A case of *Saprochaete capitata* pulmonary infection in a neutropenic HIV-infected patient

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**Abstract**

**Introduction.** *Saprochaete capitata* is an emerging opportunistic fungus that is responsible for an uncommon mycosis known as geotrichosis, mainly reported in patients with haematological malignancies. It is a life-threatening condition associated with a high mortality rate of over 52%. *S. capitata* may affect any organ, with a predilection for the lungs.

**Case presentation.** Here we report a case of pulmonary geotrichosis in a neutropenic HIV-infected patient with a prior history of treated tuberculosis. The main risk factor for pulmonary geotrichosis is profound and prolonged neutropenia. To our knowledge, this is the first reported case of *S. capitata* infection occurring on top of probable active miliary tuberculosis.

**Conclusion.** The clinical and radiological features are non-specific and similar to those of other pulmonary fungal diseases, hence the importance of mycological examination to confirm the diagnosis. Through this report, we urge clinicians to vigilantly consider *S. capitata* as an aetiological agent in the differential diagnosis of fungal infections in HIV-infected individuals and to routinely screen for associated infections.

**INTRODUCTION**

*Saprochaete capitata* (previously known as *Blastoschizomyces capitatus* or *Geotrichum capitatum*) is an emerging fungus belonging to the genus *Geotrichum*. *Geotrichum* species are ubiquitous micro-organisms found in environmental soil, water, air, plants and dairy products. They colonize the skin, gastrointestinal and respiratory tracts of 18–31% of healthy people [1–3]. *S. capitata* is a filamentous yeast-like fungus that is responsible for an uncommon infection, termed geotrichosis [3]. The spectrum of involvement goes from localized infections, primarily in the lungs, to disseminated forms. It is a life-threatening condition associated with an overall mortality of 52–57% [4]. Infections with *S. capitata* have mainly been documented in patients with haematological malignancies. They are now increasingly being described in other non-haematological immunocompromised states, such as organ transplants, diabetes mellitus, HIV infection and chronic underlying lung pathologies, such as chronic obstructive pulmonary disease (COPD) and post-tuberculosis (TB) lung disease, and rarely in the immunocompetent [1, 3–5]. These fungal infections have been reported frequently in Europe, particularly from the Mediterranean regions (87%), followed by Asia (7%) and the USA (5%). In other countries, such as those in Africa, the incidence rate is very low (1%). This non-homogeneous geographical distribution of *S. capitata* infections could be related to climatic factors [6–8]. We report here a case of pulmonary geotrichosis in old tuberculous lungs, associated with probable miliary tuberculosis in an HIV-infected patient.
A 54-year-old male, HIV-infected, undergoing antiretroviral therapy, with a history of pulmonary TB, was admitted to the infectious diseases department for dyspnoea, fever and asthenia. Two months previously, he had completed a 6-month course of anti-TB drugs with poor compliance. Clinical symptoms date back to these 2 months: persistent cough, low-grade fever, night sweats, fatigability and weight loss of 5 kg. On admission, the physical examination revealed mucocutaneous pallor, dyspnoea with decreased breath sounds in both lungs, fever (38.5–39 °C) and a weight of 47 kg.

Laboratory investigations showed anaemia (haemoglobin: 10.5 g dl⁻¹), leucopenia (1.38 10⁹ l⁻¹), neutropenia (0.96 10⁹ l⁻¹) and lymphopenia (0.32 10⁹ l⁻¹). The CD4⁺ T-cell and CD8⁺ T-cell counts were 140 cells µl⁻¹ and 180 cells µl⁻¹ respectively, and the CD4⁺/CD8⁺ cell ratio was 0.78. The CRP level was high (171 mg l⁻¹). A chest CT scan with maximal intensity projection showed scattered nodular consolidation with a tree-in-bud pattern predominantly in the upper lobe (Fig. 1). Testing for mycobacteria (Ziehl–Neelsen stain and GeneXpert), routine bacterial cultures and screening for respiratory viruses using the FilmArray respiratory panel with multiplex PCR were negative. The RT-PCR for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and blood cultures were also negative. The patient was treated as a likely miliary TB and placed on empirical anti-TB drugs. He also received a combination of third-generation cephalosporin with aminoglycoside without significant clinical improvement.

