



Case report

Rhodococcus hoagii bloodstream infection in an allogeneic hematopoietic stem cell transplantation patient: Case report and review of literature



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ABSTRACT

We report a case of bloodstream infection caused by *R. hoagii* in a woman with acute myeloid leukemia, 37-years-old, who received an allogeneic hematopoietic stem cell transplant. She developed cutaneous and gastrointestinal tract graft versus host disease, respectively on day 29 and day 69. On day 157 she developed to acute severe respiratory failure. *Rhodococcus* sp was identified by MALDI-TOF and 16S rRNA sequencing from blood culture as *Rhodococcus hoagii*. The patient was a nurse that lived in urban areas, and stated no recent trips to countryside areas neither contacted with animals. Despite of the treatment with antibiotics with action against *R. hoagii* such as linezolid and meropenem the patient evolved to multiorgan dysfunction and death. Our case-report emphasizes the importance of early diagnosis and the use of 16S rRNA sequencing to confirmed the identification of species of *Rhodococcus* infection.

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Introduction

Rhodococcus is a Gram-positive coccobacillus that belongs to the *Actinomycetae* order [1]. This microorganism has been described as cause of infection in immunocompromised host such as Human Immunodeficiency Virus (HIV) and solid organ transplantation patients [1,2]. Moreover, few cases have been reported in hematopoietic stem cell transplantation (HSCT) patients, mostly in allogeneic (allo) patients with graft versus host diseases (GVHD) [3].

Case report

We present the case of a 37-year-old woman with acute myeloid leukemia (AML), colonized by vancomycin-resistant *Enterococcus* (VRE) who received an allo-HSCT from HLA compatible donor 5 months prior to admission. Buseriphan, Fludarabine and Alemtuzumab were used as conditioning agents. The patient developed cutaneous and gastrointestinal tract GVHD, respectively on day 29 and 69. On day 69, she presented reactivation of cytomegalovirus (CMV) (RT-PCR CMV 6027 UI/mL, negativation within 3 weeks).

On day 119, she was admitted to the hospital with dyspnea and cough, the baseline liver enzymes were normal (ALT 10 U/L and AST 15 U/L) and blood count (Hb = 7,0 gm/dL; Ht = 20,9%; leukocytes 940 cells/m³; neutrophils 790 cells/m³ and platelets 159,000). The chest computer tomography (CT) revealed opacities in the upper lobe of right lung and absence of halo sign, both galactomannan on bronchoalveolar lavage fluid and serum were positives (0.5 ODI and 0.73 ODI respectively) (Fig. 1). Thus, she started voriconazole (200 mg IV q 12 h), that was replaced later on

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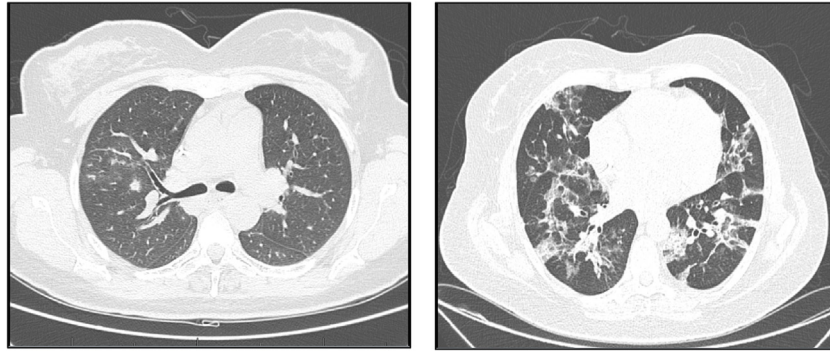


Fig. 1. Pulmonary CT before HSCT.
Pulmonary CT day 119 HSCT.

by liposomal Amphotericin B (LAmB) 300 mg/d because of increased rates of liver enzymes (ALT 166 U/L and AST 85 U/L). Voriconazole was reintroduced (200 mg IV q12 h) when the liver enzymes were normal. There was improvement of pulmonary symptoms and radiological images with non-invasive ventilation after 23 days of antifungal drugs and GVHD treatment (methylprednisolone 90 mg/d) (Fig. 1). The patient was discharged from the hospital on day 142.

On day 145, three days after she was discharged, the patient was hospitalized with dyspnea, acute kidney injury and CMV reactivation (RT-PCR CMV 401UI/mL) that was treated with ganciclovir (2,5 mg/kg/d IV q 12 h) adjusted for kidney function (KDIGO II). Blood cultures were collected, voriconazole was replaced by LAmB (3 mg/kg/d) and piperacilin-tazobactam (4,0 mg IV q6h) was introduced. On day 157 she evolved to acute severe respiratory failure and renal replacement therapy. She was transfer to the intensive care unit and mechanic ventilation was started. In this context, cultures were collected and trimethoprim/sulfamethoxazole (trimethoprim 15 mg/kg/d IV q6h), meropenem (1g IV q12h), colistin 2,5 mg/kg/d IV qDay), amikacin (15 mg/kg/d q24h) and linezolid (600 mg q12h) were given. Bronchoalveolar lavage was performed and Ziehl-Nielsen staining, bacteria and fungi cultures, Multiplex PCR for virus and galactomannan were negatives. Pulmonary CT before HSCT showed sparse and bilateral micronodules, measuring up to 0.3 cm and stable calcifications. Pulmonary CT on day 119 HSCT showed sparse nodules and micronodules, pneumonic foci in organization and opacity in frosted glass (Fig. 1).

After five days, blood cultures were positive for *Achromobacter* sp. and *Rhodococcus* sp. using VITEK[®] Biomerieux-France and matrix-assisted laser desorption ionization with time of flight (MALDI-TOF-Biomerieux-France). We performed the sequencing of 16S ribosomal RNA gene (16S rRNA gene) of *Rhodococcus* sp to confirmed the identification that revealed 100 % of identity with *Rhodococcus hoagii* according to the National Center for Biotechnology Information (NCBI) database. Genbank access number SUB4217796 Seq1 MH539885.

