



Case report

Mycotic aneurysms due to *Trichosporon asahii* in a patient with ulcerative colitis under immunosuppression

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ABSTRACT

Yeast fungi of the genus *Trichosporon* spp. can colonize the gastrointestinal tract in humans. In recent decades, the pathogenic role of *Trichosporon asahii* has been increasingly acknowledged especially in the setting of neutropenic patients with hematological malignancies. However, non-neutropenic patients who are immunosuppressed for other reasons are also at risk of developing invasive forms of this mycosis. We present the case of a 62-year-old male, with a history of ulcerative colitis under immunosuppressive treatment and previous exposure to antibiotics for various bacterial infections, who was admitted to the emergency department with a mycotic aneurysm of the abdominal aorta and left common iliac secondary to *T. asahii* infection. A multidisciplinary approach of the case (both early medical and surgical interventions) allowed the patient's favorable outcome. The patient was followed for more than two years with no evidence of relapse. We postulate that the diagnosis of invasive Trichosporonosis should be considered in patients with inflammatory bowel disease (IBD) under immunosuppressive treatment and with prior exposure to antibiotics.

Introduction

Trichosporon asahii, previously known as *T. bigelli*, is a yeast-like fungus of the phylum basidiomycete, ubiquitous in water, plants, soil, and even constitutes part of the human microbiota of the skin and digestive tract [1–3]. Human infection by this pathogen is rare, and clinical manifestations depend on the immune status of the host [1,2]. This can range from superficial skin or hair disorders in immunocompetent patients, to disseminated infections such as meningitis, pneumonia, endocarditis, and fungemia in immunocompromised patients [2]. The latter constitutes the most frequent form of invasive Trichosporonosis (IT), with high lethality [1,4].

During the last decades, the pathogenic role of this fungus has been

increasing, especially in patients with hematological malignancies, critically ill with invasive devices, long hospital stays, and prolonged broad-spectrum antibiotic therapy. Disseminated infection manages to reach mortality rates between 42% and 90% [1,3,5–8].

The clinical complexity of this mycosis is increased by the lack of early diagnostic methodologies [3], as well as the poor response to empirical antifungal therapy such as amphotericin B or echinocandins. Azole antimycotics, preferably voriconazole, are the therapy of choice, which reduce mortality [2–4,7].

Cases of Trichosporonosis in non-hospitalized patients with IBD are extremely rare. However, few reports suggest that in this subgroup of patients with disruption of the intestinal mucosa due to the underlying disease (ulcerative colitis or Crohn's disease) who additionally receive

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high doses of corticosteroids or immunosuppressants, could be susceptible to disseminated infection by fungal translocation [9,10].

Additionally, the isolation of *Trichosporon* spp as the cause of mycotic aneurysm of the abdominal aorta is even rarer. The most frequent aetiologies are bacterial, such as *Staphylococcus aureus*, species of *Streptococcus* and *Salmonella* spp, and very rarely fungal like *Aspergillus* spp and *Candida albicans* [11,12]. To our knowledge, this is the first case report of a mycotic aneurysm caused by *Trichosporon asahii*.

We present the case of a 62-year-old man from Lima, Perú with a history of ulcerative colitis treated with high doses of corticosteroids and immunosuppressants, in whom *Trichosporon asahii* was isolated from purulent samples of a mycotic abdominal aortic aneurysm. The early multidisciplinary approach was crucial for the favorable outcome of the patient.

Case

A 62-year-old male from Lima, Peru, with a past medical history of ulcerative colitis undergoing mesalazine and prolonged immunosuppressive therapy (i.e. starting with prednisone at 50 mg/day, however after multiple unsuccessful attempts of tapering the steroids due to severe disease exacerbations, azathioprine 150 mg/day was added and finally a gradual prednisone dose reduction was achieved at 20 mg/day; of note, this patient was a candidate for biological therapy, but unfortunately, he never had access to); hypertension, paroxysmal atrial fibrillation; and benign prostatic hyperplasia. Two months before admission he was diagnosed with spondylodiscitis D11-D12 due to nontyphi *Salmonella*, complicated with paravertebral abscesses, for which he was treated with ceftriaxone (2 g/day) for 6 weeks, showing favorable clinical and radiological evolution. He did not require surgical intervention.

