

TB or not TB in HIV infection

Tuberculoza: a fi sau a nu fi în infecția HIV

Diana Veronica

Costache^{1,3}, Ina Isac^{2,3},
Traian Mihăescu^{1,3},
Carmen Manciu^{2,3}

1. Clinic of Pulmonary Disease,
Iași

2. "St. Parascheva" Infectious
Disease Hospital, Iași

3. "Grigore T. Popa" University
of Medicine and Pharmacy Iași

Corresponding author:

Diana Veronica Costache
Pulmonology resident, Clinic of
Pulmonary Disease, Iași, Str. Dr. I.
Cihac, no. 30, Iași
E-mail: costachedianaveronica@
gmail.com

Abstract

The progression of tuberculosis (TB) is significantly faster in patients with HIV infection. TB is also the main cause of death for HIV-infected individuals, resulting in fatality for 1 of 3 patients. We present the case of a 26-year-old male who arrived at the hospital having previously been diagnosed with HIV in 2014, but was not compliant to the ARV treatment prescribed. The patient presented with acute onset of fever, cough, hemoptysis and malaise. Investigations such as sputum samples and a lymph node biopsy revealed the presence of *M. tuberculosis* in optic microscopy, which led to a diagnosis of pulmonary and ganglionic TB. As one of the first opportunistic infections that occur in HIV-infected individuals, TB may be one of the earliest clues of an HIV infection. Current guidelines recommend that all individuals diagnosed with HIV should also undertake testing for TB infections.

Keywords: HIV, pulmonary tuberculosis, ganglionic tuberculosis, treatment adherence

Rezumat

Progresia tuberculozei (TB) este semnificativ mai rapidă la pacienții infectați cu HIV. TB este și principala cauză de deces la cei infectați cu HIV, conducând la un deces din trei cazuri. Prezentăm cazul unui pacient de 26 de ani diagnosticat cu infecție cu HIV în 2014, care nu a fost compliant la tratamentul antiretroviral. Pacientul a prezentat debut brusc cu febră, tuse, hemoptizii și alterarea stării generale. Examenele de spută și biopsia ganglionară au relevat prezența *M. tuberculosis* la examenul microscopic, conducând la diagnosticul de TB pulmonară și ganglionară. Fiind una din primele infecții oportuniste care apar la indivizii infectați cu HIV, tuberculoza poate fi unul din primele indicii ale unei infecții cu HIV. Ghidurile actuale recomandă ca toți pacienții infectați cu HIV să facă și teste pentru infecția tuberculoasă.

Cuvinte-cheie: HIV, tuberculoză pulmonară, tuberculoză ganglionară, aderență la tratament

Introduction

According to UNAIDS, 42 million people in the world have HIV infection. Unprotected sex is the main method of transmission of HIV in patients newly diagnosed with the disease. Voluntary counseling and testing may cause changes in the sexual behavior of individuals, prompting them to use condoms, thereby reducing the rate of infection. Globally, undiagnosed and late stage diagnosed HIV infection is a feature of many epidemics in the developed world.

The World Health Organization (WHO) is estimating that one third of the world's population is infected with *Mycobacterium tuberculosis*, which results in an estimated 9 million new cases of active TB in 2010. Worldwide, 14.8% of TB patients manifest an HIV coinfection. The incidence of TB in association with HIV is believed to have reached a maximum at 1.39 million in 2005 and is currently decreasing. On the other hand, globally, TB is still the most common cause of death throughout patients with AIDS, causing fatalities for 1 of 3 patients.

Case report

We present the case of a 26-year-old male patient who first presented to the Infectious Disease Hospital presenting nausea, vomiting, diarrhea, fever and chills. The symptoms had an insidious start two days prior to hospitalization. Personal history: he had not been hospitalized prior to coming to the clinic. The medical history revealed a significant weight loss (10 kg in two months), a progressive deterioration of health with an increase in physical asthenia and a prolonged fever. One significant detail was the account given by the patient for an unprotected sexual contact that he had with a female who was

registered in the database of the HIV regional center in Iași. The physical examination of the patient revealed an influenced general state, dry skin, coated tongue, submandibular, sublingual and bilateral laterocervical lymphadenopathy and painful abdomen on palpation. The blood tests showed an important inflammatory syndrome, and hepatocytolysis. The chest X-ray was normal, but the abdominal ultrasound showed a splenomegaly. Candidosis has also been found in oral secretions culture. During hospitalization, the patient received antibiotic treatment (ampicillin), metoclopramide, therapy with B₁ and B₆ vitamins, ranitidine, pyridoxine hydrochloride and aspartic acid, as well as intravenous electrolyte rebalancing with a favorable evolution. The unprotected sexual contact, the atypical evolution of the fever, and the poliadenopathy during hospitalization have raised the suspicion of an HIV infection. The HIV testing and CD4 serology count revealed a positive outcome, respectively a CD4 count of 26 cells/mm³. The patient was released with antiretroviral therapy.

