Medical Mycology Case Reports 22 (2018) 65–68

Contents lists available at ScienceDirect

Medical Mycology Case Reports

journal homepage: www.elsevier.com/locate/mmcr

Blastoschizomyces capitatus pneumonia in a patient with untreated chronic lymphocytic leukemia

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ARTICLE INFO

Keywords:
Pneumonia
Blastoschizomyces
Chronic lymphocytic leukemia
Diagnosis
Therapy

ABSTRACT

Several cases have been reported of *B. capitatus* infections in immunocompromised patients. Acute leukemia is the main predisposing factor. Chronic lymphocytic leukemia (CLL) is not usually associated with opportunistic infections. We report a case of pulmonary infection by *B. capitatus* in a patient with untreated chronic lymphocytic leukemia. Although the patient had a complete recovery, we believe that this report will alert clinicians to consider *B. capitatus* as possible cause of severe pneumonia in untreated CLL.

1. Introduction

Invasive fungal infections are increasingly important as causes of morbidity and mortality especially in immunocompromised patients. *Saprochaete capitata*, (Teleomorph: *Magnusiomyces capitatus*, previously named *Geotrichum capitatum*, *Trichosporon capitatum* or *Blastoschizomyces capitatus*) [1] is a cosmopolitan and ubiquitous fungus, widespread in nature, that can be found in the normal microbial flora colonizing humans. It rarely causes invasive human infections, usually in immunocompromised individuals [2]. Lung infection can develop as an opportunistic infection in patients with haematological malignancies, severe neutropenia, cytotoxic chemotherapy, and corticosteroids use [3]. However, it can occur also, in very rare case-reports, in immunocompetent patients without chronic underlying lung disease [4,5]. We report a case of pulmonary infection by *B. capitatus* in a patient with untreated chronic lymphocytic leukemia (CLL). All previous reported events of *B. capitatus* pneumonias in patients with CLL occurred in subjects who were previously treated for CLL. In fact, untreated CLL is not usually associated with opportunistic infections.

2. Case

A 86 year-old male patient presented to our Department of Pneumology with fever (39 °C), general sickness, breathlessness and productive cough (day 0). Although treated at home with cephalosporins (ceftriaxone) and paracetamol, he did not respond to drugs. Patient had a history of chronic lymphocytic leukemia, in follow up and not treated, diagnosed in 2006; renal failure of undefined origin; and abdominal aortic aneurysm with surgical repair. Admission laboratory studies showed Hb 9,1 g/dl, total leucocyte count 6800/μl with differential leucocyte count (DLC) $P_{55,4}$ (polimorph) $L_{37,5}$ $M_{6,7}$ $E_{0,3}$ $B_{0,1}$ and platelets 81 × 103/μl (normal range: 150–400 × 10^3 μl). The level of serum urea was 133 mg/dl (normal range: 17–43 mg/dl), and creatinine level was 4,6 mg/dl (normal range: 0,7-1,2 mg/dl). Elevated inflammatory markers, such as C-reactive protein 164,5 mg/l (normal range 0–5 mg/l) and erythrocyte sedimentation rate 51 mm (normal range 0–20 mm) were present. Results of liver function tests, and coagulation studies all were normal. Electrolyte levels were within the reference range. At physical examination, his respiratory rate was 28/min, blood pressure 130/80 mmHg, heart rate 85/min and arterial oxygen saturation was 89% on room air; and increased to 92% on 96% oxygen via a face mask. Rales were present in one third of the lung field bilaterally. Additionally, his blood gas results were pH 7,46; PaO_2 64 mmHg; $PaCO_2$ 25 mmHg; HCO_3- 20,9 mmol/l; BE -5,1 mmol/l; and SaO_2 93% on room air. A chest radioghraph showed consolidation in the right lower lobe (Fig. 1) (day +1). Chest CT scan (Fig. 2) revealed areas of ground-glass attenuation with (alveolar) consolidation in posterior segment of the upper left lobe, in the middle lobe and lower lobes; bilateral pleural effusion; limphadenopathy; and scattered micronodules could be observed; ectasia of the thoracic aorta; Intrathoracic mediastinal thyroid goiter (day +3).

