CASE REPORT: PULMONARY MUCORMYCOSIS AND RHODOCOCCOSIS IN A RENAL TRANSPLANT PATIENT

RELATO DE CASO: MUCORMICOSE PULMONAR E RODOCOCOSE EM PACIENTE TRANSPLANTADO RENAL

REPORTE DE CASO: MUCORMICOSIS Y RODOCOCOCIS PULMONAR EN UN PACIENTE TRASPLANTE RENAL

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ABSTRACT

Pulmonary mucormycosis is a rare, rapidly progressive, and often fatal opportunistic fungal infection, especially in immunocompromised patients. Rhodococcus equi, in turn, is an intracellular opportunistic bacterial pathogen that is uncommon in humans, but shows higher prevalence in kidney transplant recipients. We report the case of a 76-year-old male patient, 15 months post-renal transplantation, under immunosuppressive therapy. The clinical course was marked by progressive deterioration of renal function, respiratory failure, need for intensive care support, and administration of multiple antimicrobial agents, including liposomal amphotericin B, vancomycin, and rifampicin. After extensive investigation with computed tomography, fiberoptic bronchoscopy, biopsy, and microbiological cultures, a diagnosis of pulmonary coinfection by mucormycosis and Rhodococcus equi was established. Despite intensive therapeutic measures, the patient progressed to death following clinical deterioration. This case highlights the diagnostic and therapeutic challenges of coinfection with two rare opportunistic pathogens in a transplant recipient, reinforcing the importance of early recognition, prompt management, and aggressive intervention in such scenarios.

Keywords: Mucormycosis. Rhodococcus Infections. Kidney Transplantation. Opportunistic Infections. Coinfection. Immunocompromised Host.

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RESUMO
A mucormicose pulmonar é uma infecção fúngica oportunista rara, de evolução rápida e frequentemente letal, especialmente em pacientes imunocomprometidos. O Rhodococcus equi, por sua vez, é um patógeno bacteriano intracelular oportunista de ocorrência incomum em humanos, com maior prevalência em transplantados renais. Relato de um paciente do sexo masculino, 76 anos, transplantado renal há 15 meses, em uso de imunossupressores. O curso clínico foi caracterizado por deterioração progressiva da função renal, insuficiência respiratória, necessidade de suporte intensivo e administração de múltiplos antimicrobianos, incluindo anfotericina B lipossomal, vancomicina e rifampicina. Após investigação extensa com tomografia, fibrobroncoscopia, biópsia e culturas, foi diagnosticado com coinfecção por mucormicose pulmonar e Rhodococcus equi. Apesar das medidas terapêuticas intensivas, o paciente evoluiu a óbito após agravamento clínico. Este relato destaca os desafios diagnósticos e terapêuticos da coinfecção por dois agentes oportunistas raros em paciente transplantado, reforçando a importância do reconhecimento precoce, manejo ágil e intervenção agressiva nesses cenários.

Palavras-chave: Mucormicose. Infecção por Rhodococcus. Transplante Renal. Infecções Oportunistas. Imunossupressão.

RESUMEN
La mucormicosis pulmonar es una infección fúngica oportunista rara, de rápida progresión y a menudo mortal, especialmente en pacientes inmunodeprimidos. Rhodococcus equi, a su vez, es un patógeno bacteriano intracelular oportunista poco común en humanos, con una mayor prevalencia en receptores de trasplante renal. Este informe describe a un paciente masculino de 76 años, receptor de trasplante renal 15 meses antes, que estaba usando inmunosupresores. La evolución clínica se caracterizó por un deterioro progresivo de la función renal, insuficiencia respiratoria, la necesidad de cuidados intensivos y la administración de múltiples antimicrobianos, incluyendo anfotericina B liposomal, vancomicina y rifampicina. Después de una extensa investigación con tomografía computarizada, broncoscopia, biopsia y cultivos, se le diagnosticó coinfección con mucormicosis pulmonar y Rhodococcus equi. A pesar de las medidas terapéuticas intensivas, el paciente falleció después del deterioro clínico. Este informe destaca los desafíos diagnósticos y terapéuticos de la coinfección por dos agentes oportunistas poco frecuentes en un paciente trasplantado, lo que refuerza la importancia del diagnóstico temprano, el tratamiento oportuno y la intervención agresiva en estas situaciones.

Palabras clave: Mucormicosis. Infección por Rhodococcus. Trasplante Renal. Infecciones Oportunistas. Inmunosupresión.

1 INTRODUCTION

Zygomycosis, also known as mucormycosis, is a rare but extremely aggressive opportunistic fungal infection characterized by a rapid process of tissue invasion in addition, the patient was diagnosed with *Rhodococcus equi,* a rare condition in which they hardly appear concomitantly This condition is caused by fungi belonging to the class Zygomycetes, especially of the orders **Mucorales** and **Entomophthorales and the second by** Rhodococcus equi, which naturally causes pneumonia in cattle, and affects humans who have low immunity. Mucorales are responsible for the most common and severe form of the disease, they tend to affect individuals with some degree of immunosuppression, such as patients with decompensated diabetes, hematological neoplasms or in prolonged use of corticosteroids. Entomophthorales are more associated with subacute presentations, usually in immunocompetent individuals, with involvement mainly of subcutaneous tissues.

Rhodococcus equi is a **facultative gram-positive**, aerobic, intracellular bacterial pathogen widely recognized for causing **pyogranulomatous bronchopneumonia in horses**, especially in young foals. It is a microorganism present in the soil, particularly in rural environments, where contamination occurs mainly by inhalation of particles containing the bacteria. In humans, *Rhodococcus equi infection* is considered **rare** but potentially severe, occurring predominantly in individuals with **immunosuppression**, such as patients living with HIV/AIDS, solid organ transplant recipients, individuals on long-term corticosteroid use, or undergoing chemotherapy. The most common clinical manifestation is **pneumonia**, often with subacute or chronic evolution, and may present with the formation of lung abscesses, cavitations, and systemic dissemination.

