Summary

The filamentous or arthrosporic fungi *Saprochaete capitata* (previously named *Geotrichum capitatum*) is a genus of fungi widely distributed in nature as a component of the soil, water and plants. Also it is often isolated as a colonizer of the respiratory and gastrointestinal tract in 30% of the healthy population. Fungemias caused by *S. capitata* are extremely rare. In fact, invasive infections due to *S. capitata* have been reported almost exclusively in neutropenic, oncohematological patients. In this report, we describe a case of fungemia caused by *S. capitata* in a patient with chronic hematological and neurological disease, hospitalized for a long period in an Intensive Care Unit. The prompt identification of *S. capitata* is extremely important because of its intrinsic resistance to echinocandins.
Introduction

Invasive fungal infections (IFI) are frequently observed in patients hospitalized in Intensive Care Unit (ICU) and the majority of such IFI are caused by Candida spp. On the contrary, fungemia caused by filamentous or arthrosporic fungi, such as Saprochaete capitata/Magnusiomyces capitatus (previously named Geotrichum capitatum), is extremely rare. S. capitata is a genus of fungi widely distributed in nature as a component of the soil, water and plants. Also it is often isolated as a colonizer of the respiratory and gastrointestinal tract in 30% of the healthy population, and it might be also present in the human cutaneous microbiome. S. capitata causes infections mainly in immunosuppressed patients with very high mortality rate and rarely in immunocompetent patients. More in details, S. capitata infections were observed in neutropenic oncohematological patients (87%) and more rarely (9%) in patients with non-haematological conditions such as diabetes, solid neoplasms, solid organ transplants, endocarditis and chronic obstructive pulmonary disease.

In this report, we describe an unusual case of Saprochaete capitata fungemia in an immunocompromised patient with a clinical history of chronic hematological and neurological disease.

Case report

A 63-year-old man was admitted in February 2015 to Euroclinic Hospital presenting symptoms of tachycardia, dyspnea, hypoxia and hypertension. Based on his clinical history the patient has been treated for Hodgkin lymphoma and Amyotrophic Lateral Sclerosis (ALS) (Motor Neuron Disease) for the last 15 years. Neurological examination revealed progressive deterioration of ALS during the last year, causing recurrent respiratory system infections, progressive exacerbation of dyspnea episodes, heart failure, hypokinesia of the tongue and feeding disability. Due to complications of his underlying disease, the patient was hospitalized for a long time in ICU and underwent gastrostomy tube placement, tracheostomy and mechanical ventilator respiratory support. Chest X-ray revealed infiltrations and interstitial thickening in both lung fields consistent with inflammatory process. Further lab examinations showed: WBC: 8600 (75% neutrophils), Ht: 28.7%, PLT: 89000, schistocytes (++), CRP: 216 mg/L. Bronchial secretions cultures were obtained during his hospitalization and various pathogens were isolated (Acinetobacter baumannii, Serratia marcescens, Klebsiella pneumoniae, Staphylococcus aureus and carbapenemes-resistant Pseudomonas aeruginosa), hence the patient was treated with meropenem, colistin, amikacin and vancomycin, based on antibiotic sensitivity tests.

On September 2016 the clinical condition of the patient deteriorated and paired blood culture sets were obtained during febrile episodes. Lab examination of the blood cultures resulted in isolation of Gram-negative rods and fungi, which were further identified as Stenotrophomonas maltophilia and Saprochaete capitata respectively.

Fungal growth was clearly visible after 24h incubation and more evident after 48h incubation onto Sabouraud Dextrose Agar. Isolated colonies were whitish and butyrous (Figure 1). Microscopic examination with lactophenol blue (x400) from isolated colonies showed cylindrical-clavate conidia and rectangular arthroconidia (Figure 2). For the identification of the yeast API 32C (Biomerieux) was used (ID profile bionumber 2000010003 [99.9% - excellent identification]) (Figure 3). Antifungal susceptibility testing was performed using Microdilution test (MICRONAUT-AM, MERLIN, Gesellschaft für mikrobiologische Diagnostika mbH). The minimum inhibitory concentration (MIC) value was the concentration of drug yielding no fungal growth at visual reading after 48h incubation at 37°C; Candida parapsilosis ATCC 22019 and C. krusei ATCC 6258 were included as quality controls. Results of MICs
Colonial appearance of *Saprochaete capitata* after 48h incubation onto Sabouraud Dextrose Agar. Isolated colonies were whitish and butyrous.

Microscopic examination with lactophenol blue (x400) from isolated colonies of *Saprochaete capitata* showed cylindrical-clavate conidia and rectangular arthroconidia.

Results of API 32C (Biomerieux) for *Saprochaete capitata* showed ID profile bionumber (2000010003) and excellent identification after 48h incubation (99.9%).
are shown in Table 1. High MIC values were observed for echinocandins, especially for anidulafungin, as well as for azoles, especially fluconazole and itraconazole.

The patient unfortunately died in September 2016 hospitalized in ICU, from sepsis and multi-organ failure syndrome resulting from complications of his underlying condition.

