

Letter to the editor

Fabio Miglietta¹
Claudio Palumbo¹
Maria Pizzolante¹
Maria Letizia Faneschi¹
Marco Cucurachi²
Luciano Velardi³
Giambattista Lobreglio⁴

A rare case of *Saprochaete capitata* fungemia in a critical ill patient without hematologic and oncological disorders

¹Laboratory of Microbiology, Vito Fazzi Regional Hospital, Lecce, Italy.

²Anesthesiology Unit, Vito Fazzi Regional Hospital, Lecce, Italy.

³Istituto di Nanotecnologia, CNR-NANOTEC, Bari, Italy.

⁴Laboratory of Clinical Pathology, Vito Fazzi Regional Hospital, Lecce, Italy.

Sir,

Increasingly, invasive fungal infections (IFI) are occurring in non-neutropenic patients treated in Intensive Care Unit (ICU)¹. The majority of fungal infections in ICU is due to *Candida* species whereas fungemias due to filamentous or yeast-like fungi have rarely been encountered in the intensive care settings. Invasive geotrichosis has been reported exclusively in patients that showed signs of severe immunodeficiency, particularly those affected by hematological malignancies². We describe a rare case of *Saprochaete capitata* fungemia preceded by RSV community-acquired pneumonia with secondary lung infection due to *Pseudomonas aeruginosa*. This patient showed no signs of immunosuppression at the time of hospital admission; medical record and cell blood count test did not disclose any hematologic and oncological disorder; HIV, HBV and HCV tests resulted also negative. A previously healthy 60 year-old man was admitted to our hospital in May 2014 because of dry cough, fever (37.3°C), wheezing and rare signs of dyspnea. The laboratory data on hospital admission included white blood-cells count (WBC) of 12.2×10^9 /L with a differential of 39.6% neutrophils, 55.1% lymphocytes, 4.5% monocytes, 0.6% eosinophils, 0.2% basophils, C-Reactive protein of 12.1 mg/L (reference < 10 mg/L) and Procalcitonin < 0.05 ng/mL (reference < 0.05 ng/mL). At admission, he resulted positive for IgM class antibodies anti-Respiratory Syncytial Virus; RSV infections was, at a later stage, confirmed through Real-time RT-PCR assay from bronchoalveolar lavage (BAL) fluid in absence of other microbial isolates from BAL culture. For worsening of dyspnea, the patient was transferred in ICU. Chest computed tomography (CT) scan performed on day +7 showed small mediastinal lymph nodes and bilateral subpleural areas of airspace opacity

with air bronchograms. A supportive therapy with the administration of antipyretics and intravenous fluids was performed, with an empirical antibiotic treatment with clarithromycin (for 5 days) to prevent possible secondary bacterial infections. In the first week of ICU hospitalization, the patient showed an initial improvement of the clinical picture and hemogasanalysis parameters and a reduction of fever and WBC count. Unfortunately at day +12, he showed increasing signs of respiratory failure and fever (38.7°C) as well as a cough with purulent sputum and pleuritic chest pain. Physical examination indicated a blood pressure of 110/70 mm Hg with a respiratory rate of 29 breaths/min.

A *P. aeruginosa* ESBL producing strain (according to EUCAST criteria) was isolated on day +13 from a purulent sputum with 10^6 colony forming units/mL in absence of other microbial isolates in the lower respiratory tract. The sputum gram stain showed numerous neutrophils with intra and extra-cellular gram-negative rods suggestive of *P. aeruginosa*. Antimicrobial therapy with ciprofloxacin and imipenem was started. In the following week his condition rapidly deteriorated leading to the definition of severe acute respiratory distress syndrome (ARDS) according to the Berlin definition³, moreover hemogasanalysis parameters confirmed a significant worsening of the respiratory functions. For these reasons, the patient was intubated and connected to the automatic respiratory system and subsequently to extracorporeal membrane oxygenation treatment (ECMO). A new chest CT scan showed the presence of pneumomediastinum, right pneumothorax with worsening of the areas of parenchymal consolidation. In absence of improvements in the pulmonary framework, antimicrobial therapy was modified using meropenem and colistin in aerosol. At day +26, abdominal ultrasound showed the appearance of consolidations, absent at the time of hospital admission, in the liver parenchima. In the following 48 hours β -D-Glucan of 97 pg/mL (reference < 60 pg/mL) was detected and *S. capitata* was isolated in two blood cultures (figure 1).