Abdominal ultrasound showed an increased liver volume with steatosis, enlarged spleen, and kidneys had normal size, with some cysts. Additionally laboratory tests were done; blood and urine cultures

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https://doi.org/10.1016/j.mmcr.2018.09.004
Received 14 August 2018; Received in revised form 13 September 2018; Accepted 20 September 2018
Available online 21 September 2018

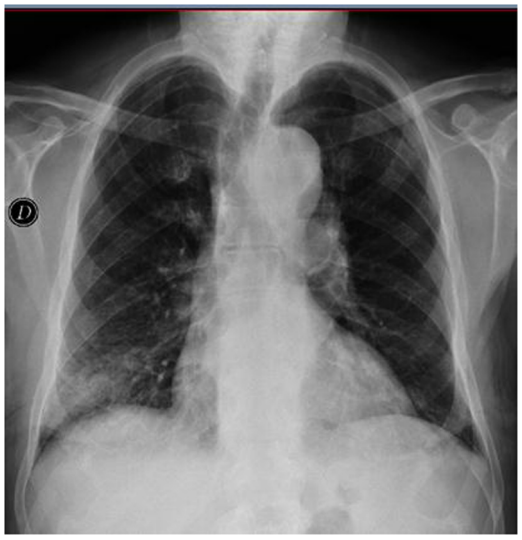

Fig. 1. Chest radioghraph: consolidation in the right lower lobe (patchy right lower lobe infiltrate).

were negative. Viral and bacterial investigations including Cytomegalovirus, echovirus, coxsackie, legionella, *Mycoplasma pneumoniae* showed negative results. The biomarker 1,3-β-D-glucan, performed by means of Fungitell kit (Associates of Cape Cod Inc., Falmouth, Massachusetts), was positive (91 pg/mL) (day +4). The patient had been given piperacillin with tazobactam intravenous 4,5 g every 8 h daily; sulfamethoxazole and trimethoprim oral 160/800 mg twice daily. He was also treated with immunoglobulin intravenous and erythropoietin. A sputum sample was send for the research of *Pneumocystis* DNA, for direct microscopic examination and fungal culture in Sabouraud's dextrose agar medium supplemented with chloramphenicol and gentamycin (day +5). The RIDA®GENE *Pneumocystis jirovecii* real-time PCR assay (R-Biopharm, Darmstadt, Germany) was use for the qualitative detection of *Pneumocystis jirovecii* DNA. PCR was performed on the CFX96™ (Bio-Rad) and DNA was extracted by using the EZ1 DNA tissue kit (Qiagen) and following the manufacturer's instructions. Direct microscopic examination with 15% potassium hydroxide (KOH) showed numerous thin, septate, hyaline hyphae while *Pneumocystis* DNA was negative (day +5). After 72 h of incubation at 32 °C growth of numerous cream colored colonies was seen (Fig. 3).

Identification of the yeast isolate was performed by conventional methods [1,6] including morphologic examination on corn meal Tween 80 agar. These colonies were identified as *Blastoschizomyces capitatus* by cornmeal agar medium with the addition of Tween-80, according to the Dalmau plate technique and by analysis of biochemical patterns by ID32C kit (bioMérieux, Marcy l'Étoile, France) [6] (day +10). Matrix-assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOT MS) on a Microflex LT (Bruker Daltonics, Bremen, Germany) platform after ethanol-formic acid extraction identified the isolate as *Blastoschizomyces capitatus*. Susceptibility to fluconazole, itraconazole, voriconazole, posaconazole, flucytosine, caspofungin, anidulafungin, micafungin, amphotericin B, was evaluated by the Sensititre®YeastOne method. MIC values of 2 μg/mL for fluconazole, 0.12 μg/mL for itraconazole, 0.03 μg/mL for voriconazole, 0.25 μg/mL for posaconazole, 32 μg/mL for flucytosine, 8 μg/mL for caspofungin,