Ten days before admission, he developed stabbing left flank pain, of moderate intensity, partially controlled with analgesics. Outpatient workup showed a urine culture positive for extended-spectrum beta-lactamase (ESBL) *Escherichia coli*, thus ertapenem (1 g/day) was started. However, the pain intensified and he developed a fever. At that time, a decision was made to admit the patient to our center. The physical examination was relevant for cushingoid fascia and pain in the palpation of the left iliac fossa without peritoneal signs; vital signs were stable.

Complete blood count highlighted leukocytosis with neutrophilia and elevated inflammatory markers. Blood cultures were negative. Kidney and liver function tests were within normal ranges. Abdominal computed tomography (CT) showed two mycotic aneurysms; one in the left infrarenal aorta (35 × 32 × 21 mm) and the other in the left common iliac artery (7 × 86 × 69 mm), both with suggestive signs of rupture (Figs. 1 and 2). Likewise, there was evidence of left pyelocalyceal dilatation with contrast extravasation through the renal pelvis and multiple retroperitoneal abscesses located along the left flank with extension to the anterior intraperitoneal and perisplenic space, and inferiorly to the left pelvis and inguinal region. Finally, an abscess was observed in the left iliac muscle measuring 46 × 22 mm and bilateral posterobasal pleural effusion. Endocardial, pulmonary and cerebral compromise was ruled out through echocardiographic study and tomographic scan respectively.

For this reason, antibiotic therapy was rotated to meropenem plus vancomycin and highly complex multidisciplinary emergency surgery was scheduled. First, cardiovascular surgery performed 2 arterial bypasses, one right subclavian-femoral, and the other left femoro-femoral and then performed an exploratory laparotomy followed by general surgery who performed a complete dissection and medial mobilization of the entire left colon towards the splenic flexure in order to gain access to the retroperitoneum and large vessels. Subsequently, a 500cc giant retroperitoneal abscess was drained. This abscess involved both the left paracolic and psoas muscles. Next, cardiovascular surgery completed the surgical repair of 1) the ruptured infrarenal aortic aneurysm (3.3 cm of diameter) and 2) the ruptured left common iliac aneurysm (7.8 cm of

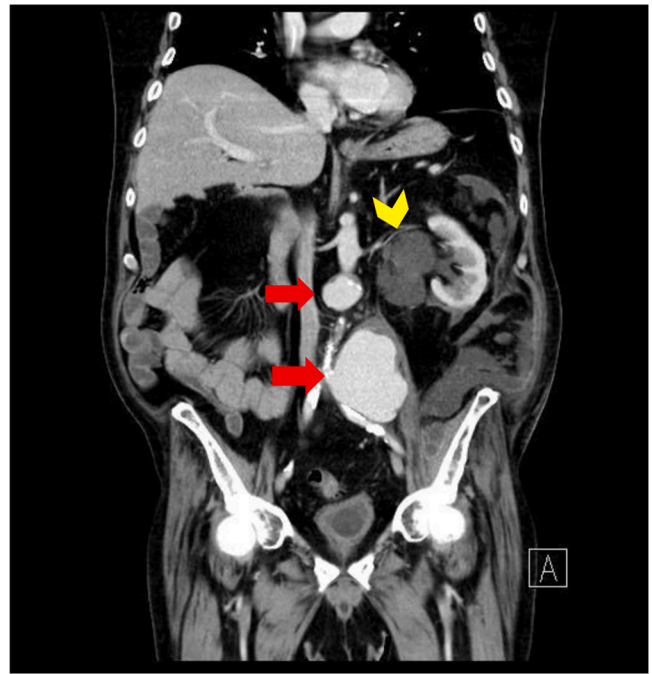


Fig. 1. Abdominal CT show two large aneurysms (red arrows) located on the left infrarenal aortic and the other one on the left common iliac artery, both with suggestive signs of rupture. Renal artery abscess is also shown (yellow arrow), associated with surrounding inflammation.

