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Case Report

Leprosy and Tuberculosis Coinfection : The Strength of Neglected Diseases

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This study reports a case of a patient with simultaneous clinical manifestation of tuberculosis and leprosy. The patient was treated for pneumonia with respiratory quinolone describing improvement in respiratory symptoms. A latter diagnosis indicated dimorphous lepromatous leprosy. Then, the patient reported a productive cough and fever. Chest radiography investigation of respiratory symptoms showed fibroreticularis infiltrate in the upper lobes and the bilateral peri-hilar region. Sputum smear microscopy for tuberculosis showed positive BAAR. The PCR analysis confirm the *M. tuberculosis*. In conclusion, leprosy patients should be properly investigated for tuberculosis for achieving optimum therapeutic outcomes for both the diseases.

Key words : Coinfection, Tuberculosis, Leprosy

Introduction

Leprosy and tuberculosis are granulomatous and caused by gram-positive bacilli (Donoghue 2019). The *Mycobacterium leprae* (*M.leprae*) is a weakly acid-resistant bacillus, unable to grow in vitro culture, an obligate intracellular pathogen that shows a tropism for Schwann cells (Mattos et al 2011). *Mycobacterium tuberculosis* (*M. tuberculosis*) is a strongly acid-resistant bacillus, an extra or intracellular pathogen in macrophages, cultivable in vitro (Huang et al 2015). These diseases are transmitted through the airways.

Leprosy initially adheres to the nasopharynx mucosa, while tuberculosis in the peripheral areas of the lungs. Tuberculosis characteristically manifests through respiratory symptoms. But both diseases can manifest cutaneously (Amraoui et al 2015).

Among the 30 countries with a high tuberculosis burden, which are responsible for 87% of new cases worldwide, India leads with the highest number of cases (WHO 2020). Regarding leprosy, three countries lead the notification of new cases: India, Brazil and Indonesia. Both diseases should

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be eliminated by 2030, following the health goals of the United Nations Sustainable Development Goals (WHO 2017).

The clinical manifestations of either disease after infection occur in a small part of the population. In leprosy, 3.75% of infected patients develop disease. While in tuberculosis, 10% of patients are affected (WHO 2020).

The immune defense against the two diseases depends on adequate specific cellular immunity. There are hypotheses that the activation of the immune system against one disease would prevent susceptibility to another (Dallmann-Sauer et al 2018, Lázaro et al 2010). Other points that the susceptibility to one disease would also generate vulnerability to the other. This theory is supported by the finding of genetic material from both diseases in archaeological evidence (Donoghue 2019).

Brazil notified, from 2014 to 2018, 140,578 cases of leprosy (13.7/100,000 habitants) and, in 2019, 73,864 cases of tuberculosis (35.0/100,000 habitants) (WHO 2017, WHO 2020). It now ranks 2nd in new cases of leprosy and the 18th concerning tuberculosis in the world. Based on such data, the question is whether co-infection was being underdiagnosed and not published or if the occurrence would be rare.

This study reports a case that occurred in Cuiabá, Mato Grosso, Brazil, in 2019, from a previously healthy patient with simultaneous clinical manifestation of tuberculosis and leprosy. The clinical course was favorable, with patient adherence to treatments.

Case report

Male patient, 36 years old, born in Cuiabá, MT, Brazil, attending general services in health, without previous comorbidities, forwarded to the reference service in leprosy at Julio Müller University Hospital (HUJM), in the city of Cuiabá,

