CASE REPORT

MALDI-TOF-MS IDENTIFIED *RHODOCOCCUS HOAGIE* BACTERAEMIA IN AN IMMUNOCOMPROMISED PATIENT

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Rhodococcus hoagie, previously referred to as *R. equi*, is a Gram-positive intracellular coccobacillus that belongs to the *Nocardiaceae* family. This multi-host pathogen causes infections in farm animals, particularly foals, but also in immunosuppressed patients, mainly individuals treated with high doses of corticosteroids, subjected to organ transplant, or infected with human immunodeficiency virus Objectives of the study are to report a bloodstream infection in an immunocompromised patient. Immunocompromised patients with advanced HIV who presented bloodstream infection, residing in an urban setting and having undertaken no trips to the countryside or elsewhere during the COVID-19 pandemic. Blood culture by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) was done in order to identify the bacteria. The immunocompromised female patient presented bloodstream infection by *Rhodococcus hoagie*, which was identified using MALDI-TOF-MS. *R. hoagie* can cause a severe infection with a high mortality rate if prompt treatment with a combination of antibiotics is not established. A high level of suspicion is required to establish the diagnosis, as it may be misdiagnosed as pulmonary tuberculosis. On gram stain, *R. hoagie* may appear as beaded to solid staining coccobacilli, which can be dismissed as a "diphtheroid" contaminant. The infection was identified using MALDI-TOF-MS.

Keywords: *Rhodococcus equi*; Advanced HIV; MALDI-TOF-MS

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INTRODUCTION

Rhodococcus hoagie, previously referred to as *R. equi*, is a Gram-positive intracellular coccobacillus that belongs to the *Nocardiaceae* family.[1] This multi-host pathogen causes infections in farm animals, particularly foals, but also in immunosuppressed patients, mainly individuals treated with high doses of corticosteroids, subjected to organ transplant or infected with human immunodeficiency virus (HIV). Accordingly, exposure to farm animals is a relevant factor in transmitting the infection to humans.[2–7] Here, we describe an immunocompromised patient with advanced HIV who presented bloodstream infection by *R. hoagie* despite residing in an urban setting and having undertaken no trips to the countryside or elsewhere during the COVID-19 pandemic. This case shows the importance of recognizing severe infection, discerning the failure of antibiotic therapy, and changing to more appropriate antimicrobials to ensure survival.

CASE REPORT

A single 25-year-old female living in the metropolitan area of Belo Horizonte, Minas Gerais, south-eastern Brazil, attended a Basic Health Care Unit and reported progressive dyspnoea, cough, asthenia, excessive night sweating, weight loss (around 15 kg since the onset of the condition), unmeasured fever peaks and sporadic blood-tinged sputum that had begun two months earlier. The patient's medical history included a smoking load of 10 pack years, social drinking, use of illicit drugs (cocaine and marijuana) and anaemia. The patient had been diagnosed with HIV infection in 2016 during a serological screening for pregnant women, and a viral load of 4,243 copies/mL and a CD4 cell count of 232 cells/mm^3 were recorded at that time. The patient was prescribed antiretroviral therapy (ART) but abandoned the treatment after

giving birth because of personal difficulties and the stigma associated with the disease. Although no follow-up was performed, the patient reported being asymptomatic after treatment abandonment and presented no opportunistic infections.

Upon arrival at a Basic Health Care Unit, the patient presented a haemoglobin (Hb) concentration of 6.9 g/dL, required oxygen therapy to re-establish normal saturation levels, and received a transfusion of red cell concentrate (600 mL). Since the respiratory symptoms were compatible with COVID-19 and the patient showed general clinical worsening, a nasopharyngeal swab was taken, which was negative. The patient was summarily treated for pneumonia by administration of ceftriaxone (1g, q12h), azithromycin (500 mg, q1d), and hydrocortisone (100 mg, q8h). Two days later, the patient was transferred to a hospital specialized in infectious diseases for ongoing care at Hospital Eduardo de Menezes. The chronological sequence described below records events from day 1 of hospital admission to the first follow-up at the outpatient clinic after discharge from the hospital (day 40). On the first day, by physical examination of the patient revealed the presence of tachycardia [heart rate (HR) of 126 beats/min), tachypnoea [respiratory rate (RR) of 26 breaths/min], hypoxemia (oxygen saturation of 93%), and lesions in the oral mucosa suggestive *Candida* spp infection. In addition, the patient presented hepatosplenomegaly, as shown by the palpable liver at 5 cm below the right costal margin and palpable spleen at 2 cm from the left costal margin. The complex constellation of symptoms suggested a multisystemic syndrome that could include sarcoidosis and lung cancer. However, given the probability of advanced HIV, the main diagnostic hypothesis was a systemic infection process of pulmonary origin. The hypoxemic patient continued receiving non-invasive oxygen therapy. An empiric chemotherapy regimen for tuberculosis (TB) was initiated comprising a combination of rifampicin/isoniazid/pyrazinamide/ethambutol (RHZE-FDC; 150/75/400/275 mg; q8d)., according to Brazilian Health Ministery[7] In addition, sulfamethoxazole/trimethoprim was prescribed for pneumocystosis prophylaxis, and intravenous administration of ceftriaxone (1 g, q12h), clarithromycin (500 mg, q24h), and fluconazole (150 mg, q24h) was prescribed. X-ray (Figure-1) and computed tomography (CT) scans of the chest showed the presence of diffuse consolidations with multiple cavitations in the left hemithorax, associated with adjacent branching opacities (tree-in-bud pattern) compatible with an active granulomatous process with endobronchial dissemination (Figure-2).