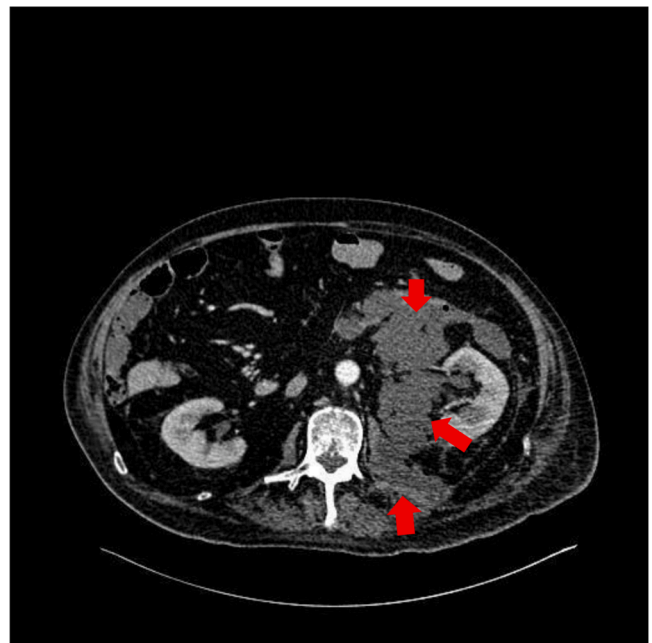


Fig. 2. Abdominal CT revealing multiple retroperitoneal abscess (red arrows) of different sizes located throughout the left flank.

diameter), after which selective ligation of bilateral external and internal iliac arteries was accomplished. Finally, the urologist achieved a left nephrectomy due to a left perirenal abscess (250cc approximately) associated with perirenal fat fibrosis and severe friability of the renal pelvis. All samples were sent to microbiological cultures. Lastly, the abdominal cavity was washed with physiological saline solution plus gentamicin and tubular drainages were left. After 12 h in the operating room, the patient was transferred to the intensive care unit (ICU) for

hemodynamic and ventilatory monitoring.

In the ICU, broad-spectrum antibiotic treatment was continued and caspofungin was added empirically because of sustained hypotension. Serum cryptocolateral was negative. Then, on the fourth postoperative day, *Trichosporon asahii* was isolated from all samples sent for culture, including a urine culture upon admission. It was decided to continue with initially intravenous voriconazole (6 mg/kg bid for one day and then 4 mg/kg bid) and later, once hemodynamic stability was achieved, it was continued orally (200 mg bid). The susceptibility of the microorganism to voriconazole was subsequently confirmed.

The clinical evolution was favorable, without the need for renal replacement therapy or additional surgical interventions. Oral voriconazole was continued for 1 year. After 2 years of outpatient follow-up, the patient fully recovered with no recurrences.

Discussion

A case of IT with a mycotic aneurysm is described in a patient with ulcerative colitis treated with high-dose corticosteroids and immunosuppressants. In recent decades, *Trichosporon* spp has emerged within the microorganisms that cause nosocomial infections, occupying the 1st or 2nd place of invasive fungal infection (IFI) by non-*Candida* spp yeast in immunocompromised patients [13]. Classically, IT has been described in patients with hematological neoplasia, reaching a prevalence of up to 47.7% of all cases in some series [3,4]. Li et al., reported that previous antibiotic exposure was present in 46.4% of patients with IT [1]. Another major risk factor is the use of invasive devices like central venous catheter reaching up to 82.9% of patients with IT in the literature [3,4,6]. On the other hand, Dabas et al., described a higher frequency of IT in patients with gastrointestinal pathology [14].

Trichosporon asahii is the most frequently isolated species in human samples and the most frequent opportunistic pathogen in invasive forms, including bloodstream infection (BSI) [1,4,13]. This patient was probably colonized by *T. asahii* before the development of invasive disease. Colonization of the skin and mucous membranes from the respiratory and gastrointestinal tracts have been described previously [9,10,14], so we postulate that in this patient, other variables must also have coexisted for the invasion of the fungus, including the existence of a “gateway” for the fungus to enter the system and some “type” of immunosuppression. *Trichosporon* spp has been reported as an opportunistic pathogen in patients with inflammatory bowel disease such as Crohn’s disease or chronic granulomatous disease complicated by colitis who require immunosuppressive therapy with corticosteroids, azathioprine, or cyclosporine [9,10,15]. Probably, in this patient, the inflammatory nature of the gastrointestinal tract together with the colonization by this fungus, favored by the previous administration of antibiotics, plus drug-induced immunosuppression was the sufficient combination for the development of this pathology.

