Mycobacterium simiae infection in an immunocompetent elderly woman: case report in Roraima state of Brasil

Infecção por *Mycobacterium simiae* em paciente idosa imunocompetente: um relato de caso no estado de Roraima

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ABSTRACT

A *Mycobacterium simiae* pulmonary infection in an eighty-year-old patient attended to at the Tuberculosis Secondary Referral Outpatient Clinic in the city of Boa Vista, Roraima between 2016 and 2019. This study aims to report the symptoms, diagnostic methods, and treatment of the patient because for this rare case in Brazil, and this patient had a late and difficult diagnosis. Due to this difficulty, the patient was treated for pulmonary tuberculosis for years without being cured. Finally, after a correct diagnosis, the treatment was stopped due to failure.

KEYWORDS: Mycobacteriosis; Tuberculosis; Multirresistance.

RESUMO

Trata-se de um estudo de caso sobre infecção pulmonar por *Mycobacterium simiae* em uma paciente de 80 anos de idade, atendida no Ambulatório de Referência Secundária em Tuberculose da cidade de Boa Vista, estado de Roraima a partir do ano de 2016. O objetivo do estudo foi relatar os sintomas, métodos diagnósticos e tratamento da participante da pesquisa, por tratar-se de uma patologia pouco incidente no Brasil e caracterizada por diagnóstico tardio e difícil. Devido a essa dificuldade a paciente foi tratada durante anos para tuberculose pulmonar sem alcançar a cura. Por fim, após o diagnóstico correto, o tratamento foi encerrado por falência terapêutica.

PALAVRAS-CHAVE: Micobacteriose; Tuberculose; Multirresistência.

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INTRODUCTION

Mycobacterium simiae (Latin, simiae: monkey) is a non-tuberculous mycobacterium (NTM) rarely associated with diseases in humans[1]. Moreover, this is the only niacin-positive non-tuberculous mycobacterium, which may lead to a misdiagnosis of *M. tuberculosis*[1,2,3]. This mycobacterium was first described in 1965 as a new mycobacterium isolated from *Macacus rhesus* and *Cercopthecus aethiops* monkeys transported from India to Hungary[1,4]. In Brazil, the mycobacterium was first isolated from sputum samples of an HIV-positive patient in Araraquara, São Paulo in 1995. In 2001, the mycobacterium was isolated from blood samples of another patient with Acquired Immunodeficiency Syndrome (AIDS)[5]. In Israel, *M. simiae* is endemic. It has become the most isolated NTM in a microbiology laboratory of a local tertiary care center over the past few years[6].

Considering it's rarity in Brazil, and diagnosis and treatment difficulties, this study aims to report the first *Mycobacterium simiae* infection case in humans in the state of Roraima. Researchers suggest *M. simiae* enters the body via aerosol inhalation, water ingestion, other environmental sources, and infected animals and people. This ubiquitous mycobacterium has been isolated from multiple animal sources and environmental sites such as soil, milk, moss, food, and water, including drinking water and water used in hospital equipment[1,2]. However, no evidences of animal-to-human or human-to-human transmission have been found[2]. Medical diagnosis of *M. simiae* infection is late, due to it's infrequency and it's non-specific symptoms, usually mimicking pulmonary tuberculosis[1]. Treatment of NTM infections are difficult to diagnose as a result of the multiresistance to traditional antituberculosis drugs[7]. Therefore, identifying different species of NTM involved in infection cases, as well as developing in vitro studies to determine the most suitable treatment, are fundamental in such situations[1].

CASE REPORT

D.C. is a, 80 years old female, single, lawyer, who lives with two of her nephews and a cat in a brick house with a concrete roof in an upscale neighborhood in the city of Boa Vista – Roraima. She smoked for 40 years with a 60 pack per-year history. She stopped smoking 23 years ago and denied having any chronic diseases. She underwent a pulmonary tuberculosis treatment in 1982. She sought medical care at the Tuberculosis Secondary Referral Outpatient Clinic in Roraima in November 2016 and she reported having lost weight and a cough productive of yellow, sometimes bloody sputum. Nevertheless, she denied having a fever, chills or sweating. During physical examination, she was 1.68 meters tall, emaciated, weighing 54Kg, had normal lung auscultation, no hilar adenopathies or other relevant symptoms. In subsequent follow-up, crackles in the apex of the right lung and bilateral wheezing were detected.

Due to positive sputum smears (2++), treatment for pulmonary tuberculosis combining rifampin, isoniazid, pyrazinamide, and ethambutol started on December 3, 2016. Rapid molecular test result for TB (real-

time PCR) was negative. Conversely, growth was positive in Löwenstein-Jensen medium test. After that we sent the culture to the Hélio Fraga Intitute to identify the species. It was defined as *Mycobacterium simiae* through PRA-restriction enzyme technique (PCR using PRA restriction enzyme). On May 15, 2017, she started being treated with moxifloxacin (400mg/day), ethambutol (1,000mg/day), clarithromycin (1g/day) and intravenous amikacin (500mg three times per week). The latter being interrupted after the 40th dose due to partial hearing loss. Afterward, the sputum smear microscopy results were negative, but they went back to positive in the third month and kept being positive (2++) during the entire treatment. Concurrently, the patient took symptomatic relief medications due to gastrointestinal complaints.