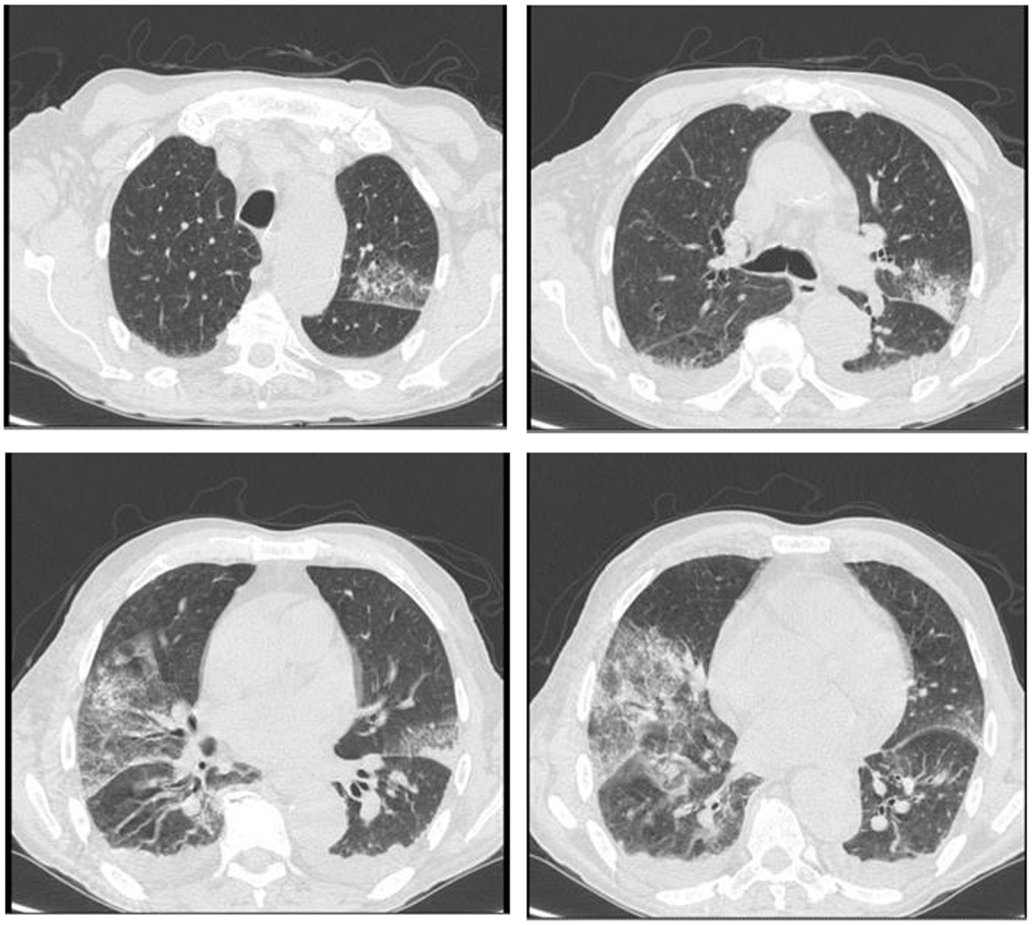

Fig. 2. Chest CT scan: areas of ground-glass attenuation with (alveolar) consolidation in posterior segment of the upper left lobe, in the middle lobe, and lower lobes; bilateral pleural effusion; limphadenopathy; and scattered micronodules could be observed. Ectasia of the thoracic aorta.

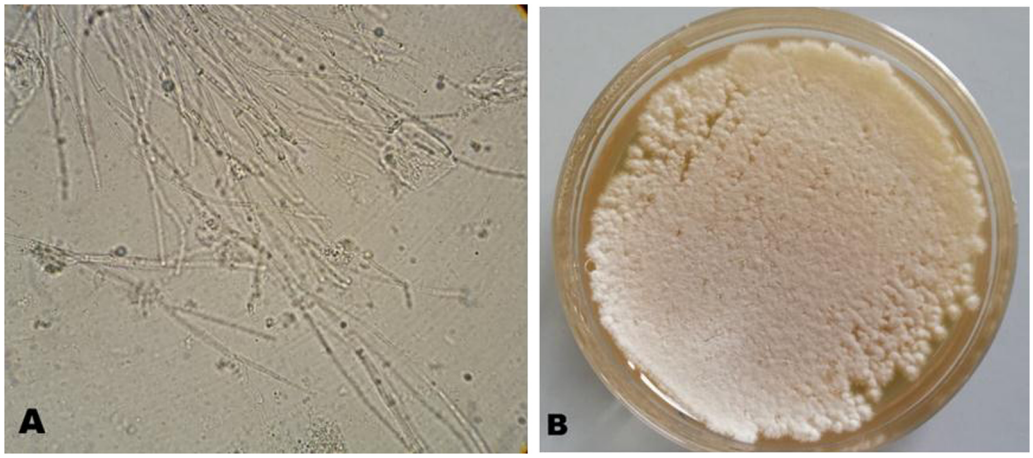

Fig. 3. Direct examination of sputum sample with 10% KOH (A) (original magnification × 40), (B) growth on Sabouraud Dextrose Agar after 72 h at 32 °C.

8 μg/mL for micafungin, 4 μg/mL for anidulafungin, 1 μg/mL for amphotericin B were obtained. Patient was put on itraconazole 100 mg/die orally (day +8). He responded well after 5 days. Before discharge Chest CT (Fig. 4) was performed and revealed a prominent reduction of ground glass opacities and consolidation in all involved lobes. Arterial blood gas levels in room air were as follows: pH 7.38; PO2 88 mmHg; PCO2 29 mmHg; HCO3-std 19,4 mmol/L; BE -7,1 mmol/L; SaO2 97%. The patient was discharged with improvement of dyspnea, oxygenation and radiological findings (day +16). He had to continue treatment for the next 30 days.

