

## The First Reported Case of *Trichosporon asahii* in Systemic Lupus Erythematosus (SLE) from Riyadh, Saudi Arabia

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### ABSTRACT

**Background:** Trichosporonosis is an emerging invasive opportunistic fungal infection in immunocompromised patients.

**Case presentation:** We report an unusual clinical presentation of a rare invasive fungal infection secondary to *Trichosporon asahii* in a 26-year-old female. This was initially a known case of Systemic Lupus Erythematosus (SLE). The patient presented with abdominal pain and distension secondary to bowel perforation. She was admitted for urgent sigmoid resection and colostomy. The surgical histopathology reported excessive infiltration of fungal elements but was inconclusive. The patient was started on ambisome; PCR then showed *Trichosporon* species and later the blood culture grew yeast for which caspofungin was added. However, the final identification was that of *Trichosporon asahii*, which is resistant to echinocandins and sensitive to amphotericin B and voriconazole. The patient stayed in the ICU for more than one month. She received broad-spectrum antibiotics and had a central venous catheter, arterial, and Quinton lines inserted for an average duration of 30 days. Ultimately, the patient died due to disseminated infection, multiple episodes of ICU acquired infections, and multi organ failure. This is the first case of *Trichosporon* in a SLE patient to be reported from Saudi Arabia, Riyadh at the Prince Sultan Military Medical City.

**Conclusion:** *Trichosporon* is an opportunistic fungal infection that requires a high index of clinical suspicion. Molecular diagnosis is a rapid, highly sensitive and reliable diagnostic tool that plays a crucial role in speeding up diagnosis.

**Keywords:** Trichosporon; SLE; Yeast; Voriconazole; Ambisome; ICU

### BACKGROUND

*Trichosporon asahii* is yeast originating from the Basidiomycetes class. It is considered a life-threatening opportunistic pathogen, most prominently for neutropenic and immunocompromised patients [1]. Invasive infections have also been documented in immunocompetent patients as well those in post-surgery [2-4]. *Trichosporon* spp is widely present in nature and isolated from soil and water as well as colonising the oral, skin, and gastrointestinal tract of normal human flora [1]. Amphotericin B has exhibited limited *in vitro* efficacy against the *Trichosporon* [5]. *In vitro* data has suggested that voriconazole is the antifungal agent of choice for a disseminated Trichosporonosis [6,7].

### CASE PRESENTATION

A 26-year-old female diagnosed as SLE complicated with lupus nephritis for 7 years (for which she was on 10 mg of prednisone), presented to the emergency department with a history of fever and abdominal pain for 12 days. She reported fever of more than 38.2 degrees together with pain. There was no history of diarrhea, skin rashes, joint pains, or any neurological symptoms. She sought medical advice in a private hospital where she was found to be pancytopenic. The patient underwent a CT scan of the abdomen and pelvis which showed intramural thickening in cecum with mild free fluid in the right iliac fossa. She was treated with broad spectrum antibiotics and, owing to low

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complements levels suggestive of active lupus, pulse steroids were administered. The patient showed slight clinical improvement and was discharged from the hospital. Two days later, the patient presented to our hospital with severe abdominal pain and fever. A clinical examination revealed a temperature of 36.1 degrees, a pulse of 114/min, blood pressure of 115/55, and a respiratory rate of 16/min with normal O<sub>2</sub> saturation at room air. She reported a diffusely tender abdomen. Her blood counts on admission were within normal limits. A CT scan of the abdomen showed hyper enhancement of the sigmoid colon with mild thickening and submucosal edema with an adjacent focal collection measuring 3.3×2.7 cm abutting its wall. There was extensive free air, primarily around the sigmoid colon, descending the colon and splenic flexure, as well as beneath the anterior abdominal wall. The patient was immediately taken for exploratory laparotomy and resection of the perforated sigmoid colon, following which she was transferred to the Intensive Care Unit (ICU). The following day she was extubated with a Glasgow Coma Scale (GCS) of 15/15, representing stable haemodynamic status. On the second day, the postoperative patient developed tachycardia with a pulse rate of 120 and her hemoglobin fell from 9.8-3 gms/dl. There was evidence of coffee brown aspirate from the nasogastric tube plus signs of active bleeding in the colostomy bag.

An endoscopy showed diffuse ulceration and active bleeding from the mid and lower oesophagus. Left gastric artery embolisation was present and she was transfused with 3 pints of packed RBCs. On the third day, the treating physician noticed a blackish encrusted rash in her nasal and oral areas, which raised the possibility of invasive fungal infection in an immunocompromised patient, and she was referred to the infectious diseases specialty for further assessment. Based on the overall clinical context of the patient's condition, she was started on liposomal amphotericin 5 mg/kg to cover the high possibility of invasive fungal infections, namely *Mucor* mycosis. This usually tends to manifest as profuse bleeding due to severe angioinvasion, which is characteristic in a high risk group of patients.

