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Case report

Mycobacterium tuberculosis infection in a HIV-positive patient

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ABSTRACT

Mycobacterium tuberculosis (MTB) and human immunodeficiency virus (HIV) coinfection remains a global public health challenge. We report a 40 year old African American male who is a known HIV-positive patient, non-compliant with his antiretrovirals and developed pulmonary tuberculosis. His chief complaints were chronic cough, fever, night sweats and undocumented weight loss. He had a prior positive T-SPOT-TB test; however, chest radiograph and sputum smear examination revealed normal results. PCR-based GeneXPERT MTB/RIF assay was ordered and confirmed MTB infection. The sputum cultures grew MTB and sensitivities showed susceptibility to all primary anti-tuberculosis medications. A delay in diagnosis and initiation of MTB therapy, in the setting of HIV or AIDS, may result in rapid disease progression and worse clinical outcome.

1. Introduction

Mycobacterium tuberculosis (MTB) and human immunodeficiency virus (HIV) co-infection is one of the major public health burdens globally. According to the World Health Organization (WHO), nearly 15% of individuals diagnosed with MTB were HIV positive and a total of 360,000 deaths were attributed to MTB-HIV coinfection alone [1,2]. Clinical evidence suggests that MTB is the most common opportunistic infection causing exacerbation of viral load and diminished CD4 count in HIV patients. It also remains the leading cause of death in patients with Acquired Immunodeficiency Syndrome (AIDS) [2–4]. Reciprocally, by decreasing the body's cell mediated immunity, HIV increases the risk of MTB progression and reactivation of latent TB infection (LTBI) [5]. HIV coinfection can alter the pathogenesis of MTB and lead to negative sputum smear results, atypical radiographic manifestations and extrapulmonary manifestations, which poses difficulty in diagnosing MTB disease [6,7]. The synergistic repressive effect of MTB and HIV on the immune system, drug interactions and their overlapping toxicities, and the existence of a condition called immune reconstitution inflammatory syndrome (IRIS) complicate the co-treatment of MTB and HIV [8,9]. Here we report a patient previously diagnosed with HIV and a history of non-compliance with his anti-retroviral medications, who subsequently developed MTB disease.

2. Case report

A forty-one year old African American male with a history of HIV infection was arrested and sent to jail for his offense. He was previously diagnosed with HIV in 2005. He had a history of non-compliance with his highly active antiretroviral therapy (HAART) and was currently not on any medications. He was screened at the correctional facility for complaints of fever, night sweats, cough and undocumented weight loss for the past four weeks. The laboratory studies demonstrated a white blood cell count of $3.73 \times 10^3/mm^3$, normal liver function profile, CD4 count of $130/mm^3$ and viral load of >500,000 copies/ml. The chest x-ray obtained was normal. The patient's T-SPOT.TB *(Oxford Immunotec Inc, Marlborough, MA*; TST), an Interferon Gamma Release Assay (IGRA) test, performed a year ago, was positive. Unfortunately, no further evaluation was done by the primary physician at the time. The sputum collected during the current work up was smear-negative, but the PCR-based analyses with the GeneXPERT MTB/RIF assay detected *M. tuberculosis* in the specimen and showed no rifampicin (RIF) resistance. The patient was initiated on four drug anti-tuberculous therapy with isoniazid (INH), rifampin (RIF), ethambutol (EMB) and pyrazinamide (PZA). The sputum culture grew *M. tuberculosis* after four weeks of incubation and sensitivities showed the organism to be susceptible to all the aforementioned primary anti-tuberculous drugs.

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3. Discussion

The case report describes a known HIV-positive patient who presented with signs and symptoms of active tuberculosis such as chronic cough, fever, night sweats and weight loss of approximately four weeks duration. However, his normal chest x-ray and smear-negative sputum exam was misleading from the diagnostic viewpoint. Clinical evidence has shown that the likelihood of misdiagnosing MTB is higher in patients infected with HIV [10]. The diagnostic difficulty arises from non-specific symptoms, absence of typical radiological presentations and sputum smears that are negative for acid fast bacilli (AFB), which are more frequently observed in HIV co-infected patients. Studies have shown that radiographic presentations of MTB among HIV-infected patients are either unremarkable or would appear as adenopathy rather than lung consolidation/cavitation commonly seen in non HIV patients [11]. A low CD4+ lymphocyte level has also been linked to the atypical chest x-ray findings seen in MTB-HIV coinfections [12]. Down-regulation of the body's immune response to MTB infection in HIV/AIDS compounded by high viral load is a potential reason for the diagnostic dilemma [13]. A high index of suspicion should be exercised in HIV infected patients with pneumonic presentations because delayed initiation of anti-tuberculosis therapy, especially in patients with advanced immunosuppression, may lead to MTB progression, decreased survival and higher mortality rate. The diagnosis of MTB is confirmed by a combination of various factors including clinical and radiological features, IGRA, Tuberculin skin test (TST), AFB, culture and GeneXPERT MTB/RIF assay [14,15].