This study is justified by the need to report a clinical case of zygomycosis in a kidney transplant patient, who, when evaluating the condition of mucormycosis, was identified in parallel with Rhodococcus equi infection, as the patient is a kidney transplant recipient, a condition that makes him particularly vulnerable to the development of opportunistic infections due to the continuous use of immunosuppressive drugs. In view of this scenario, it is recognized that other similar cases may emerge, requiring the care team to act quickly and accurately to implement appropriate interventions. In addition, co-infection by the two pathogens in the same patient represents a situation not yet described in the medical literature, configuring an additional challenge for diagnosis and treatment. This is because clinical, laboratory, and radiological findings tend to overlap with those of other infections frequently observed in clinical practice, making early identification and appropriate therapeutic management difficult.

In this context, there is a need to reflect on which interventions should be adopted in patients diagnosed with zygomycosis and Rhodococcus equi infection, especially in complex scenarios such as immunosuppressed individuals. The following questions are asked: how are **which clinical conducts are most appropriate**? **Which therapeutic approaches should be prioritized** and **what is the expected multidisciplinary action** become fundamental to guide safe and timely care? In view of these concerns, the present study aims to **describe in detail a case of zygomycosis** and Rhodococcus equi, which occurred concomitantly in a referral hospital for the treatment and follow-up of kidney transplant patients, which is part of the EBSERH network. By documenting this clinical experience, it seeks to contribute to the improvement of care practices, in addition to offering subsidies that favor early identification, decision-making, and effective management of this rare and highly aggressive fungal infection.

The methodological approach of this study is based on a **case study**, an approach widely used to investigate rare, complex or poorly described clinical phenomena in the literature. Data collection involved a thorough analysis of the patient' **s anamnesis** and **physical examination**, complemented by **diagnostic confirmation of zygomycosis and** Rhodococcus equi **infection through laboratory and microbiological tests**, which are essential to establish the etiology of the infection.

The study is organized into several sections to comprehensively address the proposed theme. The introduction provides a detailed contextualization of the theme, justifying the importance of the study, outlining the objectives, methodological approaches and theoretical bases that underlie the research. Then, there is a section of theoretical foundation that explores the main concepts worked in the research and epidemiological aspects related to the identification, treatment and management of zygomycosis and what are its clinical and epidemiological trends. Then, the methodological procedures, results and discussions are presented, with a detailed analysis of the data collected. The study concludes with final considerations on the researched topic, including the limitations and implications for future studies.

This article aims to improve strategies for diagnosis, management, treatment, and care in patients with zygomycosis, promoting the strengthening of surveillance, alertness, and response related to opportunistic diseases.

2 CONCEPTUAL THEORETICAL FRAMEWORK

2.1 CLINICAL-EPIDEMIOLOGICAL ASPECTS OF ZYGOMYCOSIS

Zygomycosis, also called mucormycosis, is a rare and highly aggressive opportunistic fungal infection, characterized by rapid tissue invasion. It is caused by fungi of the class *Zygomycetes*, especially of the orders **Mucorales** and **Entomophthorales**, recognized for their high potential for dissemination in vulnerable individuals. From a clinical point of view, zygomycosis presents in different manifestations, most frequently in **the rhinocerebral, pulmonary, gastrointestinal,** and **cutaneous forms**, all of which are characterized by rapid evolution and the potential for severe outcomes, especially in immunosuppressed patients or those with predisposing comorbidities. Transmission occurs predominantly by **inhaling spores** present in decomposing organic materials, such as fruits, breads, and plant residues. Other forms of contamination include **ingestion of contaminated food** and **skin or mucosal inoculation**, especially in situations of disruption of the skin barrier or by contact with feces of infected animals or spores dispersed in the environment (Brazilian Ministry of Health, 2024).

The development of opportunistic fungal diseases is strongly associated with the presence of immunodeficiency, especially in individuals exposed to risk factors such as solid organ transplantation, chemotherapy and immunotherapy treatments, as well as decompensated diabetes mellitus (Song et al., 2017). In these contexts, the reduction in immunological competence favors proliferation and tissue invasion by highly pathogenic fungi, including the etiological agents of zygomycosis (Cohen et al, 2022).

Data from the Brazilian Ministry of Health (MS, 2022) show that, between 2018 and 2022, **206 cases of mucormycosis were recorded** in the country. The year **2021** had the highest number of notifications, totaling **99 cases**, of which **47 were associated with COVID-19 co-infection.** This significant increase in the pandemic period reinforces the association between SARS-CoV-2 infection, intensive use of corticosteroids, and the risk of developing opportunistic fungal infections, highlighting the need for expanded clinical surveillance in patients with immune compromise.

Immunosuppression resulting from solid organ transplantation, especially when mediated by the continuous use of drugs such as mycophenolate mofetil, tacrolimus, and cyclosporine, significantly compromises the patient's immune response. This scenario increases vulnerability to opportunistic infections, both fungal and bacterial, including those caused by microorganisms of the genus **Rhodococcus**, a pathogen initially classified as of animal origin and composed of 27 described species (Dandu et al, 2024).

Among these species, **Rhodococcus equi (R. equi)** stands out as the main agent of clinical relevance for humans. It is a gram-positive, facultative intracellular bacterium, widely distributed in the soil and recognized as a saprophyte of the intestinal tract of herbivores, particularly horses (Gürtler et al., 2004). *R. equi* infection, called **rhodococcosis**, is considered rare in humans and occurs predominantly in immunocompromised individuals, including transplant recipients, people with HIV/AIDS, and patients on intense immunosuppressive therapy. In Brazil, the first documented cases were recorded in Rio Grande do Sul in 1989, marking the beginning of the national description of this emerging agent (Severo et al., 2001).