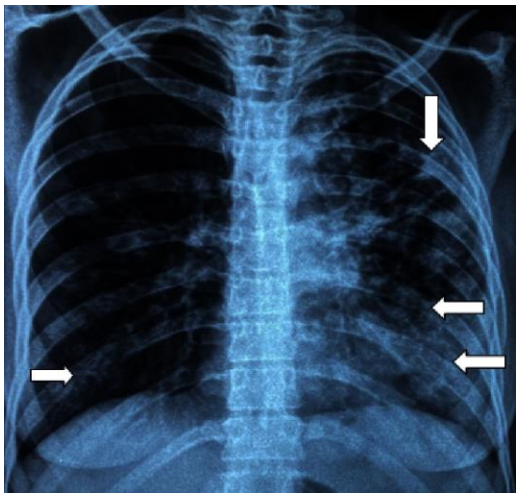

Figure-1: Chest X-ray of the patient on the first day.
The image displays bilateral diffuse interstitial infiltrates and irregular consolidations, primarily in the left hemithorax

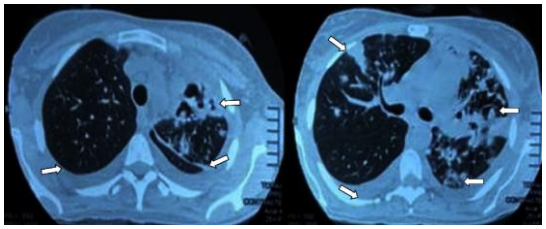

Figure 2: Chest computed tomography (CT) on the first week.
The scan shows diffuse consolidations in the left hemithorax, featuring multiple cavitations and an adjacent tree-in-bud pattern. This is consistent with active granulomatous disease with endobronchial dissemination.

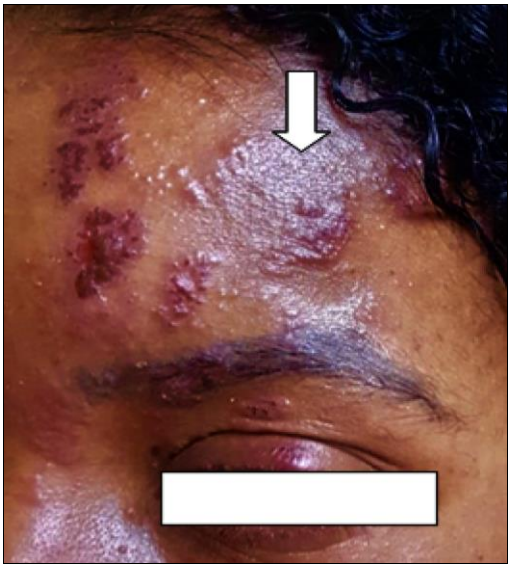

Figure 3: Diagnosis of herpes zoster 20 days post-discharge.
Characterized by typical blisters on the forehead and eyelid, this may represent an instance of immune reconstitution syndrome following initiation of antiretroviral therapy, as indicated by the typical presentation of herpes zoster in these regions.

