CASE REPORT

Miliary tuberculosis as a complication of untreated AIDS: a case report

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Abstract

Introduction: Miliary tuberculosis (TB) is the most common bacterial opportunistic infection in patients with advanced stage of acquired immunodeficiency syndrome, particularly in those not undergoing antiretroviral therapy (ART). The described patient was admitted to the infectious diseases ward due to disseminated TB affecting multiple organs.

Case description: The patient was diagnosed with human immunodeficiency virus (HIV) infection 20 years ago, and initially received ART with good results. However, due to discontinuing ART for several years resulting in significant immunosuppression, the patient developed pulmonary TB at the end of 2020. Initial treatment was effective, but six months later, there was a recurrence in the form of severe miliary TB. The patient's condition was critical upon admission. Antituberculosis treatment and ART were applied, leading to an improvement in his condition. A year after *Mycobacterium tuberculosis* infection, follow-up renal function test revealed permanent kidney damage.

Conclusions: This case highlights the importance of strict adherence to medical recommendations and consistent intake of ART. In the case of HIV/TB co-infection, attention should be given to efficient infection diagnosis and prompt initiation of antituberculosis treatment and ART. Severe opportunistic infections in HIV-infected patients can lead to chronic kidney diseases, which should be considered when planning the continuation of ART.

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Key words: tuberculosis, AIDS, kidney failure, antiretroviral drug therapy.

Introduction

Infection with *Mycobacterium tuberculosis* is an acquired immunodeficiency syndrome AIDS-defining illness and a major cause of deaths among people living with human immunodeficiency virus (HIV) [1-4]. This co-infection nearly doubles mortality rate. Without tuberculosis (TB) treatment and antiretroviral therapy (ART), mortality rate reaches nearly 100% [5]. Here, we presented a case with miliary TB as a relapse of pulmonary TB effectively treated in the first half of 2021.

Case description

A 53-year-old man with a 20-year history of HIV and hepatitis C virus (HCV) co-infection was admitted to the Department of Infectious Diseases on May 26, 2021, due to a severe cachexia, weakness, high-grade fever, persistent abdominal pain, recurrent diarrhea, and loss of appetite. He was referred from a HIV/AIDS clinic, where he presented for a check-up after treatment interruption. The patient has been receiving ART from 2009 to 2014, but discontinued the treatment for unspecified reasons. He was infected with HIV through in-

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travenous drug use (currently abstinent), and had a history of alcohol abuse and smoking. Due to pulmonary TB diagnosed in December 2020, he was treated in a TB clinic for weeks before the current admission. The patient was taking antituberculosis drugs till May 2021.

On admission, physical examination revealed signs of cachexia and dehydration as well as a soft enlarged lymph node on the right side of the neck and an organizing abscess (1 cm in diameter) on the left side. Auscultation of the lungs revealed no pathological findings.

Laboratory tests showed anemia (red blood cell [RBC], 4.2 × 10^6/μl; hemoglobin [Hgb], 10.8 g/dl; hematocrit [HCT], 32.6%), hyponatremia, hypochloremia, significantly elevated levels of D-dimers (7246 ng/ml), C-reactive protein [CRP] (193.99 mg/l), procalcitonin [PCT] (0.907 ng/ml), and creatinine (1.37 mg/dl) as well as presence of HCV RNA and high cytomegalovirus (CMV) viremia. CD4+ T cells count was 16 cells/μl, while HIV RNA was 106,899 copies/ml. Other infections were excluded. However, TB bacilli was found in a sputum smear and BAL (bronchoalveolar washing).

In chest X-ray and computed tomography (CT) scan, numerous small nodular changes with a diameter of 3 mm and a tendency to coalesce, small amount of fluid in the pleural cavity, and enlarged mediastinal lymph nodes (14 × 11 mm) were found. On the fourth day of the patient's hospital stay, standard antituberculosis treatment was initiated consisting of isoniazid, rifampicin, ethambutol, pyrazinamide, and streptomycin. During second week of hospitalization, signs of upper gastrointestinal bleeding were observed due to numerous ulcers in the stomach and esophagus typical of CMV-induced inflammation. Treatment with ganciclovir and PPIs resulted in cessation of bleeding. At the same time, ART was initiated with dolutegravir, emtricitabine, and tenofovir disoproxil. Additionally, the patient received ceftriaxone and metronidazole (due to recent laparoscopic appendectomy), prophylactic co-trimoxazole (*Pneumocystis jiroveci* pneumonia prevention), and symptomatic treatment. Despite the applied treatment, the patient's condition deteriorated, with fever rising up to 38.5°C, slow movement, time and place disorientation, no focal neurological signs, increased PCT up to 20 ng/ml and CRP up to 218.1 mg/l, recurrent renal dysfunction after initial improvement, hypoprothrombinemia, and pancytopenia. During hospitalization, lumbar puncture and magnetic resonance imaging (MRI) of the head were not performed.

A non-contrast head CT revealed hypodense areas in the left parietal and occipital lobes of unclear nature, small hypodense aggregation near the body of the left lateral ventricle, in the left centrum semiovale, and in both cerebellar hemispheres. Abdominal and pelvic CT showed hepatomegaly and splenomegaly, hypodense aggregation in the spleen, and an infarct-like area in the lower pole as well as hypodense area in the right kidney (infarct-like) and enlarged heterogeneous prostate gland with a gas-containing hypodense focus consistent with an abscess. Numerous enlarged lymph nodes with signs of necrosis were found in the liver hilum, around the celiac trunk, in the mesentery, and the periaortic and perirectal areas on the right side.