In mucormycosis, the fungal genus **Rhizopus** is identified as the most prevalent etiologic agent. However, other species are also implicated in human infection, including representatives of the genera **Mucor, Rhizomucor, Absidia, Apophysomyces, Saksenaea, Cunninghamella, Cokeromyces** and **Syncephalastrum**. These taxonomic variations reflect the diversity of fungi belonging to the order *Mucorales* that can trigger severe clinical conditions in susceptible individuals. The form of clinical presentation is directly related to the **predisposing conditions of the host**, especially immunosuppression states, metabolic alterations, and structural impairments that favor tissue invasion. Thus, the clinical spectrum of mucormycosis tends to vary according to the patient's immunological profile and associated comorbidities (Dravid et al, 2022).

The clinical manifestations of mucormycosis are mostly severe and are often characterized by an initial picture of sinusitis that progresses rapidly to rhino-orbital infection, especially in immunocompromised individuals. Among the most severe forms, **rhino-orbital-cerebral mucormycosis stands out**, usually associated with angioinvasive species such as *Rhizopus* and *Rhizomucor*. These fungi have the ability to invade the vascular space, leading to tissue necrosis in structures such as the nasal septum, palate, orbit, and paranasal sinuses. The progression of the infection to the central nervous system can result in severe neurological complications, including **cavernous sinus thrombosis, seizures, and stroke of thrombotic origin**, configuring a condition of high lethality that requires immediate therapeutic intervention (Junqueira et al, 2022).

The incidence of mucormycosis has shown a progressive increase in the last two decades, a phenomenon associated, above all, with the increase in the number of patients undergoing immunosuppressive therapy and the widespread use of broad-spectrum antibiotics (VASUDEVAN, 2021). At the same time, several clinical conditions contribute to greater susceptibility to infection, including **diabetes mellitus**, with or without ketoacidosis, **hematological and solid neoplasms, organ transplants, prolonged neutropenia,**

trauma, iron overload, use of intravenous illicit drugs, and **prematurity and malnutrition**. Although most cases occur in immunocompromised individuals, immunocompetent patients can also develop mucormycosis when there is **direct inoculation of spores into the skin**, especially in situations involving trauma, burns, or other injuries that break the integrity of the skin barrier (Skiada; Pavleas; Drogari-Apiranthitou, 2020).

The management of mucormycosis requires **early clinical recognition** and understanding of the different patterns of disease presentation. Diagnosis depends on a high degree of suspicion, especially in immunocompromised patients, and includes **direct mycological examination, fungal culture,** and, when possible, **histopathological evaluation**, fundamental methods for identifying the agent and confirming tissue invasion.

Treatment should be maintained until **resolution of imaging findings** and **adequate reconstitution of the** patient's immune system, since persistent immunosuppression favors relapse and worsening of the prognosis. Regarding pharmacological management, the use of antifungals is indispensable, especially **liposomal amphotericin B,** administered intravenously, which is considered the therapy of choice. In refractory cases or as a maintenance strategy, second-line antifungals such as **isavuconazole** or **posaconazole** are used, which have good tissue penetration and proven efficacy. Regarding surgical treatment, **aggressive debridement of necrotic tissue** may be necessary to control the spread of the fungus, reducing the infective load and increasing the chances of survival. Although the surgical impact varies according to the extent and location of the lesion, this approach is often considered an essential component of combination treatment (Sipsas et al., 2018; Cornely et al., 2019).

Tertiary level hospitals must be structured to recognize, diagnose and manage severe fungal infections, which often require complex surgical interventions and the use of high-cost antifungals. Given the severity and rapid progression of these infections, it is essential that these institutions have advanced diagnostic resources, trained multidisciplinary teams, and timely access to first-line pharmacological therapies. Currently, the treatment of mucormycosis and other invasive mycoses is based on a **multimodal therapeutic approach**, which includes: **early identification and correction of predisposing factors**, such as strict glycemic control or immunosuppression adjustment; **immediate administration of active antifungals in appropriate doses; and complete surgical removal of the affected tissue**, when indicated. This integrated strategy has shown a significant increase in survival rates, especially in patients with a high degree of immune impairment (Farias et al., 2021; Jeong et al., 2019).

The prevalence of mucormycosis is estimated at approximately **1.7 cases per million inhabitants per year**, according to data from studies carried out in the United States. However, this rate may be significantly higher in specific populations, reaching **2 to 3% among patients undergoing bone marrow transplantation**, a group known to be vulnerable due to the intense degree of immunosuppression presented. Several risk factors have been associated with the increased incidence of these infections. Among them, **diabetes mellitus stands out**, particularly when accompanied by ketoacidosis, as well as **leukemias, lymphomas,** and other **malignant hematological neoplasms**, which often course with severe immunosuppression and prolonged neutropenia. The **use of corticosteroids**, especially in high-dose or long-acting therapeutic regimens, is also an important determinant for the development of the disease. In the pediatric population, although cases are less frequent, there is an association with **low birth weight, persistent diarrhea, and malnutrition**, conditions that weaken the immune system and increase susceptibility to invasive fungal infection (Eshraghi et al, 2024).

The **primarily cutaneous form** of mucormycosis is characterized by intense **angioinvasion**, accompanied by **venous thrombosis** and rapid **tissue destruction**, resulting in extensive lesions that can evolve aggressively if not treated early. Despite this invasive behavior, cutaneous mucormycosis is the clinical presentation with **lower lethality rates** when compared to the rhinocerebral, pulmonary, or disseminated forms. Another relevant aspect is that this manifestation tends to be **less related to systemic predisposing factors**, occurring more frequently after **trauma**, **burns**, invasive procedures, or direct contamination of the skin by environmental spores. Thus, although it can affect immunocompromised individuals, cutaneous mucormycosis is also observed in previously healthy patients, as long as there is a rupture of the skin barrier that allows inoculation of the fungal agent (Ganfhi et al, 2023).

