

Case Report: Pulmonary Tuberculosis Reactivation in Patients with Human Immunodeficiency Virus: A Case Report

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1. Abstract

We present one case of co-infection with *Mycobacterium tuberculosis* (MTB) in a patient with Human Immunodeficiency Virus (HIV). It's a case of a 27-year-old woman admitted at the Clinical Hospital of Infectious Disease and Pneumology "Dr. Victor Babes" Timisoara. The patient was known to be HIV-positive since 2019 and developed pulmonary tuberculosis during the therapy. The patient was non-compliant at antiretroviral therapy and developed pulmonary tuberculosis first time in December 2020. One year later, the same patient was admitted in the hospital with pulmonary manifestations and a reactivation of pulmonary tuberculosis was once again confirmed.

2. Introduction

Human immunodeficiency virus and *Mycobacterium tuberculosis* co-infection represents a global public health problem [1]. Co-infection with *Mycobacterium tuberculosis* is the leading cause of death in HIV-1 infected individuals [2]. HIV infection promotes

the progression of the infection with MTB to active tuberculosis, both in patients recently infected and in patients with latent infection. HIV infection increases the risk of transmission of multi-drug resistant tuberculosis (MDR-TB), unless effective and continuous measures are taken to control the infection. Clinical data suggests that MTB is the most common opportunistic infection causing exacerbation of viral load and low values in CD4 count in patients diagnosed with HIV. Mutually, HIV increases the risk of MTB progression and reactivation of latent TB infection by decreasing the body's cell mediated immunity. HIV co-infection raises difficulties in diagnosing MTB disease by altering the pathogenesis of MTB. This can lead to atypical radiographic and extrapulmonary manifestations and negative sputum exams. There is also a clear association between pulmonary tuberculosis and other opportunistic infections. Tuberculosis is an independent risk factor for HIV progression to AIDS. Therefore, co-infections provide mutual advantages for both pathogens. Despite being curable and prevent-

able, tuberculosis is the leading cause of HIV-associated mortality. The risk of developing tuberculosis is 30 times higher among people living with HIV than among people who do not have HIV infection [3]. The first step to prevent this co-infection is to ensure that people living with HIV are tested for *Mycobacterium tuberculosis* infection. If found with *Mycobacterium tuberculosis*, further tests are needed to rule out tuberculosis disease. The next step is to start treatment for latent tuberculosis infection or tuberculosis disease based on tests results [4].

3. Case Report

We present the case of a 27-year-old female from the urban environment, first diagnosed with HIV infection in September 2019. She tested positive for MTB infection in December 2020 and developed relapse in December 2021. In December 2020, she presented with fever (38.5°C), headache, productive cough and fatigue. Stetacoustically, she presents bilateral basal subcrepitan crackles. Emergency department performed a CT scan of the thorax which showed dense left perihilar condensation process, microcalcifications and a cavitory image of 6 mm. The conclusion of the CT scan was secondary cavitory-caseous pulmonary tuberculosis of the superior left lobe. Blood cell count presented normal white blood cells ($6.4 \times 10^3/\mu\text{L}$), low hemoglobin (11.3 g/dL) and hematocrit levels (34.3 %), thrombocytosis ($447.000/\mu\text{L}$) and lymphopenia ($360/\mu\text{L}$). The C-reactive protein level was markedly elevated (118.41 mg/L). Hepatic and renal function were normal. She also tested positive for syphilis infection (192.6 IOC) and urinalysis tested positive for *Escherichia coli* (>100.000 CFU/mL). CD4 cell count showed a value of 6 cells/ mm^3 and a viral load of 603.000 copies/mL. The microscopic exam tested positive for *Mycobacterium tuberculosis*. MTB DNA was detected using PCR (GeneXpert MTB/RIF assay) without Rifampicin resistance. Both MGIT and Löwenstein-Jensen cultures tested positive. During the hospitalization, the patient received antitubercular therapy with Isoniazid, Rifampicin, Pyrazinamide and Ethambutol. She continued the antiretroviral therapy with Emtricitabine/Tenofovir and Isentress and after she was stabilized she was discharged with a follow-up appointment. Being uncompliant to the treatment the patient developed one year later in December 2021 a relapse and was again admitted in the hospital. She presented with fever, productive cough, posterior thorax pain, fatigue, loss of appetite and muscle pains. The CT scan of the thorax showed modifications compatible with diagnosis of caseous-cavitory secondary pulmonary tuberculosis of the left superior lobe and ulcerated infiltrative of the right superior lobe and right medium lobe. Blood cell count showed low red blood cells ($3.31 \times 10^6/\mu\text{L}$), low hemoglobin (10.1 g/dL) and hematocrit levels (28.6 %) and normal platelets and white blood cell count ranges. Lactat dehydrogenase and C-reactive protein levels were 319 U/L, above reference limits (135-214 U/L) and 203.08 mg/L respectively. AST, ALT and creatinine levels were in normal ranges. Like in the previous presentation, she tested

