Case Report

Purpureocillium lilacinum as unusual cause of pulmonary infection in immunocompromised hosts

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Abstract

Purpureocillium lilacinum (P. lilacinum) is an emergent pathogenic mold that presents more commonly as an ocular infection, cutaneous and/or subcutaneous infections in patients that are usually immunocompromised. A pulmonary presentation is rare, the clinical presentation is fever and cough with radiographic presentation as pleural effusion, single-lung consolidation, and cavitary pulmonary disease. We present a case of a patient with hematologic malignancy with febrile neutropenia; after receiving chemotherapy, the patient developed a pulmonary infection with multiple bilateral consolidations shown in the thoracic computed tomography scan. Fever persisted in spite of the use of wide-spectrum antibiotics and amphotericin. Bronchoalveolar lavage was performed and the samples were cultured, isolating in the Sabouraud Dextrous Agar a filamentous fungi growth with purple colonies that were identified morphologically as P. lilacinum and later it was confirmed by molecular methods. Once the infectious agent was identified, we continued amphotericin and oral voriconazole was added to the treatment with complete resolution of the infection. The report aims to create awareness of this emerging infectious disease, as there is little information concerning the treatment and the prognosis of patients infected by P. lilacinum with a pulmonary presentation.

Key words: purpureocillium lilacinum; fungal infection; mycology; pneumonia; immunocompromised host; infectious diseases.


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Introduction

Purpureocillium lilacinum (P. lilacinum), previously known as Paecilomyces lilacinus is an emerging pathogenic mold found worldwide in soil, decaying vegetation, nematodes and as a contaminant in laboratory air. This agent is known to cause predominantly ocular and subcutaneous infection, and in rare cases, there have been reports of pulmonary infections [1-2]. We present the first case of bilateral pneumonia due to P. lilacinum in a hospitalized immunocompromised patient and a review of the literature. The first aim of this report is to describe the clinical evolution, treatment options and prognosis of this emerging infectious disease.

Case Report

A 51-year-old female with no relevant medical history was admitted to the Emergency Department (ED) with a history of 6 months with malaise and dyspnea. At physical examination, the patient presented general paleness and no other relevant data. Vital signs were stable with blood pressure 110/70 mmHg, heart rate 74 beats per minute, respiratory rate 14 breaths per minute and temperature of 36.2 degrees Celsius (°C). Laboratory tests showed hemoglobin of 4.68 g/dL, white blood count of 1.68 K/µL, with neutropenia of 0.618 K/µL, and thrombocytopenia of 23.4 K/µL. Peripheral smear showed the presence of blasts, therefore a bone marrow aspirate was performed confirming the diagnosis of acute myeloid leukemia (FAB M4) by cytogenetics and cytometry evaluation.

The patient was admitted to the internal medicine ward for the administration of chemotherapy consisting of cytarabine and mitoxantrone 150 mg and 20 mg once daily (QD) for 5 days, respectively. Prophylactic itraconazole, acyclovir, and levofloxacin were initiated on admission due to severe neutropenia which persisted throughout the hospitalization; the patient also required
multiple transfusions of packed red cells along with two platelet apheresis due to persistent pancytopenia. On day fifth, the patient presented a fever of 38.6°C which did not respond to acetaminophen, dyspnea, and non-productive cough; thus imipenem 500 mg every 6 hours was started. Because of the new-onset fever, a chest X-ray and a sinus computed tomography (CT) scan was taken. Sinus CT scan was unremarkable but the chest X-ray showed a right lung infiltrate. A thorax CT scan was performed reporting bilateral lung infiltrates in the right lower lobe with the presence of a ground-glass opacity surrounding a pulmonary nodule (halo sign) and in the left lung two smaller consolidations in the lower lobe (Figure 1a and Figure 1b). Based on the image and the clinical presentation we added intravenous vancomycin 1g twice daily (BID) and amphotericin B (AMB) deoxycholate 50 mg QD to the treatment because of the suspicion of invasive pulmonary aspergillosis. Fever persisted (38-39°C) in spite of the wide spectrum treatment, thus we performed a bronchoscopy with bronchoalveolar lavage (BAL) and samples were taken for cultures of bacteria, fungi, mycobacteria, diverse cytology, and GeneXpert MTB/RIF.

Figure 1. Chest CT scan.

![Chest CT scan](image1a)

1a. Black arrow indicates a lung consolidation with halo sign in the posterior segment of right lower lobe typically seen in fungi and mycobacterial infections and the white arrow indicates a consolidation in the left lung (coronal thorax CT view); 1b. Black arrow indicates a big consolidation in the posterior segment of right lower lobe typically seen in fungi and mycobacterial infections and the yellow arrows indicates smaller consolidations in the left lung (axial thorax CT view).

![Chest CT scan](image1b)

Figure 2. Macro-view and microscopic view of P. lilacinum culture.