In general, the etiologic agents of mucormycosis are unable to penetrate an **intact skin barrier**, which reinforces the importance of skin integrity as the primary defense mechanism against invasive fungal infections. Thus, any condition that causes **disruption of this barrier**, whether due to trauma, burns, invasive procedures, or repetitive friction, substantially increases the risk of developing the **cutaneous** form of the disease. In the case mentioned, the patient was more vulnerable to infection due to **frequent changes in orogastric tube fixation**, a process that can generate microlesions, continuous irritation, and progressive impairment of local skin protection. This clinical situation illustrates how routine interventions, when repetitive or poorly tolerated by the tissue, can serve as a

gateway for opportunistic pathogens, favoring the establishment of cutaneous mucormycosis in already fragile individuals (Hussain et al, 2023).

2.2 CLINICAL-EPIDEMIOLOGICAL ASPECTS OF RHODOCOCCUS EQUI

Rhodococcus equi is a gram-positive, aerobic, opportunistic, and facultative intracellular bacterium, widely recognized as the etiological agent of severe pneumonia in horses, especially in young foals. In the veterinary environment, it stands out for causing pyogranulomatous bronchopneumonia, which is often associated with high morbidity and mortality rates when not properly treated (Jain et al, 2023).

In humans, *Rhodococcus equi infection* is considered rare and occurs predominantly in immunosuppressed individuals, such as patients living with HIV/AIDS, transplant recipients, on long-term corticosteroid use, or undergoing immunosuppressive therapies. In these populations, the microorganism can cause pneumonia of subacute or chronic evolution, often with the formation of lung abscesses and a clinical presentation similar to tuberculosis, which can make the differential diagnosis difficult (Keshri et al, 2023).

Although *Rhodococcus equi* is classified as a zoonosis and is commonly present in soil contaminated by equine feces, most human cases described in the literature do not have a direct or proven relationship with contact with animals. Infection in humans seems to be more associated with environmental exposure and the condition of immunosuppression of the host than with direct animal-to-human transmission. Thus, early recognition of the pathogen and clinical suspicion in vulnerable populations are critical for timely diagnosis and proper management of infection (Khare et al, 2022).

In humans, *Rhodococcus equi* is an important etiologic agent of pneumonia, lung abscesses, and systemic infections, especially in immunocompromised individuals. Its high clinical relevance in patients living with HIV/AIDS is highlighted, in whom immunosuppression favors the onset and progression of the infection. In these patients, the disease may present a subacute or chronic course, with persistent respiratory manifestations, formation of cavitary lesions, and hematogenous dissemination, resulting in multiple organ involvement. In addition, infection with *Rhodococcus equi* can mimic other pulmonary pathologies, such as tuberculosis, making diagnosis difficult and delaying the initiation of appropriate treatment, which reinforces the importance of clinical suspicion and microbiological investigation in vulnerable populations (Kirkan et alm 2025).

In the state of Rio Grande do Sul, the infection has a higher occurrence, a fact that can be attributed to the condition of endemic region for *Rhodococcus equi*. This endemicity is related, above all, to local environmental and socioeconomic characteristics, such as the

strong agricultural activity, especially equine farming, which favors the presence and persistence of the microorganism in the soil. In addition, climatic and ecological factors can contribute to the maintenance of the pathogen in the environment, increasing the population's exposure. In this context, a higher risk of infection is observed, particularly among immunosuppressed individuals, which reinforces the need for epidemiological surveillance, early diagnosis, and the adoption of appropriate preventive measures in the region (Kulkarni et al, 2022).

3 MATERIAL AND METHOD

This is a descriptive study, of the **clinical case report type**, developed from the retrospective analysis of the electronic medical record of a 76-year-old male patient, with kidney transplantation, hospitalized at the Miguel Riet Corrêa Junior University Hospital/EBSERH/UFRS, a reference institution in the extreme south of Brazil. The collection of information included clinical, laboratory, evolutionary, and therapeutic data recorded during the hospitalization period, allowing a detailed reconstruction of the clinical course and the interventions performed. This design makes it possible to document the complexity of the case and contribute to the understanding of rare conditions or challenging management in the high-complexity hospital context (Mackenzie et al, 2023).

Clinical, laboratory, and imaging information recorded throughout the hospital stay were collected, with special attention to the evolution of the condition, the diagnostic procedures, the therapeutic interventions adopted, and the clinical outcome. The data were obtained exclusively through consultation of the electronic medical record, characterizing a secondary source of information. The entire collection and analysis process strictly respected the ethical principles applicable to research involving human beings, ensuring confidentiality, anonymity, and full protection of information, as established by Resolution No. 466/2012 and Resolution No. 510/2016 of the National Health Council (Brasil, 2016).

The study was submitted to the Research Ethics Committee (CEP), ensuring full compliance with the ethical precepts that guide research involving human beings. The fundamental principles of bioethics, autonomy, beneficence, non-maleficence and justice, which guide both the decision-making process and the responsible conduct of the report, will be observed. The case was described in a strictly anonymized manner, without any data that allows the direct or indirect identification of the patient, ensuring the protection of privacy and the confidentiality of sensitive information. Considering that the patient died, the Informed Consent Form (ICF) was requested from the legally responsible family member, in

accordance with current ethical regulations, ensuring transparency, respect, and legitimacy in the use of clinical information for scientific purposes (Medeiros et al, 2023).

The case report is characterized as a type of descriptive study that records, in a detailed, organized and contextualized way, the clinical trajectory of a patient or a small group of patients. This format includes information on history, signs and symptoms, complementary tests, diagnosis, therapeutic conducts adopted, clinical evolution and observed outcomes. This is an essential modality for the scientific literature, as it allows documenting **uncommon, rare, or particularly relevant clinical situations for care practice**, such as diseases of low prevalence, atypical presentations of known pathologies, unexpected adverse reactions, or singular responses to therapeutic interventions (Megale et al, 2024).

In addition to its descriptive function, the case report plays a strategic role in generating **new hypotheses**, expanding the understanding of little-explored clinical phenomena, and sensitizing health professionals to conditions that require early diagnosis or differentiated management. Although it does not have statistical power to establish causal relationships, this type of study has recognized scientific value for subsidizing the construction of knowledge in emerging areas and guiding future investigations of greater methodological rigor (Rakowska et al, 2023).