positive for MTB in the microscopic exam and GeneXpert MTB/RIF assay without Rifampicin resistance and cultures on Löwenstein-Jensen and MGIT both came out positive. She received antitubercular medication with Isoniazid, Rifampicin, Pyrazinamide and Ethambutol and the antiviral therapy with Emtricitabine/Tenofovir and Isentress and was transferred at the local Pneumology Hospital with recommendation of follow-up after discharge.

4. Discussion

HIV-MTB co-infection is prevalent worldwide - especially in low-income and developing countries - and its clinical consequences are well known. Tuberculosis is the most common opportunistic disease and tends to be lethal in HIV-positive patients. HIV-positive patients with MTB latent infection have a higher risk of reactivation and developing severe forms of the disease. Disseminated disease and extrapulmonary forms occur more frequently in HIV, especially in patients with high viral load and low values at T-CD4 cell count [5]. Clinical studies have shown that tuberculosis is likely to be undiagnosed in HIV-positive patients; this error may occur due to non-specific symptoms. A suspicion of tuberculosis should be considered in HIV infected patients with pneumonic manifestations; delayed initiation of anti-tubercular therapy, may lead to disease progression, decreased survival rates and higher mortality rate, especially in patients with advanced immunosuppression [6,7]. The diagnosis of tuberculosis is confirmed by a combination of factors, such as clinical and radiological features, microscopic exam, cultures and GeneXpert MTB/RIF assay [8]. GeneXPERT MTB/RIF assay is considerably more effective at detecting TB than sputum microscopy with no significant difference in performance by sex or HIV status [9]. This case report describes a known HIV-positive patient who presented with signs and symptoms of active tuberculosis, such as fever, productive cough and fatigue. The CT scan of the thorax showed cavitory-caseous pulmonary tuberculosis of the superior left lobe. The patient had a history of irregular antiretroviral treatment, detectable high viral loads (603.000 copies/ml) and low T-CD4 lymphocytes count (6 cells/ mm^3). MTB DNA was detected using PCR (GeneXpert MTB/RIF assay) without Rifampicin resistance.

Challenges in the co-management of HIV and MTB include additive drug toxicities, potential medication interactions and complications, including IRIS or multi-drug resistant TB (MDR-TB) [10]. IRIS (Immune reconstitution inflammatory syndrome) may evolve in HIV and MTB co-infected subjects who receive treatment with both anti-tubercular medication and antiretroviral drugs [11]. Risk factors for IRIS include low CD4 count (values lower than 50 cells/ mm^3), severity of tuberculosis disease and less than 30-day interval between initiation of TB and HIV therapy. Inadequate initial treatment may increase the possibility of progressing to MDR-TB, even if the prevalence is low. MDR-TB remains a preoccupation not only because of its longer duration and difficult

treatment management, but also because of its associated higher transmission risk among contacts and increased mortality rates in HIV co-infected subjects [12,13,14,15].

5. Conclusions

To summarize all this, challenges in the diagnosis and therapy of HIV-MTB co-infection involve precision of standard diagnostic techniques than can often conduct to false-negative results, challenges such as patient's therapy compliance, potential drug toxicities and interactions. Complications such as IRIS may sometimes raise diagnostic challenges and influence management results. In general, concomitant therapy is preferred rather than a delay in therapy for both diseases [11,12].

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