The central venous catheter was removed, moreover, despite the treatment with active antibiotics against *R. hoagii* as linezolid, amikacin and meropenem for 14 days, the patient evolved with multi organ dysfunction syndrome and death on day 172 (Fig. 2).

Discussion

We present here a case report of a bloodstream infection (BSI) caused by *R. hoagii* in an allo-HSCT patient who evolved to death. This bacterium has been associated with severe infections such as BSI and pneumonia with high mortality in this population of patient; mainly allo-HSCT patients (Table 1).

Rhodococcus has been associated to exposure to rural areas. Its transmission usually occurs by inhalation of contaminated soils; as the soils of horses 's farmers contains highly concentration of this bacteria [1,4,5]. Recently its taxonomy changed based on sequencing methods, thus, *Rhodococcus equi* was named as *R. hoagii* according to the rules of the Bacteriological Code [14]. Although the 16S rRNA gene sequencing analysis is an useful method to identify the Rhococcus; this gene is unable to differentiate some of *Rhodococcus* species [15,16]. Thus, this technique can result in misidentification of species. Up to now, whole genome sequencing (WGS) analysis is consider the trustworthy method to identify the species in this genus [15–17]. Moreover, the WGS is not available as routine in most of low income countries. In our case report the 16S rRNA sequencing revealed 100% of identity with *Rhodococcus hoagii* according to NCBI database.

The development of the infection by *Rhodococcus* occurred later than day 100 in most of cases of HSCT [4,6–15]. Regarding risk factors; it has recently been shown, in a case-control study that O2 conditions (diabetes mellitus and a prior opportunistic infection) might increase the risk of infection caused by *Rhodococcus* [3]. Other authors, however, did not evidence any risk factors [4,6–15]. In our report, the patient was a nurse that lived in urban areas, and stated no recent trips to countryside areas neither contact with animals. Infections caused by *Rhodococcus* are underreported and

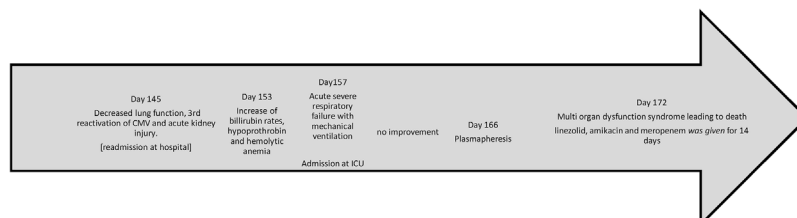


Fig. 2. Timeline showing main events that occurred during patient treatment.

Table 1
Cases of *Rhodococcus* in allo-HSCT patients described in the literature.

Year (Reference)	Age years	Gender	Rhodococcus species	Comorbidities	Clinical diagnosis	Treatment	Outcome
1995 (10)	29	Male	<i>R. equi</i>	Lymphoma	Pneumonia	Not reported	Death
2008 (4)	61	Male	<i>R. equi</i>	Lymphoma	Pneumonia	Vancomycin (treatment failure); ertapenem and rifampicin	Cure
2012 (11)	60	Male	<i>R. equi</i>	T-cell prolymphocytic Leukemia	Lung nass, pleural malakoplakia	Right upperlobe lobectomy	Cure
2012 (5)	64	Male	<i>R. corynebacteoides</i>	Myelodysplastic syndrome	Bacteremia	cefepime and ceftazidime	Death
2012 (8)	68	Male	<i>R. equi</i>	Not Informed	Mediastinitis	Vancomycin and ciprofloxacin	Not reported
2013 (7)	61	Male	<i>R. globerulus</i>	Acute Myelomonocytic Leukemia	Bacteremia	Vancomycin and ciprofloxacin	Cure
2017 (present case)	37	Female	<i>R. equi</i>	Acute Myeloid Leukemia	Pneumonia	Meropenem, amikacin and linezolid	Death

probably misdiagnosed because of a conjunction of factors that include the difficult of identification of genus and species by traditional techniques, and the importance of history as previous exposure to rural area, contact with animal as horse which should always prompt investigation. In addition, *Rhodococcus* is a diverse spectrum of disease [17]. Immunocompromised patients can present pneumonia, BSI, malakoplakia and mediastinitis caused by *Rhodococcus* [17]. This clinician characteristic makes the diagnostic hypothesis even more challenging.

Most of the cases reported in transplantation patients described the lung as the mainly route of infection [4,6–17]. Around 80 % developed pulmonary cavity, and among immunocompromised populations, it is often observed disseminated disease as well [1]. Our patient presented respiratory symptoms but the respiratory cultures were negative. Although, she received a multidrug treatment including antibiotics with action against *Rhodococcus* such as linezolid, amikacin and meropenem [13,14] she evolved to death. The literature recommends at least combination of two antibiotics such as vancomycin, carbapenems, aminoglycosides and quinolones, to treat infections caused by this microorganism [4,6–15]. As for systemic infections, monotherapy might result in emergence of resistance [4,6,7–15]. But, there is no robust data to establish the proper antibiotic regime to treat infections caused by this organism.

Conclusion

Our case-report emphasizes the importance of early diagnosis and the use of 16S rRNA sequencing as a tool to confirmed the identification of species of *Rhodococcus* infection.

Author contribution

PSC and L ZMM data collection analysis and writing; MV B; HH and FNO data collection; FR and CR laboratory and sequencing data; VR data collection and SFC data analysis and writing.

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Declaration of Competing Interest

All authors declare that they have no conflict of interest.

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