The case reports follow a systematized structure that seeks to ensure clarity, rigor and reproducibility. Among the main methodological elements, the following stand out: **Case identification**: objective description of the patient, preserving anonymity, and presentation of the reason for care; **Detailed clinical history**: temporal evolution of signs, symptoms and relevant events, including personal, family and epidemiological history; **Complementary tests**: laboratory findings, imaging or other diagnostic methods that support the analysis of the case; **Diagnosis and rationale**: clinical reasoning that led to the diagnostic definition, including differential diagnoses considered; **Treatment and interventions**: therapies instituted, justifications, adjustments made and responses observed; **Evolution and outcomes**: clinical follow-up, complications, regression or progression of the condition, and impact on quality of life; **Discussion**: critical analysis that relates the case to the existing scientific literature, highlighting unpublished, rare, or relevant aspects and **ethical aspects**: obtaining free and informed consent and ensuring confidentiality (Riet-Correa et al, 2022).

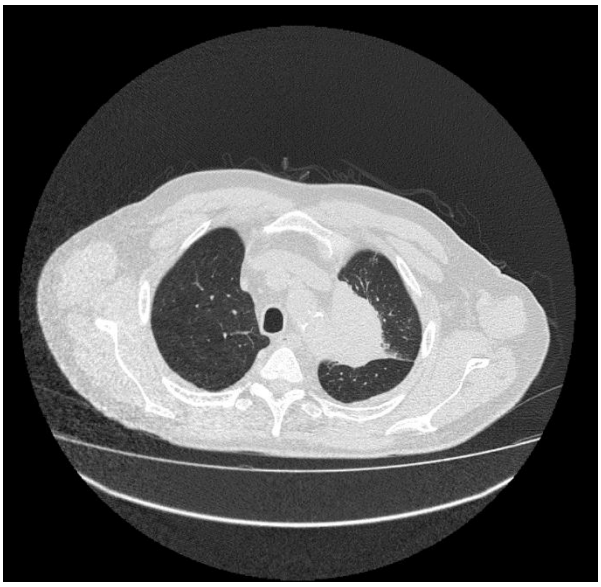
4 RESULTS

A 76-year-old male patient with chronic kidney disease due to obstructive uropathy, with a right kidney transplant for 15 months, using immunosuppressants (Tacrolimus, Mycophenolate sodium, Prednisone), hypertensive and non-insulin-dependent type 2

diabetic, presenting dyspnea at rest, associated with mild/moderate respiratory effort, requiring supplemental oxygen, low fever (38.5º), asthenia, dry cough, anorexia and worsening of renal function with serum creatinine levels of 3.40 mg/dL (previous creatinine 2.23mg/dL- 03/22/24). The patient was internal and performed on a chest CT scan, showing the presence of a mass with an infiltrative component in the left upper lobe, measuring approximately 8.5 cm in the largest diameter (Figure 1). Piperacillin + Tazobactam 18g/day was started for 10 days in the meantime, fiberoptic bronchoscopy was performed, demonstrating extrinsic compression of the anteroposterior segment of the left upper lobe, with transbronchial biopsy and bronchoalveolar lavage.

Figure 1

Initial CT scan



Source: CT scanner at the Miguel Riet Corrêa Junior University Hospital/EBSERH/UFRS.

The possibility of lung neoplasia, tuberculosis, or fungal infection was raised as differential diagnoses. After completion of antibiotic therapy, the patient showed partial improvement of symptoms, tolerating weaning from oxygen therapy, and was discharged from the hospital, with outpatient return for pending test results.

After 7 days at home, the patient presented worsening of the condition with dyspnea at rest, fever, dry cough, malaise, and worsening of renal function (creatinine 4.4mg/dl). During care at the renal transplant unit with cytopathological results of bronchoalveolar lavage with absence of neoplastic cells, presence of fungal hyphae is indicated hospitalization.

The patient was readmitted 1 month after the last admission for treatment based on mycological culture collected by fiberoptic bronchoscopy from the previous hospitalization,

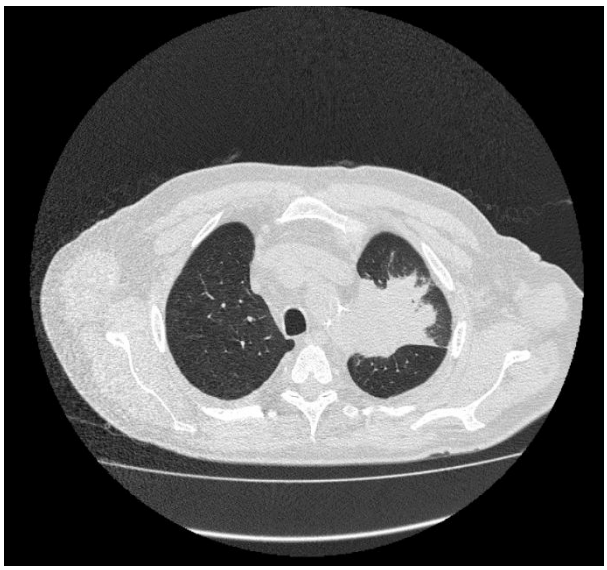
showing the presence of zygomycetes (possibility of sample contamination was considered), in addition, the cytopathological result of the transbronchial biopsy describes the bronchial mucosa with an acute inflammatory process with fibrinoneutrocyte exudate and suggests the presence of fungal hyphae. AFB and Genexpert collections in bronchoalveolar lavage were negative.

In addition, the cytopathological examination of the transbronchial biopsy described a bronchial mucosa affected by an acute inflammatory process, characterized by fibrinoneutrocytic exudate, in addition to suggesting the presence of fungal hyphae, a finding that reinforces the suspicion of invasive fungal infection. Investigations for tuberculosis, performed by means of the search for acid-fast bacilli (AFB) and rapid molecular testing (GeneXpert) in bronchoalveolar lavage, showed negative results, contributing to the exclusion of this diagnostic hypothesis and directing clinical reasoning towards alternative infectious etiologies.