On day 15 of admission, a chest CT scan showed the appearance of a pleural effusion and worsening of consolidation (Fig. 1). A bronchoscopy with bronchoalveolar lavage (BAL) was performed. At this time, the patient had a fever of 40 °C, respiratory distress and an increased CRP level of 243 mg l⁻¹. Antibiotic therapy was changed to a combination of imipinem and aminoglycoside, together with trimethoprim/sulfamethoxazole and fluconazole (FLC) (200 mg/day). Direct examination of BAL fluid showed septate hyphae and annelloconidia (Fig. 2). The smears obtained by cytocentrifugation of BAL fluid were stained using the May–Grünwald–Giemsa method and examined under a light microscope with ×40 and ×100 objectives, ruling out Pneumocystis pneumonia.

Culture on Sabouraud media showed the growth of cream-coloured, dry, cottony and circular colonies after 48 h of incubation at 35 °C (Fig. 3). Lactophenol cotton blue preparation showed true hyphae with rectangular arthroconidia without blastoconidia (Fig. 4). Identification was done by the VITEK-2 System (bioMérieux, France) using a YST card with a probable value of 99%.
Species confirmation was carried out using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) (Bruker Daltonik, Bremen, Germany). The FLC treatment was continued.

The susceptibility testing was performed using Fungitest (BioRad, France). The strain was sensitive to amphotericin B (AMB) and 5-flucytosine (5-FC) with a minimum inhibitory concentration (MIC) <2 μg ml⁻¹ each, with intermediate susceptibility to FLC (8 μg ml⁻¹ < MIC < 64 μg ml⁻¹). A second BAL was performed 1 day later and revealed similar results. Galactomannan antigenemia and blood cultures were negative.

On day 20 of hospitalization, day 4 of FLC therapy, the patient was switched to AMB. However, the patient’s clinical condition deteriorated rapidly, and he died due to septic shock. The patient was neutropenic with an absolute neutrophil count of 0.93 10⁹ l⁻¹ upon admission and 0.86 10⁹ l⁻¹ on the day of death. No autopsy was conducted.
DISCUSSION

The taxonomy of Geotrichum spp. has undergone multiple revisions, with the two most clinically relevant species now included in the genus Saprochaete: S. capitata and S. clavata. A second group encompasses Geotrichum anamorphs, with G. candidum being the most frequently identified species from clinical specimens [9].

The first cases of S. capitata infections were observed in the 1960s [10]. These opportunistic mycoses emerge as a result of a dynamic interaction between altered hosts, permissive environmental conditions and antifungal selective pressure [11]. Invasive infections caused by Geotrichum species are rare, accounting for less than 1% of non-Candida fungal infections [12]. Profound neutropenia, especially when lasting more than 7 days, is a well-recognized risk factor for invasive mycosis and has also been reported in patients with S. capitata infections [2]. Several conditions may induce neutropenia, including haematological malignancies and their cytotoxic regimens, long-term corticosteroid use, immunosuppressive therapy and HIV infection [13]. In our patient, the disease occurred during a period of profound neutropenia.

Invasive S. capitata infections are the most frequent presentation. They can be misinterpreted as disseminated candidiasis because of their similar clinical features. Single organ involvement can affect any organ with a predilection for the lungs, especially when their structural integrity is damaged by an underlying disease such as TB or COPD [1, 5]. In a multicentre study reporting 35 cases of S. capitata infections, localized forms mainly affected the lungs (14.3%), with 1 case of focal renal lesion, 1 focal hepatosplenic involvement and 1 case of meningitis [6]. Most of these infections occur in patients with haematological malignancies.

To our knowledge, this is the first reported case of S. capitata pulmonary infection in association with probable miliary TB occurring in an HIV-infected patient.

The diagnosis of pulmonary geotrichosis relies primarily on obtaining monomorphic and abundant cultures of S. capitata from BAL samples, with a positive direct examination and in the presence of clinical signs consistent with respiratory involvement [14]. The radiological findings are non-specific and similar to those of other lung mycoses, hence the importance of mycological examination to confirm the diagnosis [13].
The mycological diagnosis is based on the detection of hyaline septate mycelia and arthrospores on direct examination. *S. capitata* grows on Sabouraud’s media as yeast-like, white-to-cream-coloured, smooth to wrinkled colonies. Microscopy of lactophenol cotton blue mount made from fungal growth reveals true hyphae and pseudohyphae with typical annelloconidia and arthroconidia and an absence of arthrospore budding. *S. capitata* is thermotolerant (up to 45°C), resistant to cycloheximide, and unable to assimilate a large number of carbohydrates (except glucose and galactose) or hydrolyse urea, which helps distinguish it from *Trichosporon* spp. [5, 15]. Morphologically, *Saprochaete* species are identical. *S. capitata* isolates can be identified using yeast identification systems such as VITEK2 (ID-YEAST card; bioMérieux) and API ID32C galleries (bioMérieux); however, neither system covers *S. clavata*. Advanced diagnostic modalities such as MALDI-TOF MS or PCR sequencing of the ITS and partial large subunit (LSU) loci can discriminate between these two species [16].