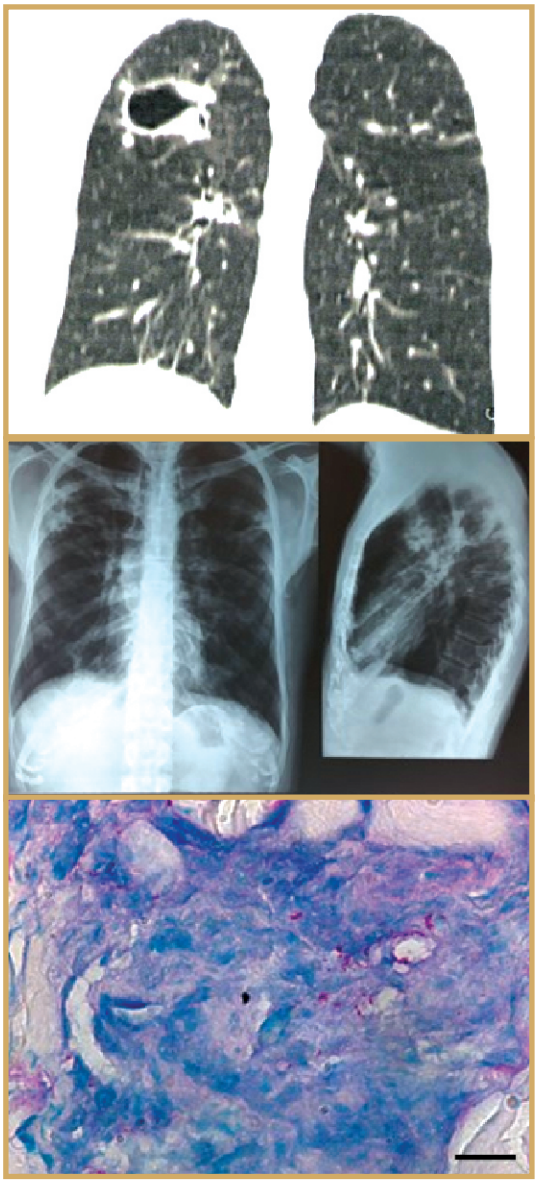

Fig. 1 : (a) Chest radiography and baciloscopy of patient with leprosy and tuberculosis co-infection. Fibroreticular infiltrates in the upper lobes and bilateral perihilar region, with small cavities in permeate. Elevated right diaphragmatic domes and specific pulmonary inflammatory process. (b) Tomography showed cavities. (c) Histopathological analysis shows bacilli stain with Fite-Faraco in the dermis. Bar=50 m.

MT, Brazil. Participant agreed to take part in the study. He initially signed the informed consent form, approved by the Committee for Ethics in Research of HUJM (CAAE No. 09292319.0.0000. 5541), taking into account the Resolutions no. 466/12 of the National Health Council and international ethical guidelines (Declaration of Helsinki).

The patient was treated for pneumonia with a quinolone (levofloxacin 500 mg/day for 05 days) describing improvement in respiratory symptoms. He was then diagnosed with dimorphous lepromatous leprosy with concomitant type 1 and 2 reactions due to bilateral ulnar abscesses with neuritis and knotty erythema (Ridley & Jopling 1966). The attending physician prescribed corticosteroid therapy (prednisone 80 mg/day), anti-helminthic treatment (albendazole 400 mg/day for 05 days) and polychemotherapy multibacilary (PCT/MB) for leprosy (150 mg rifampicin, 300 mg clofazimine, and 100 mg dapsone). Additional tests revealed lymph smear microscopy for leprosy with an index of 4.25 and presence of globi (right ear +4, left ear +5, right elbow +4, left elbow +4). In the skin biopsy, the bacilloscopy with Fite-Faraco indicates an index of +6 (Fig 1c). The biopsy also showed an intense and diffuse lymphoplasmacytic infiltrate, suggestive of lepromatous leprosy. After 1 month, the patient´s follow up reported productive cough, chest, and back pain, daily fever not measured in the morning and at dawn, chills, however, without weight loss, lasting more than 2 weeks. Chest radiography investigation of respiratory symptoms showed fibroreticularis infiltrate in the upper lobes and the bilateral peri-hilar region, with small intervening cavities, elevated right diaphragmatic domes and specific pulmonary inflammatory process (Fig 1a). Tomography showed characteristic findings (Fig. 1b). Sputum smear microscopy for tuberculosis (BAAR) in 2 positive samples (+++), with visualization of globi in both. He was started on treatment with 150 mg rifampicin, 75 mg isoniazid, 400 mg pyrazinamide, and 275 mg ethambutol (RIPE) concomitantly with the second PCT/MB blister.