CT scan with maintenance of the lesion and findings of replacement of the lung parenchyma of the left upper lobe, small bilateral pleural effusion, atelectasis, and mediastinal lymph node enlargement, of a possible reactional nature (Figure 2).

Figure 2

Maintenance tomography scan (after 1 month of onset)



Source: CT scanner at the Miguel Riet Corrêa Junior University Hospital/EBSERH/UFRS.

After discussion with a pulmonologist, a new collection of material by fiberoptic bronchoscopy was recommended for subsequent initiation of antifungals due to the risk of contamination of the sample described by the laboratory. Suggested collection, it was performed approximately 30 days after the previous examination.

While awaiting bronchoalveolar lavage analysis, the patient presented progressive worsening of renal function (Creatinine 5.45 - 6.38mg/dL) associated with oliguria, worsening of respiratory effort with pulmonary congestion, mental confusion, decreased level of consciousness, and severe anemia. Renal replacement therapy was instituted (last hemodialysis session prior to kidney transplantation).

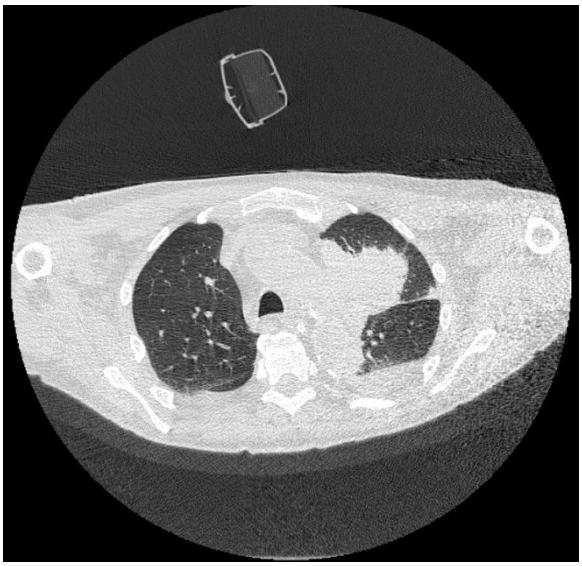
Due to the worsening of the general and especially respiratory condition, liposomal amphotericin B was started, even without the result of the second sample. Cryptococcosis, aspergillosis, and histoplasmosis were ruled out. Hemodialysis and use of oxygen therapy were maintained. He presented refractory hypotension requiring vasoactive drug use, and was transferred to an ICU bed 72 hours after starting liposomal amphotericin B (5mg/kg - 400mg/day) and empirically added Meropenem and Vancomycin. On the fourth day of intensive care, the result of blood culture showed growth of Rhodococcus equi, and it was not possible to perform an antibiogram because "this species is not included in the taxonomy for performing an antibiogram in the Phoenix system" as released by the unit's laboratory. On the recommendation of the infectology, Rifampicin 600mg/day associated with Vancomycin is started and Meropenem is suspended. In addition, the nephrology team advises suspension of immunosuppressants (Tacrolimus and Mycophenolate sodium) and maintenance of corticosteroids (Hydrocortisone 100mg/day).

The patient presents progressive worsening of the respiratory condition, fever and maintenance of hemodynamic instability, already on the eighth day of ICU, evolving to orotracheal intubation. Bronchoalveolar lavage was 19 days after collection, mycological culture results show mixed growth of zygomycete, hyalohyphomycete, and dematiaceous fungi.

A new CT scan of the chest was performed on the following day, an expansive approach with attenuation in soft tissues in the perimediastinal region occupying the left upper lobe, with heterogeneous contrast enhancement, measuring 6.8 x 6.5 x 6.2 cm, involving bronchial branches and arteries of this pulmonary lobe, which presents partially atelectasis and moderate bilateral pleural effusion **(Figure 3).** Prominent and enlarged lymph nodes in the left, paratracheal, and subcarinal hilar chains that measure up to 2.2 cm, and may represent lymph nodes of secondary involvement.

Figure 3

Post-intubation tomography (40 days after the onset of the condition)



Source: CT scanner at the Miguel Riet Corrêa Junior University Hospital/EBSERH/UFRS.

Patient with unfavorable evolution, maintaining fever peaks despite antimicrobial therapy with liposomal amphotericin B 400mg/day (20 days), vancomycin 1g (18 days) and rifampicin 600mg/day (13 days), properly adjusted for renal function. The patient died after 17 days in the ICU.

5 DISCUSSION

The present report documents an unusual case of pulmonary mucormycosis in a renal transplant patient, complicated by secondary infection with *Rhodococcus equi*, a condition rarely described in the medical literature. The coexistence of these two opportunistic infections, both of high severity and low prevalence, configured a particularly challenging clinical scenario, making it difficult to establish the differential diagnosis and directly influencing the elaboration of the therapeutic approach. The overlap of nonspecific clinical manifestations, the atypical evolution of the respiratory condition, and the significant immunosuppression resulting from transplantation contributed to the complexity of the case, highlighting the importance of rigorous clinical surveillance, in-depth microbiological investigation, and a multidisciplinary approach in immunocompromised patients (Rakowska et al, 2023).

Mucormycosis is a rare and extremely invasive opportunistic fungal infection, characterized by rapid progression and high lethality, especially in the pulmonary form, whose mortality can reach up to 87%. This mycosis predominantly affects individuals with some degree of immunosuppression, including solid organ recipients, people living with HIV/AIDS, patients undergoing continuous immunosuppressive or corticosteroid regimens,

as well as individuals with diabetes mellitus of previous, decompensated, or drug-induced origin, and users of alcohol or illicit drugs (MAHAPATRA et al., 2023; SONG et al., 2017).