Discussion

In immunocompromised patients, conditions such as profound neutropenia, cytotoxic chemotherapy, which is known to alter the integrity of the intestinal mucosal barrier and the presence of central venous catheter (CVC) are identified as important risk factors for *Saprochaete* infection. This yeast can also become a pathogen in subjects with other risk factors commonly occurring in patients in ICU, such as antibiotic therapy, use of immunosuppressive drugs, surgery, the presence of CVC and total parenteral nutrition. Therefore, although in the majority of cases fungemia in patients in ICU is due to *Candida* species, an opportunistic pathogen such as *S. capitata* may represent a risk also in a critically ill patient. These infections are potentially fatal, mortality rate ranging from 50% to 90%.4

Though epidemiological and microbiological investigations so far did not identify with certainty the source of infection, some studies considered the possibility of a food borne origin or a transmission through contaminated medical devices.5 Furthermore, one study described cases of invasive geotrichosis in patients with urinary tract infections documented by multiple urine cultures positive for *G. capitatum*.6

No consensus regarding the optimal treatment for invasive *S. capitata* infections has been reported and antifungal clinical breakpoints are not available for this yeast. In vitro testing results and clinical experience suggest the use of amphotericin B, possibly associated with 5-flucytosine. However, clinical failure of treatment with high-dose (7 mg/kg) liposomal amphotericin B has been described in hepatosplenic infection and sepsis in the neutropenic patient.2 Because this yeast seems intrinsically resistant to echinocandins (in vitro MIC values are high), the role of this class of antifungal agents in the therapy of *S. capitata* infections remains to be elucidated. Several cases of *S. capitata* IFI have been reported in neutropenic patients, while receiving echinocandin treatment.7

A prompt identification of arthrosporic yeasts by direct microscopic examination of blood cultures is essential for a correct therapeutic management. However, the diagnosis of *S. capitata* may be difficult and time-consuming and newer approaches are required including the MALDI-TOF technique. MALDI-TOF is an excellent diagnostic tool to provide reliable identification of most (98%) of the tested arthroconidial yeasts strains to the species level, with good discriminatory power.8,9 In our case, the identification with conventional method (API 32C) was also very helpful, as it was indicated and by Cavanna et al.10

The clinical spectrum of disseminated infections due to *S. capitata* is very similar to that produced by the far more common *Candida* spp. Therefore, avoidance of misdiagnoses and rapid microbiological identification is essential for an appropriate management of such infections, especially in the light of the intrinsic resistance of these yeasts to echinocandins and of the very high mortality rate associated with IFI due to *S. capitata*.

In conclusion, the necessity of rare, opportunistic pathogen identification as causative agents of septicemia in high risk patients should be emphasized. Additionally, regular blood culture examination combined with proper detection and identification of isolated fungi is of great significance for the early diagnosis and adequate treatment of severe fungal infections.

<table>
<thead>
<tr>
<th>Antifungal drug</th>
<th>MIC (μg/mL)</th>
<th>MIC (μg/mL)</th>
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</thead>
<tbody>
<tr>
<td>Anidulafungin</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Micafungin</td>
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<tr>
<td>Caspofungin</td>
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<tr>
<td>5-Fluorocytosine</td>
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<td>Itraconazole</td>
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<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>0.25</td>
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</tr>
</tbody>
</table>

Minimum inhibitory concentration (MIC) of the antifungal agents tested using MICRONAUT-AM (MERLIN) against *Saprochaete capitata* after 24h of incubation.
Περίληψη

Μυκηταιμία από Saprochaete capitata (πρώην Geotrichum capitatum) σε ασθενή με χρόνιο νευρολογικό και αιματολογικό νόσημα

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Ο μύκητας Saprochaete capitata, προηγούμενη ονομασία του Geotrichum capitatum, είναι ευρέως διαδεδομένος στη φύση ως συστατικό του εδάφους, του νερού και των φυτών, ενώ αποτελεί αποικιστή του αναπνευστικού και του γαστρεντερικού συστήματος στο 30% του υγιούς πληθυσμού. Προκαλεί λοιμώξεις κυρίως σε ανοσοκατεσταλμένους ασθενείς, με υψηλή θνητότητα (60-70%), παρά τη χορήγηση κατάλληλης αντιμυκητικής αγωγής. Σκοπός της παρούσας εργασίας ήταν η παρουσίαση περίπτωσης μυκηταιμίας από S. capitata σε ασθενή με χρόνιο νευρολογικό και αιματολογικό νόσημα, νοσηλευόμενο για μεγάλο χρονικό διάστημα σε Μονάδα Εντατικής Θεραπείας. Η ταχεία ανίχνευση του μύκητα, σε συνδυασμό με την ορθή ταυτοποίηση, ήταν πολύ σημαντική για την έγκαιρη έναρξη της κατάλληλης αντιμυκητικής αγωγής, δεδομένου και της ενδογενούς αντοχής του ζυμομύκητα S. capitata στις εχινοκανδίνες.

Λέξεις κλειδιά
Saprochaete capitata, μυκηταιμία, ανοσοκατεσταλμένος ασθενής