Furthermore serum alkaline phosphatase went from 88 U/L

Correspondence:

Fabio Miglietta:

83, Montegrappa Street, 73018, Squinzano, Lecce, Italy.

Tel. +39 3492548568

Fax. +39 0832782033

E-mail: miglietta_fabio@yahoo.it

Antifungal agent tested	MIC (mg/L)
Amphotericin B	0.25
Micafungin	8
Caspofungin	8
Anidulafungin	4
5-Fluorocytosine	0.06
Posaconazole	0.25
Voriconazole	0.12
Itraconazole	0.25
Fluconazole	8

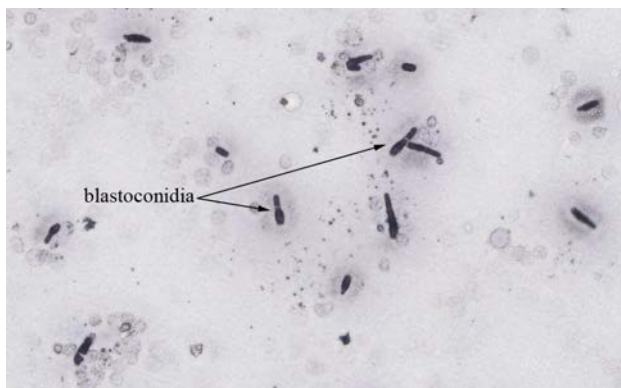


Figure 1 Microscopy of isolated *S. capitata* from Sabouraud dextrose agar visualized by Gram stain technique, 40x objective.

(day 25th) to 266 U/L (day 27th) (reference 40 – 130 U/L) while total bilirubin increased from 8.2 mg/dL (day 25th) to 17.06 mg/dL (day 27th) (reference < 1.25 mg/dL). At day +30, empiric antifungal therapy with caspofungin, begun the previous day, was replaced by combination treatment with liposomal amphotericin B and flucytosine according to MIC's information (table 1), in addition to colistin and meropenem.

In the days that followed the patient's conditions remained still severe. The clinical picture worsened dramatically at day +40 with neutropenia, signs of multiple organ failure and hypotension refractory to inotropic treatments leading to the patient death (at day +41).

Fungal isolate from blood cultures was plated on Sabouraud dextrose agar, incubated at 35°C for 24 h and identified by using Maldi-TOF analysis (Bruker Daltonik Maldi Biotyper, Germany). Molecular identification was performed by amplification and sequencing of the ITS1 region of ribosomal DNA using universal fungal primers ITS1 and ITS4. DNA extraction was carried out by NucliSens easyMAG platform (bioMérieux,

France) following manufacturer instructions. Hotstart Taq Master Mix Kit (Qiagen, Hilden, Germany) and universal fungal primers ITS1 and ITS4 were used for ITS region amplification as previously described⁴. PCR products were sequenced by ABI PRISM 3130xl Genetic Analyzer (Applied Biosystems, USA). Species identification was performed using the Basic Local Alignment Search Tool (BLAST) (<http://blast.ncbi.nlm.nih.gov>). The sequence of the 416-bp (ITS1 region) yielded a match of 100% with more than two sequences identified as *Dipodascus capitatus*. These included JN573270 and AF455443. Susceptibility testing was performed by colorimetric microdilution (Trek Diagnostic System, UK).