![Macro-view and microscopic view](image2a)

2a. Black arrow is showing a macro-view of violet-colored colonies; 2b. Black arrow indicating the chains of elliptical conidia with divergent branches characteristic of Purpureocillium lilacinum.
The patient persisted with fever but with no deterioration in her clinical status. Cultures growth were negative except for the Sabouraud dextrose agar which presented a filamentous fungi growth with a light purple coloration at the center of the colony (Figure 2a), and a microscopic view of philaids with elongated necks bearing divergent branches of elliptic conidia (Figure 2b). The fungus was identified morphologically as Purpureocillium lilacinum (*P. lilacinum*) and its identity was confirmed by molecular methods. Genomic DNA of the fungus was extracted by the use of a commercial kit (Quick-DNA™Fungal/Bacterial MiniprepKit - Zymo Research, Irvine CA, USA) and the non-coding fungal region ITS was amplified and sequenced by the Sanger method. BLAST sequence analysis led to the identification of *P. lilacinum* (GenBank accession number: MN396442). Antifungal susceptibility of the isolate was determined by the broth microdilution method in accordance with the CLSI document M38-3rd Edition [1], obtaining the following results: AMB = 8 µg/mL and voriconazole = 1 µg/mL. Antibacterial agents were suspended and voriconazole (4mg/kg BID) was added to the AMB treatment with eventual resolution of fever and improvement of the respiratory symptoms. We continued the treatment in the hospital for 21 days and finally, the patient was discharged asymptomatic with oral voriconazole for 6 weeks and follow-up in the hematology and infectious diseases clinic.

### Discussion

*P. lilacinum*, previously known as *Paecilomyces lilacinus*, is a saprophytic and filamentous mold that exists in soil and decaying vegetation, it can produce conidia and spores in human tissue and is usually not a pathogenic mold [2]; however, in recent decades it has become an emergent pathogen causing of infection mainly in immunocompromised hosts. There are risk factors associated with acquiring this infection, for example, patients receiving antibacterial treatment, oncological chemotherapy, primary or acquired immunodeficiency, bone marrow and solid organ transplantation [3,4].

*P. lilacinum* is an agent that cause hyalohyphomycosis, with a variety of clinical presentations, the most common correspond to oculomycosis and cutaneous infections, the most frequent ocular manifestations are keratitis and endophthalmitis, these are usually associated with intraocular lens implantation, non-surgical trauma with or without a foreign body, use of contact lenses and ophthalmic surgery. Cutaneous and subcutaneous infections come in a wide variety of presentations, consisting of solitary or disseminated skin eruptions,

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### Table 1. Summary of cases reported with pulmonary *P. lilacinum* infection.

<table>
<thead>
<tr>
<th>Case</th>
<th>Reference</th>
<th>Country</th>
<th>Age/Gender</th>
<th>Clinical Presentation</th>
<th>Predisposing Factor(s)</th>
<th>Diagnostic method</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Mormede et al. 1984 [8]</td>
<td>France</td>
<td>58/F</td>
<td>Pleural Effusion, Diffuse Reticulonodular Lesion</td>
<td>Interstitial lung disease, Corticosteroids</td>
<td>Pleural effusion culture</td>
<td>Antibiotics, antiinflammatory, no antifungal given</td>
<td>Died of hepatic complications</td>
</tr>
<tr>
<td>3</td>
<td>Liu et al. 1998 [9]</td>
<td>United States</td>
<td>Not available</td>
<td>Lung Disseminated</td>
<td>Acute lymphoblastic, leukemia</td>
<td>Lung biopsy culture</td>
<td>Not available</td>
<td>Recovered</td>
</tr>
<tr>
<td>4</td>
<td>Ono et al. 1999 [10]</td>
<td>Japan</td>
<td>57/M</td>
<td>Lung Abscess</td>
<td>Not available</td>
<td>Not available</td>
<td>Lobectomy</td>
<td>Recovered</td>
</tr>
<tr>
<td>5</td>
<td>Mullane K et al. 2007 [11]</td>
<td>United States</td>
<td>60/M</td>
<td>Lung Consolidation, Nodules on CT Scan, Fever, Cavitary Pulmonary Disease</td>
<td>Multiple Myeloma, Asthma, diabetes, rheumatoid arthritis</td>
<td>BAL culture</td>
<td>Posaconazole</td>
<td>Recovered</td>
</tr>
<tr>
<td>7</td>
<td>Pechin M. et al. 2013 [12]</td>
<td>Spain</td>
<td>34/M</td>
<td>Neutropenic Fever, Lung Consolidation, Neutropenic Fever, Nodules on CT Scan</td>
<td>Acute Lymphoblastic Leukemia</td>
<td>BAL culture</td>
<td>Posaconazole</td>
<td>Recovered</td>
</tr>
<tr>
<td>8</td>
<td>Hobson et al. 2013 [13]</td>
<td>United States</td>
<td>48/M</td>
<td>Neutropenic Fever, Lung Consolidation, Neutropenic Fever, Nodules on CT Scan</td>
<td>Myeloid Leukemia, Chemotherapy</td>
<td>BAL culture</td>
<td>Posaconazole</td>
<td>Recovered</td>
</tr>
<tr>
<td>10</td>
<td>Actual case</td>
<td>Mexico</td>
<td>51/F</td>
<td>Neutropenic Fever, Bilateral Lung Consolidation, Angioinvasive- Halo Sign</td>
<td>Myeloid Leukemia, Chemotherapy</td>
<td>GenBank of BAL culture</td>
<td>Voriconazole</td>
<td>Recovered</td>
</tr>
</tbody>
</table>

CT: computed tomography; F: female; M: male; BAL: bronchoalveolar lavage; n-LAB: nebulized liposomal amphotericin; COPD: chronic obstructive pulmonary disease.
macules, vesicles, papules, nodules with necrotic center and soft-tissue infections [4].