Two months later, the patient presented at the Pulmonology Hospital. The physical examination showed cachexy, axillary and laterocervical lymphadenopathy, a superficial wound in the left armpit region, pale skin and hepatomegaly. The pulmonary auscultation showed coarse crackles, peripheral oxygen saturation of 98% and a heart rate of 95 bpm.

The patient underwent a thorough investigation. The chest X-ray showed micronodular lesions disseminated in both lungs. The abdominal ultrasound revealed an enlargement of the liver with a normal echostructure. The blood test revealed a hypochromic microcytic anaemia, neutropenia and an important inflammatory syndrome.

Samples from the left armpit region revealed *Corynebacterium spp.* The patient provided sputum samples, and also underwent a ganglionic biopsy, both revealing the presence of *M. tuberculosis* in optic microscopy. Therefore, the patient was diagnosed with pulmonary and ganglionic TB, for which the quadruple tuberculosis therapy was initiated while monitoring his liver function.

Throughout hospitalization, the patient was given psychological counseling, for him to better understand the disease, the importance of therapy, but also the consequences of interrupting the treatment. Having been discharged, the patient received a revised antiretroviral therapy and was scheduled for another evaluation after 6 months. When conducted, this final examination showed a weight gain of 10 kg and an increase of the CD4 values to 187 cells/mm³.

Discussions

HIV-seropositive persons are not more likely to acquire TB infection than HIV-seronegative individuals, given the same degree of exposure. However, the risk of rapid progression from infection to disease is significantly higher in persons with HIV infection, caused by the fact that HIV impairs the host's ability to handle new TB infection. Immunocompetent individuals who are infected with *M. tuberculosis* have close to a 10% lifetime risk of developing TB, half of the risk occurring in the first 2 years after infection. In contrast, HIV-infected patients with latent TB are almost 20-30 times more likely to develop the TB disease than those who are not HIV-infected, at a rate of 8-10% per year. HIV coinfection also increases the risk of progression of recently contracted infection to active disease. In several outbreak settings, 35-40% of the HIV-infected individuals exposed to TB in health care or residential settings have developed an active TB disease within 60-100 days of exposure.

TB can manifest early in the course of HIV infection, but can occur in any timepoint. The risk of TB increases soon after infection with HIV. Although TB can be a somewhat early manifestation of the HIV infection, it is important to know that the risk of developing TB, and of a disseminated infection, increases as the CD4 cell count decreases. Even with effective immune reconstitution with ART, the risk of TB remains increased in HIV-infected individuals above the basal risk for the general population, even at high CD4 cell counts. The presentation of TB is also affected by the extent of HIV-related immunosuppression. In patients with CD4 count of more than 350 cells/ μ L, the clinical and radiographic presentation is close to that of patients without an HIV infection.

HIV-infected patients with TB usually respond well to anti-TB therapy, if the regimen includes isoniazid and rifampycin for all the duration of the TB treatment. As for HIV-uninfected patients, the standard recommendation for HIV-coinfected individuals with pulmonary TB is for a 6-month course of treatment, with extension to

9 months for patients with cavitory lung disease and culture positivity after 2 months of TB treatment.

The risk of adverse reactions to TB treatment is higher in HIV-infected individuals than in HIV-uninfected individuals, occurring in up to 25% and 13%, respectively. Hepatotoxicity is common in the treatment of TB in HIV-infected patients, and may be exacerbated by overlapping toxicities with antiretroviral (ARV) and antibiotic treatment.

Conclusions

As one of the first opportunistic infections that occur in HIV-infected individuals, TB may be one of the earlier clues of an HIV infection. Addressing TB offers the opportunity for an early HIV intervention.

HIV is a driver for the TB epidemics by increasing the incidence of TB and TB-related fatalities in a population of immunodeficient patients that are susceptible for both primary and reactivated TB. However, it remains uncertain how much HIV-associated TB contributes to the transmission of TB in the community. HIV may decrease the infectiousness of TB due to a lower probability of cavitory disease and higher frequency of smear-negative pulmonary TB and extrapulmonary TB, which decreases the mycobacterial load in the sputum.

Current guidelines are recommending that all persons should undertake testing for latent TB infection with either a tuberculin skin test (TST) or gamma interferon (IFN- γ) release assays (IGRAs) at the time of the HIV diagnosis. For those who test positive, a chest-X ray should be obtained. For those who present chest-X ray abnormalities and for those with a normal chest-X ray for whom the suspicion of disease is high (patients with symptoms and those originating from an area where the disease is endemic), guidelines are recommending that three sputum samples for AFB smear and culture should be obtained in the morning on different days as part of the initial evaluation for a suspected pulmonary TB. On the other hand, the WHO recommends symptomatic screening for active TB in HIV-infected patients. However, there is no current universal agreement on what screening involves, with many national programs screening for cough alone. Taking into account that a significant proportion of HIV-infected individuals with active TB have less specific symptoms or have no symptoms at all, screening for cough alone will miss the majority of patients with culture-confirmed TB. ■

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