Bacterial superinfections RSV-related have been often described in children, furthermore Falsey et al.⁵ affirmed that 11% to 30% of RSV-infected older patients may have evidence of mixed viral-bacterial infection. Van Ewijk et al.⁶ studied the influence of RSV infection on adherence of *P. aeruginosa* to IB3-1, HEp-2, and A549 epithelial cell monolayers *in vitro*. RSV infection of epithelial cells as well as simultaneous addition of RSV and *P. aeruginosa* to non-infected cells both strongly enhanced the pseudomonal adherence to epithelial cells. A clinical setting of severe pneumonia with the connection to the automatic respiratory system and subsequently to ECMO could open the way to systemic geotricosis together with the prolonged antibiotic therapies performed. It is important to point out that these risk factors are common to most patients hospitalized in ICU, therefore systemic geotricosis may represent a risk for critical patients, especially in geographical areas, such as Italy or Spain² in which this rare pathogen is endemic. The route of fungal infection was not clear; our patient showed no evidence of skin lesions ascribable to this fungus, moreover *S. capitata* was not isolated from urinary or respiratory tract. The appearance of consolidations in the liver parenchima made it possible to presume that the invasive fungal infection departed from gastrointestinal tract. The suspicion of liver involvement seems to be confirmed by the significant increases in serum alkaline phosphatase and bilirubin at the time of blood culture positivization, as previously described⁷. In the case series of Martino et al.⁸, which represents the largest series of patients with probable or definite invasive infection with *S. capitata*, the heterogeneity of drug combinations used did not allow, for any evidence-based, suggestions about the drugs of choice for treating this infection. No clinical breakpoints values are available for *S. capitata*, furthermore *in vitro* antifungal susceptibility findings are sometimes contradictory to those observed in the clinical practice⁹. Based on *Candida* species breakpoints, *S. capitata* seems poorly susceptible or even resistant to echinocandins; on the contrary, MIC levels for amphotericin B, voriconazole and posaconazole often fall in the susceptibility range. Clinical experience suggests that amphotericin B is the most effective treatment and most experts currently recommend this agent, alone or in combination with another drug¹⁰. In this case, the patient was unsuccessfully treated with liposomal amphotericin B and flucytosine despite their *in vitro* susceptibility.

ACKNOWLEDGEMENTS

This paper has not been presented in any congress. The authors thanks the Institute of Microbiology, Catholic University of the Sacred Heart (Rome, Italy) for technical support. Dedicated to Dr. Mina Folletto now away from here.

FUNDING

None

TRANSPARENCY DECLARATIONS

None to declare

REFERENCES

1. Bassetti M, Righi E, Costa A, Fasce R, Molinari MP, Rosso R, et al. Epidemiological trends in nosocomial candidemia in intensive care. *BMC Infect Dis.* 2006; 10:6:21.
2. Miglietta F, Vella A, Faneschi ML, Lobreglio G, Rizzo A, Palumbo C, et al. *Geotrichum capitatum* septicaemia in a haematological patient after acute myeloid leukaemia relapse: identification using MALDI-TOF mass spectrometry and review of the literature. *Infez Med* 2015; 23:161-7.
3. ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA* 2012; 307: 2526-33.
4. White TJ, Bruns T, Lee S, Taylor J. Amplification and direct sequencing of fungal ribosomal RNA genes for phylogenetics. In: Innis MA, Gelfand DH, Sninsky JJ, White TJ, eds. *PCR protocols—a guide to methods and applications*. San Diego: Academic Press. 315–22, 1990.
5. Falsey AR, Walsh EE. Viral pneumonia in older adults. *Clin Infect Dis* 2006; 42:518-24.
6. Van Ewijk BE, Wolfs TF, Aerts PC, Van Kessel KP, Fleer A, Kimpen JL, et al. RSV mediates *Pseudomonas aeruginosa* binding to cystic fibrosis and normal epithelial cells. *Pediatr Res* 2007; 61:398-403.
7. Amft N, Miadonna A, Viviani MA, Tedeschi A. Disseminated *Geotrichum capitatum* infection with predominant liver involvement in a patient with non Hodgkin's lymphoma. *Haematologica* 1996; 81:352-5.
8. Martino R, Salavert M, Parody R, Tomás JF, de la Cámara R, Vázquez L, et al. *Blastoschizomyces capitatus* infection in patients with leukemia: report of 26 cases. *Clin Infect Dis* 2004; 38: 335–41.
9. García-Ruiz JC, López-Soria L, Olazábal I, Amutio E, Arrieta-Aguirre I, Velasco-Benito V, et al. Invasive infections caused by *Saprochaete capitata* in patients with haematological malignancies: Report of five cases and review of the antifungal therapy. *Rev Iberoam Micol* 2013; 30: 248-55.
10. Chittick P, Palavecino EL, Delashmitt B, Evans J, Peacock JE Jr. Case of fatal *Blastoschizomyces capitatus* infection occurring in a patient receiving empiric micafungin therapy. *Antimicrob Agents Chemother* 2009; 53: 5306-7.