Disease caused by *T. asahii* in immunocompromised patients commonly presents as a BSI or catheter-associated infection; however, its isolation has also been described in ascitic fluid, purulent secretions, or more rarely as a causal pathogen of endocarditis or in disseminated disease with ocular, pulmonary or hepato-splenic involvement; the latter, especially in patients with hematological malignancies [1,3,16,17]. On the other hand, although mycotic aneurysms generally have a bacterial origin, *Candida albicans* and *Aspergillus fumigatus* have rarely been responsible in cancer and immunocompromised patients with prolonged use of broad-spectrum antibiotics [11,12,18]. However, to date, we have not found a report of *T. asahii* associated with a mycotic aneurysm.

Diagnoses of IT have generally been established from isolations of blood, urine, sputum, and skin cultures. For the identification of *T. asahii*, the methods used are usually morphological, biochemical, or genetic [1,5]. In this case, the pathogen was isolated both in urine and retroperitoneal abscess cultures, using a morphological identification with VITEK®2 YST identification cards. Current biomarkers such as

galactomannan or cryptococcus serum antigen have shown poor utility in IT, as they are not very sensitive or specific [3]. Other studies propose proteomic characterization by MALDI-TOF MS as a reliable method for the identification of yeasts of the genus *Trichosporon* spp., managing to identify up to 74.5% [13].

The management of the patient described was complex since it required a simultaneous multidisciplinary medical and surgical approach. Medical therapy consisted of the administration of voriconazole since *T. asahii* is intrinsically resistant to echinocandins, as well as showing poor susceptibility in vitro to polyenes and some triazoles such as fluconazole; however, voriconazole presents the lowest minimum inhibitory concentrations (MIC) for all species of *Trichosporon* spp, except for *T. mycotxinivorans*, which has been reported as the only species with high MICs for voriconazole. This is also mirrored in clinical practice, since a direct impact on mortality has been described depending on the type of antifungal used, with higher mortality when using amphotericin B or fluconazole and lower mortality when opting for voriconazole [3,4,7]. It is also known that *Trichosporon* spp has a high intrinsic capacity to produce biofilms, showed in different series that the removal of the central venous catheter resulted in greater survival [3–6]. In our patient, this was not a determining variable since he came from his home without any device, highlighting the unusual presentation outside the hospital context.

It is concluded that invasive Trichosporonosis should be suspected in patients with inflammatory bowel disease, exposed to antibiotics that promote fungal colonization, and under immunosuppressive therapy, regardless of whether they come from a nosocomial or community setting.

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Ethical approval

The case report has the informed consent of the patient and does not violate any ethical principle in its realization.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contributions

Physicians ACG, JLQ, XC, ASS, LTR, MMG, ADCM and HCC participated in the collection of information and images of the clinical history and computer system of the Clinica Angloamericana. ACG, JLQ, XC, ASS and MMG have participated in the conception of the design of the manuscript and its writing. Then, ACG, HCC, MMG, ADCM and LTR performed the analysis of the case. Likewise, ACG, JLQ, XC, ASS, LTR, MMG, ADCM and HCC critically reviewed the article separately and subsequently unified concepts. Subsequently, ACG, JLQ, LTR, ADCM, MMG and HCC made corrections to the article over time and ensured that they took responsibility for all aspects of the manuscript. Finally, all authors reviewed the manuscript and approved the final version.

CRedit authorship contribution statement

Juan Luis Quintana: Conceptualization, Methodology, Software, Data curation, Writing – original draft, Supervision, Writing – review & editing. **Xosse Carreras:** Conceptualization, Methodology, Software, Visualization, Investigation, Writing – review & editing. **Andrea S. Salcedo:** Conceptualization, Methodology, Software, Writing – review

& editing. **Lourdes Torres Ruíz:** Data curation, Writing – original draft, Visualization, Investigation. **Manuel Moreno Gonzales:** Data curation, Writing – original draft, Visualization, Investigation. **Alfonso Del Castillo Mory:** Data curation, Writing – original draft, Validation. **Hugo Cedrón Cheng:** Data curation, Writing – original draft, Validation. **Alfredo Chiappe Gonzalez:** Conceptualization, Methodology, Software, Data curation, Writing – original draft, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors have no relevant financial or non-financial interests to disclose.

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