In the case presented here, the risk of developing the infection was particularly high, since the patient had undergone kidney transplantation 15 months earlier and was regularly using immunosuppressive therapy associated with corticosteroid therapy. Such interventions, essential to prevent graft rejection, compromise the innate and adaptive immune response, facilitating the proliferation of angioinvasive fungi. In addition, these drugs can induce metabolic disorders, such as hyperglycemia and post-transplant diabetes, factors that further increase susceptibility to aggressive fungal infections, including mucormycosis (Megale et al, 2024).

The clinical manifestations of mucormycosis present wide variability, and may affect different organ systems. The most frequently described forms include rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated and, in specific cases, graft involvement in transplant patients. Each variant has diagnostic and therapeutic particularities, as well as different prognoses (Medeiros et al, 2023).

In the case under analysis, the patient developed the pulmonary form of the disease, which corresponds to approximately 13% of the cases described in the literature, as reported by Alves et al. (2002). It is a highly aggressive clinical presentation, marked by deep tissue invasion, progressive respiratory impairment, and great diagnostic difficulty. According to Hase et al. (2023), this specific form is associated with mortality that can reach up to 87%, especially among immunocompromised individuals, which reinforces its clinical relevance and the need for early intervention.

Previous reports of pulmonary mucormycosis indicate that patients often present with high fever, productive or non-productive cough, and, in some cases, hemoptysis. However, there are no pathognomonic signs or symptoms that allow this infection to be immediately differentiated from other severe lung diseases, which makes the diagnosis particularly challenging. This aspect is consistent with the case described, in which the patient sought care with dry cough, progressive dyspnea, and fever, nonspecific clinical manifestations that may suggest a wide range of differential diagnoses (Mackezie et al, 2023).

In the context of imaging studies, computed tomography of the chest plays a central role in the initial evaluation. Studies, such as the one by Liang et al. (2024), describe that the most common radiological findings include areas of consolidation, cavitations, halo-haloed nodules, irregular opacities, and pleural effusion, all of which are potential indicators of invasive fungal infection. These patterns, although not exclusive to mucormycosis, are considered important markers of severity and, when associated with immunological risk

factors, should raise clinical suspicion for this opportunistic mycosis. In addition, the correlation between the patient's immunosuppressive profile and the presence of compatible tomographic alterations reinforces the need for early microbiological investigation, since the delay in diagnosis is directly related to the worsening of clinical outcomes (Hussain et al, 2023).

The diagnosis of mucormycosis requires an integrated approach that considers risk factors, clinical presentation and, above all, histopathological and microbiological confirmation. The literature highlights that the identification of the agent depends on the direct analysis of samples obtained by pulmonary secretion, bronchoalveolar lavage or, preferably, by tissue biopsy, since angiotropic invasion is one of the main markers of the disease (Alves et al., 2002; Liang et al., 2024).

In the present case, the diagnosis was established on the basis of fragments of lung tissue obtained during fiberoptic bronchoscopy. Histological examination showed the presence of fungal hyphae compatible with fungi of the order Mucorales, associated with bronchial mucosa intensely infiltrated by an acute inflammatory process, characterized by fibrinoneutrocyte exudate. The hyphae were observed immersed in a fibrinous matrix, reinforcing the pattern of tissue invasion typical of these infections. Mycological culture complemented the findings, revealing growth of zygomycetes, as well as other fungal structures classified as hyalohyphomycetes and dematicetes. Although the possibility of laboratory contamination is recognized in this type of analysis, the set of histopathological, microbiological, and clinical findings conferred robustness to the diagnostic hypothesis of pulmonary mucormycosis (Jain et al, 2023).

A significant increase in the incidence of mucormycosis has been observed among patients undergoing kidney transplantation in the last five decades. This growth is largely related to technological advances and the improvement of diagnostic techniques, which enable faster and more accurate identification of the infection, favoring the timely initiation of treatment. However, it is important to highlight that, in the context of the Unified Health System (SUS), liposomal amphotericin B considered the first choice therapy is not part of the standardization of most hospital units due to its high cost. In these cases, its availability occurs only upon formal diagnostic proof and specific request to the Ministry of Health, which can delay the start of optimal therapy (Brasil, 2022).

In addition to antifungal treatment, the approach to mucormycosis requires, when indicated, surgical intervention to remove necrotic tissue, as well as careful evaluation to reduce the dose of immunosuppressants, in order to improve the patient's response to infection. The combination of liposomal amphotericin B and surgical debridement is currently

the gold standard for the clinical and surgical management of this invasive mycosis, as described by Song et al. (2017).

In addition to pulmonary mucormycosis, immunosuppressed patients are more vulnerable to opportunistic infections, many of which are rare and difficult to manage clinically. In the case in question, blood culture showed growth of **Rhodococcus equi**, an uncommon pathogen in humans, but associated with severe conditions in individuals with immune compromise. It is an infection of high diagnostic complexity, both due to its nonspecific clinical presentation and the low frequency of identification in routine laboratories, which can delay the start of appropriate treatment (LIANG et al., 2024b). The concomitant occurrence of mucormycosis and *R. equi* infection reinforces the need for expanded microbiological surveillance and thorough diagnostic investigation in these patients, since the coexistence of multiple infectious agents worsens the prognosis and increases the need for rapid and well-targeted therapeutic interventions.

Rhodococcosis is an opportunistic infection caused *by Rhodococcus equi*, an organism that has preferential tropism through the respiratory tract, especially in immunosuppressed individuals. Its pulmonary manifestation is the most frequent clinical form and is characterized by symptoms such as persistent cough, fever, chest pain, weight loss, and fatigue — signs that, due to their lack of specificity, can delay the diagnosis. Radiological findings are particularly important for clinical suspicion, since the disease can produce images compatible with cavitations, lung abscesses, pyothorax, pneumothorax, pleural thickening, areas of consolidation, structural invasion, and mediastinal lymph node enlargement (VAROTTI et al., 2016; LIANG et al., 2024b). In addition, the infection can evolve with **hematogenous dissemination**, resulting in extrapulmonary involvement, such as involvement of the central nervous system, bones, skin, and soft tissues, especially in patients with a profound degree of immunosuppression.