A wide variety of unusual clinical manifestations have been associated with *P. lilacinum*, there are reports of onychomycosis, sinusitis, osteomyelitis and pulmonary involvement. Pulmonary infections by *P. lilacinum* are unusual with few cases reported in the literature in both immunocompromised and immunocompetent hosts. The most frequent clinical manifestations are malaise, fever, cough, pleuritic pain and dyspnea. There are a variety of radiographic presentations reported in the literature including lung nodules, cavitary pulmonary disease, pleural effusion, lung abscess, solitary pulmonary lesion and lung consolidation [5,6]. However, there are no reported cases of bilateral lung consolidation.

At the moment of writing this paper (written in English) 9 cases have been reported in the literature describing pulmonary infections secondary to *P. lilacinum*: they are described in Table 1, with the respective thorax CT scan findings and the diagnosis methods [6-14]; all cases described in Table 1 show the pulmonary infection with morphologic criteria and positive cultures (sputum, BAL and biopsy): Only Khan et al. [6] and our case confirmed the diagnosis using the criteria previously explained and adding genotypic identification (GenBank) to give additional information about the causative pathogen.

The mean age of presentation in patients with pulmonary infection due to *P. lilacinum* was 48 years old (20-80 years old), with a predominance of the male gender (60%), the most frequent predisposing factor was hematologic malignancies (50%), the most frequent clinical presentation was fever (40%), there were a variety of radiographic presentations; unilateral lung consolidation (20%), cavitary pulmonary disease (20%) and nodules on the thorax CT scan (20%) were the most reported signs, while the most frequent outcome was a recovery from the pulmonary infection (60%) with voriconazole and posaconazole as primary therapy.

Diagnosis of *P. lilacinum* can be challenging because of the similarity on morphology when compared with Aspergillus and other agents of hyalohyphomycosis; thus, several diagnostic tools are available to aid in the correct identification of this pathogenic mold, *P. lilacinum* grows rapidly on Sabouraud glucose agar, giving rise to a white colony and gradually becomes lilac or vinaceous in color; additionally, at microscope the mold can be characterized by septate, branching hyaline hyphae with phialides tapering at its distal end [2,15]. Using genotypic identifications alongside cultures can boost the identification of fungal pathogens, the internal transcribed spacers (ITS1 and ITS2) regions of the ribosomal RNA gene cluster are molecular markers that help in the estimation of phylogenetic relationship between species: it is a well-defined barcode that has the highest probability of successful identification for the broadest range of fungi, not just *P. lilacinum*, making it a great diagnosis test [16,17].

Systemic treatment is important in patients with pulmonary involvement, *P. lilacinum* has been reported to show reduced susceptibility to AMB, echinocandins and itraconazole, but it showed good susceptibility against voriconazole and posaconazole. There are reports that voriconazole has been used to treat *P. lilacinum* successfully in a wide variety of clinical presentations (including pulmonary involvement) thus being first-choice treatment [18]. In our case, the initiation of voriconazole was accompanied by a fast recovery of symptoms.

No information about the use of primary prophylaxis was found in the cases of *P. lilacinum* with pulmonary involvement described in Table 1, except for the case of Mullane K. et al. [11] that used fluconazole in a patient with multiple myeloma disorder that underwent an autologous hematopoietic stem cell transplant. In our case we can hypothesize the presentation of this breakthrough fungal infection is due to multiple reasons. In Mexico itraconazole is exclusively available as capsules which has reduced bioavailability, measurement of serum level concentrations is not obtainable so we were unable to know if therapeutic concentrations were reached and finally the activity of itraconazole against this fungal pathogen is limited [18], all of which could have contributed to acquiring the infection in this patient.

In our review of the literature and to the best of our knowledge, we described a new radiographic presentation in a patient infected by *P. lilacinum* and we indicated in the largest list of patients with pulmonary *P. lilacinum* infection the general characteristics of these patients in hope of helping our colleagues to promptly identify and treat this infection. The relevance of this case is to remark the challenge of *P. lilacinum* as a cause of pulmonary infection due to the similarities on the clinical and radiographic presentations with other opportunistic and more common infections such as *Candida* and *Aspergillus*, because of the different effectiveness of antifungal therapies, thus remarking the importance of prompt identification of the pathogenic agent to initiate the most effective therapy.
References

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