

Case report

Disseminated tuberculosis with pulmonary and renal infections: A confirmed case in a severely immunocompromised HIV patient

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Tuberculosis continues to be a major public health issue. The advent of human immunodeficiency virus (HIV) infections led to a dramatic increase in extrapulmonary forms of tuberculosis, with a non-negligible number of cases with multifocal lesions. This study reports a disseminated tuberculosis case with pulmonary and renal localization in a severely immunocompromised HIV patient diagnosed by microscopic examination and the GeneXpert MTB/RIF on sputum and urine in the absence of a urine test, in particular, the urine lipoarabinomannan assay (TB-LAM).

Key words: Tuberculosis, disseminated, immunosuppression, HIV, Bangui.

INTRODUCTION

In 2019, the WHO reported 10 million cases of tuberculosis (TB) in the world, with 8.6% occurring in people infected with the human immunodeficiency virus (HIV) (WHO, 2019). In the reported extrapulmonary forms, which represent 15% of all TB cases, renal TB is considered to be one of the most severe forms of the disease, accounting for up to 27% of extrapulmonary TB (WHO, 2019; Altiparmak et al., 2015; Daher Ede et al., 2013). Renal TB may be due to a disseminated TB infection or to an isolated urogenital infection (Daher Ede et al., 2013). In the past, sputum smears and culture were the only diagnosis methods available. These conventional tests generally have poor sensitivity; but the

advent of automated tests, such as the GeneXpert tests, has made it possible to explore new avenues for diagnosing renal TB. Xpert MTB/RIF tests came out in 2010 and the Xpert MTB/RIF Ultra tests have been available since 2017 (Dorman et al., 2018); however, the WHO still only recommends the urine lipoarabinomannan (TB LAM) assay to diagnose TB in urine (WHO, 2015). The Central African Republic (CAR) remains a high TB burden country, with an incidence of 540 cases for 100,000 inhabitants and a prevalence of 25% for TB in patients living with HIV (WHO, 2019; Ministry of Public Health and Population, 2018). The diagnosis of TB relies mainly on hot Ziehl-Neelsen staining of sputum smears

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for microscopic examination. Since January 2019, Xpert MTB/RIF has been the first-line diagnosis method at the National Reference Laboratory for TB (NRL-TB; Institut Pasteur in Bangui, CAR) for patients with a suspicion of TB and for retreatment patients. The TB LAM test has been adopted by the National TB Control Program (NTCP) as the urine test for TB in HIV patients, but this test is not yet operational in the CAR. Here, a disseminated pulmonary and renal TB case diagnosed using microscopy and the Xpert MTB/RIF test on a severely immunocompromised HIV patient were reported.

CASE REPORT

A male patient, 47 years of age, was hospitalized in the Infectious Diseases Department at the Amitié Sino-Centrafricaine (ASC) Teaching Hospital on the 25 February 2019 for cough, inconsistent speech and fever. The patient had been coughing for three weeks with mucous expectoration; two days before hospitalization, the patient showed delusional behavior with inconsistent speech. The fever had started three weeks earlier, occurring in the evening with nocturnal sweating; the fever was accompanied by asthenia and anorexia. The patient did not have chest pains or urinary disorders.

Upon examination, the patient's temperature was 38°C, pulse of 90 bpm, respiration rate of 24 breaths/min, Glasgow score was 15/15, and body mass index was 19 kg/m²; he had no peripheral lymphadenopathy and ultrasound did not reveal any cervical lymphadenopathy. The chest X-ray was also normal. Lumbar puncture revealed clear cerebrospinal fluid (CSF) and the cytological and biochemical analyses were normal. The CSF proved to be sterile after direct observation and culture.

HIV serology was positive, CD4+ T lymphocyte was 54 mm⁻³ (FACS Canto II flow cytometer). Using the Xpert HIV-1 Viral Load kit, the HIV viral load in this antiretroviral treatment-naïve patient was 790 000 copies/mm³. A chemoprophylactic treatment based on cotrimoxazole was implemented immediately. Acid-fast bacilli (AFB) were screened for in sputum smears twice at the Bacilloscopy Unit at the ASC hospital; both samples were negative. Given the severely immunocompromised state of the patient, sputum and urine samples were sent to the NRL-TB.

There, a 10 mL urine sample was centrifuged at 3000 rpm for 15 min; using a 10 µL inoculation loop, the pellet was sampled to prepare a smear for Ziehl-Neelsen staining. The rest of the pellet was resuspended in 1.5 mL of distilled water for the Xpert MTB/RIF test according to the classic procedure. Direct observation of the urine pellet smear showed exactly 8 AFB and the Xpert MTB/RIF tests on the sputum and urine were positive for *Mycobacterium tuberculosis*, but the resistance to rifampicin was not detected. These tests made it possible

to diagnose disseminated TB with pulmonary and renal infections in a severely immunocompromised HIV patient.

In compliance with national guidelines on susceptible TB, treatment with ethambutol/isoniazid/pyrazinamide/rifampicin began on 6 March 2019. Two weeks later (21 March 2019), antiretroviral treatment with efavirenz/emtricitabine/tenofovir commenced. After six months of anti-TB medication, the patient was declared cured on 8 September 2019. The clinical and immunovirological status was favorable; the patient was asymptomatic after six months of treatment and his body mass index was 23 kg/m². The CD4+ T cell was 230 mm⁻³ and the HIV viral load <40 copies/mm³.

DISCUSSION

TB is by far the most frequent opportunistic infection in HIV patients and extrapulmonary forms are often observed in HIV patients, with sites other than the lungs being infected. Renal TB is the most common extrapulmonary TB found in HIV patients, with TB spreading from the primary site (lungs) via the circulatory system (Daher Ede et al., 2013; Hillemann et al., 2011). In the CAR, an HIV infection is often diagnosed late and frequently during an opportunistic, identifiable infection such as TB. At this stage, immunosuppression has already progressed, leading TB to develop multifocal lesions directly, as in the case reported here. In the absence of specific urine tests – albeit recommended by the WHO – the Xpert MTB/RIF was a test of prime importance for us (WHO, 2015). The usefulness of GeneXpert tests on urine has already been reported, particularly recently with Xpert Ultra tests (Hillemann et al., 2011; Tortoli et al., 2012; Atherton et al., 2018). In this case study, there were no urinary disorders and no cytological examinations had been requested or carried out on urine samples to detect a possible urinary infection. With a new grant from the Global Fund, the national TB control program plans to use the TB LAM urine test to diagnosis TB in patients living with HIV as of 2021. We hope that the TB LAM test can effectively be implemented, because it can help diagnose TB in areas where Xpert MTB/RIF tests are not yet in operation.

Conclusion

TB and HIV remain the most frequently encountered co-infections in hospitals, particularly in resource-limited countries such as the CAR, where both diseases have relatively high prevalence rates. The systematic use of TB LAM tests to diagnose TB in urine samples are necessary for the CAR health system to diagnose TB in people living with HIV, who are the most vulnerable patients and most likely to show renal TB in addition to the pulmonary form.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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