Computed tomography of the chest in November 2016 showed multiple areas of bilateral centrilobular emphysema, cavitating lung lesion at the right base, tree-in-bud pattern in both lungs, 1-centimeter nodules in the upper left lobe and no lymphadenopathies. Chest CT one year and three months after the beginning of the treatment showed no improvement in her condition.

In the 15th month of treatment, sputum microscopy tests were still positive, which led to a new bacterial culture and a request for a MIC (minimum inhibitory concentration) calculation of the identified species. However, the mycobacteria identification sector of the Professor Helio Fraga Referral Center informed us that the test would not be performed because there was no standard technique for *Mycobacterium simiae.* After the 21st month of moxifloxacin, ethambutol and clarithromycin treatment, the patient showed improvement in her respiratory symptoms but she still had positive sputum smears (2++), a 7.4-kilogram weight loss, and the CT scan showed no improvements. In addition, her condition evolved to optic neuritis caused by the use of ethambutol. Thus, it was decided to end the treatment due to therapeutic failure and to provide outpatient follow-up to monitor and treat it's complications.

Most of the scientific studies on people with pulmonary diseases caused by *M. simiae* show a prevalence in immunocompetent elderly patients with previous lung lesions, such as in this reported case[2,8]. In addition, in the research, the most common symptoms are productive cough, weight loss, dyspnea, malaise, asthenia, and night sweats. Some other symptoms are hemoptysis, moderate fever, pleural effusion, and lymphadenopathy. On physical examination, findings are not specific and may reflect an underlying lung disease such as bronchiectasis or chronic obstructive pulmonary disease (COPD). Common sounds during auscultation are rhonchi, stridors, crackles and wheezes[1,2], of which the last two were compatible with the findings in this work. Some studies show that in chest radiograph pulmonary infiltrates, nodules or cavitating lesions are found, which is also compatible with the image results in this case[1,2,8]. This infection is less frequent and tends to appear in young patients with advanced Acquired Immunodeficiency Syndrome (AIDS)[1,5], even though it has already been described in an immunocompetent elderly patient without previous lung disease, after a trauma episode and surgery in 2008[9].

A study in Israel compared characteristics and radiographic appearance of pulmonary infection by *M. simiae*

(n=102) and *M. tuberculosis* (n=121). In a group infected by *M. simiae*, there was a higher rate of females and of tobacco consumption, facts supported by the history of the patient in this case report. Ten percent of the tuberculosis patients were HIV-positive (n=12) compared to none of the patients in the *M. simiae* group. On chest radiograph, signs of chronic lung disease were common in the *M. simiae* group as well as affection of the middle and lower lobes. Chest pain, cough, fever, hemoptysis, sweating and weigh loss were more common in pulmonary tuberculosis patients[3].

Diagnosis must be made after microbiological confirmation, applying strict criteria to evaluate each isolation because it is an environmental mycobacterium[1]. It's presence in a sample indicates it is the causative agent of mycobacteriosis or a sample contamination, originating a pseudoinfection[7]. In the present case, the American Thoracic Society (ATS) and the Infectious Disease Society of America (IDSA) criteria were used to diagnose pulmonary disease caused by NTM[2].

The drug-susceptibility testing (DST) results contribution to the drug treatment decision are still limited because in vitro susceptibility and in vivo response are not established for most of the drugs[2,10]. This fact makes establishing an effective treatment difficult in this case because there are no technical standards to calculate the MIC of the *M. simiae*. In a study that evaluated susceptibility of the *M. simiae* complex to thirteen drugs, *M. simiae* showed the highest level of drug resistance in vitro, exhibiting sensitivity to clarithromycin and moxifloxacin. Only one out of twenty-two isolations was susceptible to ethambutol. Resistance to rifampicin was demonstrated to have minimum inhibitory concentration invariably high (MIC ≥ 8μg/mL) in all *M. simiae* samples[10]. Another research assessed the susceptibility of twenty-four different MNT strains to fifteen antimicrobial agents. The *M. simiae* was resistant to fourteen agents and sensitive to amikacin with an 8μg/mL MIC[11]. Recommended Treatment regimens should include a macrolide, such as clarithromycin; a quinolone antibiotic, such as moxifloxacin; and one or two other additional drugs based on susceptibility drug testing[10], which was the treatment used in this case report.

ETHICAL APPROVAL

This paper fulfilled all criteria related to research involving humans, being submitted and approved by the Research Ethics Committee of the Federal University of Roraima (Protocol number 3.237.166).

FINAL CONSIDERATIONS

In tuberculosis-endemic areas, the chances of NTM infections must always be considered after treatment failure. Despite all effort to identify the pathogenic agent and the adequate treatment, the outcome is not successful in most of the cases, including the case reported.

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