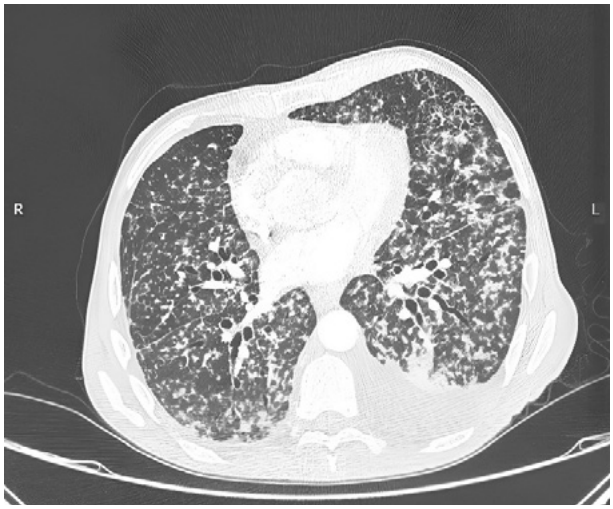

Figure 1. Computed tomography of the chest. Visible miliary, uncountable nodular changes in the lung parenchyma consistent with miliary tuberculosis

Figure 2. Computed tomography of the abdomen and pelvis. Hypodense areas are visible in the lower pole of the spleen and the right kidney, indicating dissemination of tuberculosis to extra-pulmonary organs

Finally, antituberculosis therapy was continued for 80 days in the TBC department. Clinical improvement was observed during further treatment, with 4 kg weight gain over two months, resolution of respiratory failure symptoms, and normalization of renal parameters. Three months after start-

ing antituberculosis treatment, sputum tests showed no *Mycobacterium tuberculosis*. Follow-up radiological examination indicated the persistence of small nodular changes in the lungs, but less severe compared with previous scan. Abdominal ultrasonography showed partial regression of changes, especially in the spleen, with no enlargement of abdominal lymph nodes. The patient was discharged on August 30, 2021, with a recommendation to continue antituberculosis treatment and ART.

During follow-up, hematology and renal function tests indicated slowly improving anemia and concerning increase in creatinine level (one month after the last hospital stay: 4.29 mg/dl; estimated glomerular filtration rate [eGFR], 20.56). Tenofovir with emtricitabine was discontinued, and the patient was switched to lamivudine, while dolutegravir was maintained. A year after the TB diagnosis, the patient reported dizziness, tinnitus, and diarrhea. Hospital diagnostics for chronic diarrhea excluded celiac disease. Head MRI did not identify a focal cause for the dizziness. The patient is currently in good condition, has gained 50 kg of weight from 2021, regularly attends outpatient department for HIV-positive patients, and systematically uses ART. His CD4+ T cell count is currently 328 cells/μl and HIV RNA level below detection limit (with 70 IU/ml sensitivity used). He completed successful treatment for chronic hepatitis type C.

Discussion

In the presented patient, miliary TB related to vast lymphocyte CD4+ deficiency due to untreated HIV infection was diagnosed. The patient was admitted with typical symptoms, such as infiltrative changes and lymphadenopathy [6, 7].

For diagnosis confirmation, bacteriological smear of sputum, blood culture, sputum, or BAL are necessary, but these methods used for years do not provide the whole picture of patient's disease, with additional waiting time for results ranging from 6 to 10 weeks. In the presented case, sputum culture was positive for MTC in two weeks, whereas blood culture in 4 weeks. The diagnostic method recommended by the WHO and the Polish AIDS Society is the rapid molecular test (e.g., expert MTB/RIF), which in approximately 2 hours shows information about the presence of mycobacteria or drug resistance [8]. Because of the typical clinical presentation of TB and the fact that miliary TB was recurrent to the lung TB, this test was not performed.

Medical imaging, such as chest X-ray, is helpful in assessing the spread of MTB bacilli in the body that allows to make the primary diagnosis – TB. Other authors also emphasized the great importance of X-rays in making the correct diagnosis [9]. CT scanning of the head, chest, abdominal cavity, and pelvis facilitates detection of hypodense mycobacterial aggregation in disseminated TB [10], as it was found in our patient [9, 11].

According to the recommendations of PTN AIDS and EACS, ART should be initiated immediately in a patient with TB and CD4+ T lymphocytes < 100 cells/μl, along with the use of tuberculostatic. However, we should be aware of the high-risk of immune reconstitution syndrome [8, 12]. Our patient received standard antituberculosis therapy together with ART, and gradual improvement was achieved.

The patient's follow-up examination revealed reduced renal function caused by multiple factors, such as infarct area in the kidneys (miliary disease), anti-TB drugs (particularly rifampicin), and nephrotoxicity due to tenofovir. However, in advanced TB, this therapy is absolutely recommended, and its interruption may reduce the effectiveness of systemic treatment [13, 14].

The key aspect is the patient's discontinuation of ART, despite his knowledge of the subsequent consequences, such as an increase of HIV RNA level, failure of the immune system, and recurrence of previously treated TB [15-17].

Conclusions

Even with the availability of modern and effective ART, late diagnosis of HIV infection still occurs. The awareness of having a life-threatening disease and consequences of not undertaking treatment may motivate patients to start the therapy, which offer the chance to improve their health and quality of live.

Disclosures

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4. Conflicts of interest: None.

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