The mortality rate of rhodococcosis in immunosuppressed individuals is high, ranging from **20% to 25%,** reflecting both the aggressiveness of the pathogen and the diagnostic and therapeutic challenges. Data from Macken et al. (2015) show that *R. equi* infection has a particularly high incidence in **kidney transplant recipients**, corresponding to 58.5% of the cases recorded among transplant recipients, with a marked predominance in males (82.9%). These epidemiological characteristics coincide with the profile observed in the case analyzed, reinforcing the association between post-transplant immunosuppression and the increased risk for opportunistic bacterial infections of this nature.

The diagnosis of *Rhodococcus equi* infection requires an integrated approach, combining clinical evaluation, imaging tests, and microbiological methods. Laboratory

confirmation can be obtained by **blood culture**, **sputum culture, pus, bronchoalveolar lavage,** or cytopathological and histopathological analysis of **tissue biopsies**, which allow the visualization of Gram-positive, partially acid-resistant bacilli, characteristic of the species (LIANG et al., 2024b). In immunosuppressed patients, the positivity of cultures is usually higher, reflecting the high bacterial load and the ability of the pathogen to survive and replicate in macrophages.

The treatment of rhodococcosis is based on combined regimens of **two to three antimicrobials with excellent intracellular penetration**, due to the facultatively intracellular character of the microorganism. Among the recommended classes are macrolides, rifampicin, fluoroquinolones, glycopeptides, aminoglycosides, carbapenems and linezolid, and prolonged therapies are necessary to avoid relapses, a common situation in patients with compromised immunity (VERGIDIS et al., 2017; MACKEN et al., 2015).

In the case analyzed, the patient received a combined regimen consisting of **meropenem, vancomycin, and rifampicin**, associated with previously instituted antifungal therapy with **lipid amphotericin B** for the management of pulmonary mucormycosis. Although the therapeutic choice was in line with international recommendations, the clinical response was unfavorable, with progression of the infectious condition and deterioration of laboratory parameters. The unstable clinical condition made any adjuvant surgical intervention impossible, a measure that could help control the infection in selected cases. Given the refractoriness to drug treatment and the severity of immunosuppression, the patient died (Gandhi et al, 2023).

The overlap of clinical and radiological manifestations between pulmonary mucormycosis and *Rhodococcus equi infection* represents a significant challenge for differential diagnosis, especially in immunosuppressed patients. Both conditions can present with fever, cough, dyspnea, weight loss, and tomographic alterations such as consolidations, cavitations, and pleural effusions, making it difficult to initially distinguish between etiologies. This similarity contributes to a potential diagnostic confounding bias, especially in settings where there are multiple comorbidities or concomitant co-infections (Jain et al, 2023).

In addition, laboratory confirmation often depends on the growth of cultures, a process that can take several days, delaying the initiation of specific therapy, a critical factor in severe opportunistic infections. The need to exclude relevant differential diagnoses, such as pulmonary tuberculosis, endemic mycoses, neoplasms, and other bacterial infections of subacute course, also prolongs the clinical investigation and complements the reasons why initial management may be delayed. In immunosuppressed patients, this delay has a direct

impact on prognosis, since both mucormycosis and rhodococcosis have rapid progression and high mortality when not treated early and targeted (Khare et al, 2022).

Although the patient is not HIV-seropositive, the concomitant presence of infection by *Rhodococcus equi* and mucormycosis was observed, which gives the case a high rarity and clinical relevance, since both infections are classically associated with immunosuppressive states. The coexistence of these two agents in an individual without an HIV diagnosis reinforces the complexity of the picture and broadens the discussion about other possible predisposing factors, such as underlying comorbidities, undiagnosed immune alterations, or intense environmental exposure (Dravid et al, 2022).

In addition, studies conducted in southern Brazil have already described the occurrence of *Rhodococcus equi infection* in patients without HIV infection, suggesting that the acquisition of the pathogen may not be exclusively linked to classic immunosuppression. This finding may be related to the fact that the region is considered endemic, with greater environmental circulation of the microorganism, especially in areas of intense agricultural activity. Thus, regional endemicity emerges as a relevant factor in the epidemiological chain of infection, reinforcing the importance of considering *Rhodococcus equi* in the differential diagnosis of pulmonary infections even in apparently immunocompetent patients ((Cohen et al, 2022).

6 FINAL CONSIDERATIONS

In view of the experience presented, it is found that the concomitance of two rare opportunistic infections, sharing similar signs and symptoms in an immunocompromised patient, imposes significant challenges to diagnosis and therapeutic management. The clinical overlap between the conditions delayed the etiological definition and made it difficult to initially choose the most appropriate treatment, evidencing the complexity of care in this patient profile. The case reinforces the relevance of early diagnosis, broad and systematic investigation, and timely initiation of specific therapy, which are determining factors to improve the prognosis in severe infections of rapid evolution. In addition, it emphasizes the importance of maintaining a high degree of clinical suspicion in the face of atypical presentations or refractory to conventional treatment in individuals under immunosuppression.

The present study highlights the relevance of careful clinical investigation of rare cases, such as the one described here, since these atypical cases contribute significantly to the expansion of scientific knowledge and to the improvement of clinical practice. The detailed analysis of unusual presentations allows the identification of little-recognized risk

factors, diagnostic difficulties and particularities in the clinical evolution, supporting more assertive therapeutic decisions.

In addition, the study emphasizes the importance of establishing specific clinical protocols aimed at the management of rare and complex cases, including early diagnosis strategies, appropriate therapeutic approach, and systematic follow-up of patients. The standardization of these approaches can reduce the time to diagnosis, minimize complications, improve clinical outcomes, and strengthen the capacity of health services to deal with infrequent situations, especially in endemic regions or with particular epidemiological characteristics.

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