On the fifth day of hospitalization, arterial blood gas measurements (performed while the patient received supplementary oxygen) were normal, and laboratory tests showed that lactate dehydrogenase and liver, pancreas, and kidney function indicators were within the normal range. However, the level of C reactive protein (CRP) had increased to 45 mg/L, and the complete blood cell count (CBC) indicated the presence of normocytic normochromic anaemia with Hb of 8.6 g/dL, white blood cell count (WBC) of 8,600 cells/mm^3 and platelet count of 178, 000 cells/mm^3. Direct microscopy and culture of sputum samples were negative for *Nocardia* spp. and *Mycobacterium* spp. Moreover, direct microscopy was negative for *Pneumocystis jirovecii*. Rapid immunochromatographic assays for *Leishmania* spp. and *Cryptococcus* spp. were also negative. Advanced HIV infection was confirmed with a viral load of 121,100 copies/mL and a CD4 cell count of 22 cells/mm^3. A test for syphilis and antibody tests for hepatitis B and C were negative. After one week, the patient showed no signs of improvement as demonstrated by a CRP level of 225 mg/L and low counts for all three types of blood cells, Hb of 6.9 g/dL, WBC of 2,700 cells/mm^3, and platelet count of 65,000 platelets/mm^3. Blood culture and cervical lymph node biopsy were performed to investigate the possibility of bloodstream infection or elsewhere. The patient's clinical conditions worsened despite the maintenance of antibiotic therapy and increased oxygen supplementation (to 8 L/min) using a facemask. Bronchoalveolar lavage (BAL) was performed to investigate the possible presence of fungi, bacteria, and *Mycobacterium* spp, but the results were negative. However, microscopy of the lymph node biopsy showed the presence of a nonspecific inflammatory infiltrate. Blood culture showed the presence of Gram-positive coccobacillus, but the report ascribed this finding to sample contamination. Given the patient's serious condition, the medical team opted to revise lymph node smears and requested a detailed analysis of the blood culture by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) in order to identify the bacteria. In addition, because of the persistence of hepatosplenomegaly, the patient was submitted to abdominal ultrasound, which confirmed the presence of moderate abnormalities with diffuse echogenicity of the liver parenchyma.

Considering the severe pulmonary infection and the positive blood culture, the intravenous ceftriaxone and clarithromycin treatment were interrupted on day 12. An empiric antibiotic therapy against *Listeria monocytogenes*, considering the presence of Gram-positive rods in the blood. was initiated with ampicillin (2 g; q4h) and gentamicin (80 mg; q8h). The sulfamethoxazole/trimethoprim combination was administered at an increased dose rate (800/160 mg; q6h) as therapy against possible *P. jirovecii*-induced pneumonia. Changes in the antibiotic therapy regimen resulted in significant clinical improvement as demonstrated by the reduction in CRP levels to 78 and 56 mg/L (on days 15 and 16, respectively), progressive resolution of pancytopenia, and gradual recovery of arterial oxygen levels. On day 18, the patient has weaned off oxygen supplementation. The patient's respiratory rate had reduced to 20 breaths/min, and ART was re-established with lamivudine/tenofovir (300/300 mg; q24h) together with a double dose of dolutegravir (50 mg, q12h). After 20 days of hospitalization, the patient was discharged with a recommendation to continue with ART, RHZE, and sulfamethoxazole/trimethoprim as previously prescribed. The first follow-up visit to the hospital outpatient clinic was fixed for 20 days after discharge. At this moment, the results of MALDI-TOF-MS identified the Gram-positive bacterium present in the blood culture as *R. hoagie*. A physical examination conducted during the first follow-up at empithe hospital's outpatient clinic confirmed that the patient's vital signs were normal, except for mild tachycardia (HR of 113 beats/min) and persistent hepatosplenomegaly.

Nevertheless, the patient reported sporadic coughing and daily nausea after taking RHZE. Hence this medication and sulfamethoxazole/trimethoprim were suspended and replaced with a combination of rifampicin (450 mg/day) and azithromycin (500 mg, q24h) specifically recommended for *R. hoagie*[8]. The patient exhibited herpes zoster ophthalmicus with blisters on the forehead and eyelid (Figure-3), and this development was attributed to immune reconstitution syndrome.[9]

The patient was referred to the hospital to treat herpes zoster with intravenous acyclovir. While in the hospital, the patient experienced malaise, fatigue, and fever peaks and presented severe neutropenia with a count of 356 neutrophils/mm^3. Empiric antibiotic therapy for febrile neutropenia was initiated with meropenem (800mg; q8h) and vancomycin (1000 mg; q12h) over six days. A blood culture was performed, but the results were negative. The patient was discharged after 20 days of hospitalization, presenting progressive clinical and laboratory improvement with a count of 1100 neutrophils/mm^3.

The patient is being followed-up at the outpatient clinic, and treatment against *R. hoagie* infection continues with rifampicin/azithromycin as before, in addition to ART and sulfamethoxazole/trimethoprim. Currently, the

patient shows overall health improvement, without dyspnoea, loss of appetite or other symptoms, and regained weight and strength.

MALDI-TOF-MS analysis of the blood culture proved essential in identifying the cause of bloodstream infection. It uses intact cells or cell extracts and provides a rapid, sensitive, and economical proteomic profiling method for microbial identification and diagnosis.[10] Patient's successful outcome can be attributed to the timely assessment of response to treatment, the recognition of antibiotic therapy failure, and the swift and opportune administration of alternative antimicrobials. MALDI-TOF-MS was fundamental to identifying *R. hoagii* and adjusting medication.

Conflict of interest: None declared

Ethical approval: Written informed consent was obtained from the patient for publication of this report and the images contained therein.

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