi-drug-resistant tuberculosis at Moulay Youssef Hospital. We describe the radiological, evolutionary and therapeutic clinical characteristics of resistant TB in this patient category. The average age of our patients was 36. These are 2 women and 4 men. Of which 4 were known to carry retroviral infection, followed and treated with antiretroviral therapy, there was only one diabetic patient on insulin therapy. The signs of calls were respiratory in 3 patients, digestive in one patient, neurological in one case, and an alteration of the general state in the last case. Exclusive pulmonary involvement was noted in 4 patients, associated with neuromeningeal localization in one patient and cervical lymph node localization in the last case The radiological aspect was dominated by bilateral micronodular opacities often associated with sequellary opacities. Based on the results of the xpert Tb Rif and Hain Test 1 st line and 2 nd line 3 cases of our patients were Prexdr (resistant to injectable 1/3 cases, resistant to furoquinolone 2/3 cases), MDR in one patient, two patients were classified as RR due to the unavailability of genotypic tests. The evolution during hospitalization was marked by the occurrence of pneumocystosis in 2 patients who had progressed well under Bactrim high curative dose and systemic corticosteroids, pneumothorax in one case; we deplore the death of a patient by tuberculosis meningitis. Five patients were put individualized regimen of 20-24 months and only one case on a standardized regimen for 9-11 months, antiretroviral treatment was initiated after 1 month of the start of anti-bacillary treatment in 2 cases (CD4 rate > 500). Major adverse effects were observed in 3 patients. These were bilateral deafness, significant hepatic cytolysis, and severe cytopenia which required the permanent discontinuation of amikacin, Pza, Linezolid respectively. Minor side effects, a type of digestive intolerance, were noted in 2 patients who progressed well under symptomatic treatment. Minor side effects, a type of digestive intolerance, were noted in 2 patients who progressed well under symptomatic treatment.HIV infection increases the risk of the emergence of resistant strains of the TB bacillus in HIV-positive subjects. The combination of multi-drug-resistant tuberculosis and HIV infection is a major risk factor for morbidity-mortality.

Introduction

People infected with Mycobacterium tuberculosis and HIV are much more likely to develop active tuberculosis (TB) than people with M. tuberculosis but without HIV [1]. Patients infected with multidrug resistant (MDR)-TB (defined as resistance to at least rifampicin and isoniazid, the two most powerful anti-TB drugs) require longer, more expensive treatment regimens than drug-susceptible TB, with poorer treatment success [1, 2].

Discussion

Multidrug-resistant (MDR) tuberculosis (TB) is TB caused by *Mycobacterium tuberculosis* strains resistant to at least isoniazid and rifampin; it has emerged as a global epidemic resulting largely from deficiencies in TB case management and program management [3–4]. Approximately 425,000 MDR-TB cases occur annually worldwide, representing nearly 5% of the world's annual TB burden [3].

The diagnosis of MDR-TB requires sophisticated laboratories with highly skilled microbiologists. Patients with MDR-TB require a much longer treatment period, usually 24 months, compared with the 6–8 months required for drug-susceptible TB [5]. In well-performing MDR-TB programs in settings with a low HIV infection prevalence, treatment success is generally 70%–80%; by comparison, treatments success for drug-susceptible TB in well-performing TB programs can exceed 90% [6].

Many countries have limited capacity to appropriately diagnose and treat MDR-TB [7, 8]. In addition, extensively drug-resistant (XDR) TB has emerged in every region of the world; recently, there was a highly lethal outbreak of XDRTB in South Africa [9, 10].

XDR-TB, defined as MDR-TB that includes resistance to any fluoroquinolone and one of the second-line anti-TB

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njectable agents—kanamycin, amikacin, or capreomycin—is potentially untreatable [11–12].

For persons infected with *M. tuberculosis*, HIV infection is the strongest risk factor for the development of active TB—either drug-susceptible or drug-resistant TB—after *M. tuberculosis* infection [13–14].

TB is also the leading cause of death among HIV-infected persons and may accelerate the course of HIV infection, increasing the HIV load in some patients [15, 16–17]. In addition to increasing the TB burden in general, HIV infection may also be contributing to increases in MDR-TB prevalence among patients with TB and has been associated with many MDR-TB outbreaks, as well as with acquired rifamycin resistance.

Although the evidence for HIV infection as a specific risk factor for multidrug resistance among patients with TB is variable, HIV infection has been associated with acquired rifamycin resistance among patients with TB in controlled clinical trials and other studies [18–19]

The specific genotype family of drug-resistant strains of *M.tuberculosis* may play a role in transmission, particularly among people living with HIV infection. Studies have suggested thatthe Beijing genotype family, which includes the "W" strain of *M. tuberculosis* implicated in many MDR-TB outbreaks in the United States, is more virulent and is associated with anti-TB drug resistance in specific geographic settings [20–21].

MDR-TB treatment requires a minimum of 4 effective drugs, including a fluoroquinolone, aninjectable agent (capreomycin, kanamycin, or amakacin), and at least 2 agents from the 3 remaining second-line anti-TB drug classes, including cycloserine, thioamides (ethionamide or prothionamide),and *p*-aminosalicylic acid (PAS). Treatment should also include any first-line agents beyond isoniazid and rifampin to which a patient's isolates retain susceptibility [5]. Regimens can be individualized, on the basis of drug-susceptibility testing results, or standardized, on the basis of surveillance of anti-TB drug resistance [11]. In this study five patients were put individualized regimen of 20-24 months and only one case on a standardized regimen for 9-11 months.

Furthermore, overlapping toxicities and interactions between anti-TB and antiretroviral drugs complicate treatment [22-23]. Overlapping toxicities include peripheral neuropathy (stavudine, didanosine, and ethambutol), hepatotoxicity (nevirapine,efavirenz, and pyrazinamide), rash (abacavir, amprenavir,nevirapine, efavirenz, fosamprenavir, and pyrazinamide), andocular effects (didanosine and ethambutol), among others.

Immune reconstitution inflammatory syndrome (IRIS) poses important challenges in the clinical management of HIV-TB patients initiating antiretroviral therapy (ART).

In HIV patients with TB, IRIS is thought to occur in two distinct scenarios. First, unmasking of a previously undiagnosed TB infection prior to ART initiation. Alternatively, paradoxical clinical or radiological worsening of TB in patients previously improving with antituberculousis treatment (ATT) following ART introduction and despite effective virological suppression [24]

The pathogenesis of IRIS remains incompletely understood. The most significant event leading to TB-IRIS in HIV is failure of the immune system to eliminate *Mycobacterium tuberculosis*, causing high mycobacterial burden in those with severe immunosuppression and lymphopenia prior to ART, followed by its restitution and immune activation [25].

The main risk factors of IRIS are represented by the severe immunodepression (CD4 < 50—100/mm3), the dissemination of the opportunistic infection, and the introduction of ART shortly (< 1—2 months) after the treatment of tuberculosis infection. In our study antiretroviral treatment was initiated after 1 month of the start of anti-bacillary treatment in 2 cases (CD4 rate > 500), Immune reconstitution inflammatory syndrome (IRIS) was not observed.

Conclusion

Although HIV is a powerful risk factor for all forms of TB and institutional outbreaks of MDR-TB among people living with HIV have been reported [5], population-level data on the association between HIV infection and MDR-TB are limited.

The first and most important step in averting the catastrophe of HIV-associated MDR-TB epidemics is to address the TB control program deficiencies causing ongoing generation of anti-TB drug resistance.

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