Utilization of newer laboratory methods is needed for timely diagnosis in scenarios when a definitive diagnosis of MTB cannot be formulated solely on clinical presentations. Growth based detection of *M. Tuberculosis* in cultures and molecular techniques such as Nucleic Acid Amplification Testing (NAAT) are proven to be more reliable in diagnosing MTB infection and determining drug resistance based on their reproducibility and high specificity [16,17]. However, concerns on high cost, requirement of technical expertise and strict quality control limit the use of the NAAT method. T-SPOT TB test, an Interferon gamma release assay (IGRA), is a blood test that measures immune reactivity to *M. Tuberculosis*. It must be stressed that once a prior positive IGRA or TST test has been noted, it should be rigorously followed-up [18]. However, IGRA tests cannot delineate between latent TB infection and active disease. The tests may also show both high false positives and false negatives (conversion/reversion), especially in the settings of MTB-HIV coinfections [19]. Here in belies the significance of the diagnostic capabilities of the recently introduced PCR-based GeneXPERT MTB/RIF assay, including detection of smear-negative cases and extrapulmonary tuberculosis, a frequent presentation in HIV-MTB coinfection [20,21]. GeneXPERT MTB/RIF assays have been enthusiastically introduced in regions highly affected with MTB-HIV coinfections, such as in South Africa [22,23]. The paucibacillary nature of the disease, especially in HIV-MTB coinfections, poses special problems. 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 [20,21].

Challenges in the co-management of MTB and HIV include cumulative drug toxicities, potential drug interactions, pill burden and complications such as IRIS and multi-drug resistant TB (MDR-TB) [24]. WHO and Centers for Disease Control and Prevention guidelines recommend the standard 6-month course of MTB therapy consisting of INH, RIF, EMB and PZA regardless of HIV status. However, in HIV infected individuals with CD4 count of <200 mm^3, the guidelines strongly suggest starting HAART between 2 and 8 weeks after initiation of anti-TB medications [25]. IRIS may develop in MTB and HIV co-infected patients who are treated with anti-TB medications concomitantly with HAART [26]. This risk is estimated to occur in 11%–45% of patients co-infected with TB and HIV, and is enhanced with early institution of therapy, as circulating CD4s cause exaggerated response to the macrophage-restricted *M. tuberculosis* [27]. Predictors of IRIS include CD4 count <50 cells/mm^3; higher on-antiretroviral therapy (ART) CD4 counts; high pre-ART and lower on-ART HIV viral loads; severity of TB disease, especially high pathogen burden; and less than 30-day interval between initiation of TB and HIV treatments. However, the strong emphasis is not to delay treatment for either illness [28]. On the other hand, inadequate initial treatment may lead to the possibility of development of MDR-TB, though the current prevalence is low. MDR-TB remains a concern not only because of its longer duration and complex treatment, but also because of its associated increased transmission risk among contacts and increased mortality rates in HIV co-infected patients [29].

4. Conclusion

In summary, challenges in the diagnosis and treatment of MTB-HIV coinfection include accuracy of standard diagnostic techniques which may be often reported as false-negative, challenges of polypharmacy including drug compliance, potential drug interactions and toxicities. Other complications such as IRIS may sometimes pose diagnostic challenges and affect management outcomes. In most cases, simultaneous treatment of MTB and HIV is preferred over a delay in therapy for both diseases. Moreover, the requirement for improved diagnostic methods like GeneXPERT MTB/RIF assay and aggressive MTB case detections in high risk populations especially individuals diagnosed with HIV/AIDS cannot be overemphasized.

Disclaimer

This case scenario was used in a previous review article to elucidate the importance of GeneXpert MTB/RIF assay. (Patil N, Saba H, Marco A, Samant R, Mukasa L. 2014. Initial experience with GeneXpertMTB/RIF assay in the Arkansas tuberculosis control program. *Australas Med J*. 7(5):203–207.)

Conflicts of interest

None.

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