3. Discussion

Blastoschizomyces capitatus is a rare, but emerging yeast mostly responsible for often lethal fungaemia in patients with profound neutropenia in the haematology setting [7,8]. Not much data is however available on pulmonary infection by *B. capitatus* in an immunocompetent individual. Pulmonary mycosis in non-neutropenic patient affects two main populations: the solid organ transplanted patients and patients whose local defences are altered by chronic underlying lung pathology. We report a case of severe pneumonia in patient with CLL, diagnosed 9 yrs ago, on “Watch and Wait” (W&W) follow-up and not treated. *B. capitatus* pneumonia in a CLL-patient on W&W follow-up is, to our knowledge, a rare event. In addition, the patient presented renal failure which is uncommon even in CLL. We don't know if *B. capitatus* caused renal failure in our case or this condition was pre-existent, but some case reports are described in literature. Treatment with itraconazole ameliorated also renal functionality and the

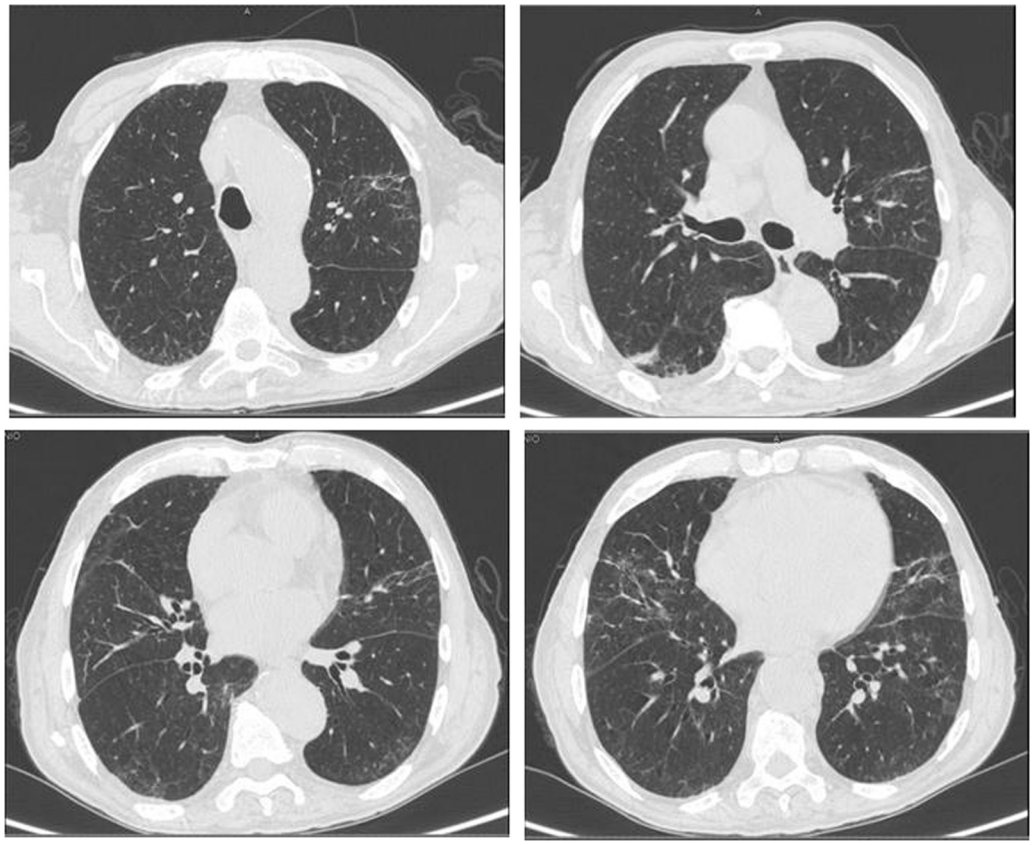

Fig. 4. Chest CT scan after treatment with itraconazole. A prominent reduction of ground glass opacities and consolidation in all involved lobes were observed.

relationship between fungal infection and renal failure is real hypothesis even not demonstrated. Although the patient had a complete recovery, we believe that this report will alert clinicians to consider *B. capitatus* as possible cause of severe and even near-fatal pneumonia in untreated CLL. Considering that *B. capitatus* is intrinsically resistant to echinocandins [1], the use of definitive diagnostic procedures and the rational application of antifungals is essential for appropriate management of these infections.

Acknowledgements

None.

Conflict of interest

There are none.

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