Molecular rapid test for tuberculosis with detection of drug sensitivity (GeneXpert MTB/RIF) was positive and did not detect resistance to rifampicin. DNA extraction was performed from intradermal scraping and sputum slides, according to Woods & Cole (1989). The PCR was purified using GFXtm PCR DNA with the PureLink™ genomic DNA extraction kit (Thermo Fisher Scientific, USA), according to the manufacturer's instructions. The second protocol for sputum slide used the primers INS1 (forward primer: 5'-CGT.GAG.GGC.ATC.GAG.GTG.GC-3') and INS2 (reverse primer: 5'-GCG.TAG.GCG.TCG.GTG.ACA.AA-3'), targeting a specific 245 bp region of the *M. tuberculosis* complex (Hermans et al 1990). The DNA sequence obtained from the positive sample for the *M. tuberculosis* PCR complex corresponded to the *M. tuberculosis* chromosome (CP046308.1). The accession number to the GenBank nucleotide sequence for the partial sequence generated in the present study is MT023079. The positivity of sputum in a molecular method for *M. tuberculosis* was important to differentiate *M. leprae* since direct visualizations of these bacilli are very similar.

Clinical follow-up of the patient demonstrated gastric intolerance controlled with symptomatic patients, the abolition of fever after 60 days of concomitant treatment, absence of laboratory changes despite the use of medications, persistent coughing until the end of antituberculosis treatment, but with a significant reduction in the frequency and productive content.

Leprosy reactions were controlled progressively. After tuberculostatic treatment, BAAR revealed bacilli absence in sputum. And control tomo-

graphy described cavitary lesions in the upper and lower right lobes, with predominantly sequelae characteristics.

After RIPE, the patient remains in clinical follow-up and continues treatment for leprosy with PCT/MB, prednisone 5 mg/day (at weaning), gabapentin, and trauma for neuropathic pain, without respiratory symptoms, with reasonable pain control and weight maintenance body.

Discussion

This case showed favorable leprosy and tuberculosis treatment without major side effects with the use of medications concurrently. However, respiratory recovery was slower.

Mangum et al (2018) have reported that leprosy patients who acquired tuberculosis had a common genetic predisposition for susceptibility. That would be contributing to microbial dissemination and is reduced in lepromatous leprosy patients (Donoghue et al 2005). Trindade and collaborators (2013) evaluated two patients with coinfection and did not observe anomalies in the presence of TCD^{4+}, TCD^{8+}, and B cells and the interleukin-12/23 receptor (IL-12/23R) and the IFN- receptor (CD119).

There is no specific recommendation in Brazil for screening reactive leprosy patients on long-term corticosteroid therapy to investigate latent or active tuberculosis. Similar situation may exist in some other countries as well. While other non-infectious and infectious diseases exist fully structured protocols for the screening of tuberculosis (Getahun et al 2015). Keragala and colleagues (2020) report that the use of steroids in the treatment of leprosy may increase the susceptibility to develop tuberculosis. Studies of Magnum and collaborators (2018) reported that 70% of cases were first diagnosed with leprosy and were late diagnosed for tuberculosis during steroids use.

Interestingly, Kama and colleagues (2019) have described a case, whereas multidrug-resistant tuberculosis may have precipitated an immunological reaction and unmasked the *M. leprae* co-infection.

It was also questioned if the use of rifampicin in the studied patient could induce resistance to tuberculosis. However, Rawson et al (2014) did not observe *M. tuberculosis* resistance after rifampicin used for leprosy. In the present case, there was no detection of resistance to tuberculosis demonstrated by GeneXpert test. Co-infected patients must be screened for resistance, especially if there are respiratory or constitutional symptoms. This is a risk that can occur in leprosy endemic countries like India and Brazil.

Conclusion

There is a need for screening for latent or active tuberculosis infection in patients diagnosed with leprosy as steroids may be required for varying periods in reaction cases. This report and earlier published studies indicate that leprosy patients should be screened for TB coinfection and likewise TB patients should be screened for leprosy so that such persons get appropriate treatment for both the conditions. Though the number may be small, consequences can be bad for patients having both the infections if not diagnosed and treated adequately.

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