In this patient, *S. capitata* was found on direct examination and in culture of BAL fluid on two occasions. The broncho-alveolar tracts are normally sterile. Any pathogen isolated in lower respiratory specimens should be taken into consideration, especially in immunosuppressed hosts. All the following epidemiological, clinical, and radiological criteria, i.e. the recent history of pulmonary TB, the chronology of respiratory and general symptoms, the chest CT scan lesions pattern and the endemic status of TB in Morocco, led us to consider TB miliary as the most probable diagnosis and to initiate anti-TB drugs despite negative microbiological tests. The absence of clinical improvement, worsening of consolidation with pleural effusion on the follow-up CT scan, and the isolation of *S. capitata* from BAL on two occasions redirected the diagnostic discussion towards two possibilities: the occurrence of *S. capitata* infection on top of a lung TB miliary or an isolated invasive *S. capitata* pulmonary infection. The tubercular origin could not be confirmed as the patient died and no autopsy was performed.

The co-occurrence of fungal infections and tuberculosis has deadly consequences, especially in immunocompromised patients. In a recent Ethiopian study, the prevalence of pulmonary co-infection with mycobacteria and potential fungal pathogens was 20%, with yeast in 81.4% of cases [17]. The association of pulmonary TB and geotrichosis was previously described in India in 2014, indicating the importance of a systematic and simultaneous search for bacterial and fungal organisms in samples from patients with a clinical picture of respiratory infection [18]. In the case of highly suspected or confirmed TB, the absence of improvement or subsequent worsening after a period of clinical improvement in response to anti-TB therapy should prompt clinicians to screen for other infections, particularly fungal ones in immunocompromised patients.

In our patient, the serum *Aspergillus galactomannan* (GM) test was negative. Cross-reactivity between soluble antigens of *S. capitata* and *Aspergillus* GM has been described [19]. However, clinical evidence consistent with pulmonary involvement in a patient with a positive GM test result should evoke invasive geotrichosis when *S. capitata* is recovered from cultures of respiratory specimens. In this context, the test could be a useful diagnostic tool in the management of these fungal infections [4, 19].

The present case of *S. capitata* pneumonia in a former tuberculous lung adds to the few reports in the literature [5, 15, 18, 20]. Even in immunocompetent individuals, TB impairs the lung structure, making it a breeding ground for opportunistic infections such as geotrichosis, as described in the three cases reported by Tanabe *et al.* [15].

To date, there are no established guidelines regarding antifungal regimens for *S. capitata* infection, probably due to the rarity of these infections and the paucity of published studies. This species is intrinsically resistant to echinocandins and has a low susceptibility to FLC. AMB, either alone or in combination with 5-FC or voriconazole, seems to be the most effective therapy for *S. capitata* infections [21]. Liposomal AMB is recommended, as it reduces side effects, such as nephrotoxicity [22].

Although rare, *S. capitata* is a potentially life-threatening opportunistic fungus, especially in neutropenic immunocompromised patients. In Morocco, only two cases of pulmonary geotrichosis have been previously reported [13, 19]. In considering this report, the fact that the incidence of these fungal pathogens may increase in Morocco should be kept in mind. It is therefore necessary to continue establishing appropriate guidelines for early diagnosis of these rare mycoses, which is of paramount importance for prompt and appropriate management. In HIV-infected individuals, clinicians should vigilantly consider *S. capitata* as an aetiological agent in the differential diagnosis of fungal infections and also routinely screen for associated infections.

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N.S. and A.S.: investigation, validation, writing – original draft preparation. E.F.H.: investigation, review. Z.Y.: investigation, review. E.H.A., T.N. and C.I.G.N.: validation, review, supervision.

Conflicts of interest
The authors declare that there are no conflicts of interest.

Consent to publish
Written informed consent for publication of the patient’s clinical details was obtained from the patient’s relative.
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