On day four, the post-surgery patient became tachypnoeic and desaturated. She was intubated with FiO<sub>2</sub> of 40% and there were blood tinged secretions from the endotracheal tube. Her renal function had begun to rise with a serum creatinine of 290 micromol/L. She was then started on two antibiotics, meropenem and teicoplanin. The patient underwent a bronchoscopy which revealed an extensive bilateral alveolar haemorrhage. The rheumatology team started her on IVIG and plasma pheresis. Bronchoalveolar lavage grew pansensitive *Pseudomonas Aeruginosa* and was negative for any fungal or mycobacterial organisms.

The histopathology of an intraoperative sigmoid biopsy reported invasive fungal infection but was in-conclusive (Figure 1). A culture of the biopsy was not sent. Formalin-Fixed Paraffin-Embedded (FFPE) tissue was sent to a reference clinical mycology laboratory for molecular diagnosis and identification using panfungal PCR and sequencing. The PCR products were sequenced and species identification was achieved using the

Basic Local Alignment Search Tool (BLAST). The sequence results showed a 100% sequence similarity to *Trichosporon asahii*.

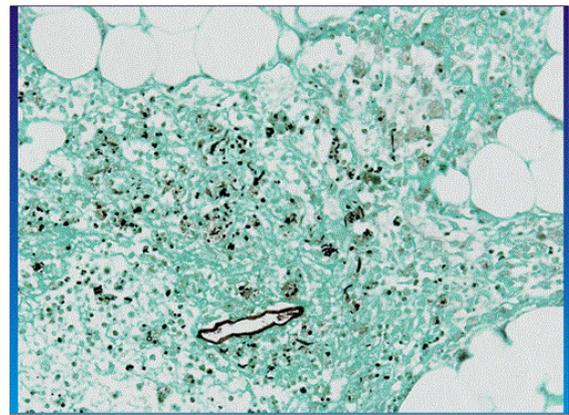


Figure 1: Histopathology of sigmoid biopsy.

The patient continued to experience active bleeding from her colostomy. An ACT scan showed mucosal thickening of the sinuses and ENT was contacted for possible debridement and biopsy. However, they could not proceed as the platelets had fallen precipitously and were refractory to any treatment and transfusions. The patient's renal profile was deteriorating daily and nephrology became involved to provide replacement therapy. Ten days later the patient started becoming hypotensive, requiring inotropic support and hypothermic. Her blood culture grew Extensive Drug Resistant (XDR) *Klebsiella*. The patient was started on ceftazidime avibactam to which the organism was sensitive. All her central lines were changed and she was able to clear her bacteremia and her vital signs improved. The result of a rectal swab culture as part of ICU surveillance for Multi-Drug Resistance (MDR) showed fungal growth consistent with *Trichosporon* spp. This was sensitive to the ambisome the patient was receiving. The patient went through several events of bleeding secondary to severe pancytopenia for which she received blood products, IVIG, and plasma exchanges.



Figure 2: Blood culture: Yeast growth in Sabouraud dextrose agar.

Three weeks later the Quinton line blood culture grew yeast, for which caspofungin was added to liposomal amphotericin.

However, the patient died due to intractable sepsis, bleeding, and a flare up of SLE six weeks after her admission into hospital.

The yeast isolated from the blood culture was identified as a *Trichosporon* species using API 20C AUX (bioMérieux, Mercy l'Etoile, France), which was sensitive only to voriconazole and flucytosine using Sensititre YeastOne® (Thermo Scientific) (Figures 2 and 3).



**Figure 3:** Blood culture: Yeast growth in CHROMagar.

## DISCUSSION

SLE is an autoimmune disease that in most cases requires a potent immunosuppressant treatment, including a high dose of corticosteroids. These play a major deregulatory role in immune status leading to varying vulnerability to several types of fungal infections with substantial mortality and morbidity [8]. The most common corticosteroids associated with invasive fungal infections in SLE are *Aspergillus*, *Candida* and PCP [9-11]. Over the last few decades a non-*Candida* yeast infection known as *Trichosporon* species has emerged in immunocompromised hosts, mostly in hematological malignancies where it is considered the second leading cause of fungaemia after *Candida* species [1]. *Trichosporon* is basidiomycetous yeast that consists of septate hyphae, arthroconidia and pseudohyphae. It exhibits the same mycological characteristics as the *Geotrichum* species as both can produce arthroconidia and true hyphae from cultures. However, *Geotrichum* results in a negative urease test, unlike the *Trichosporon* species [5]. *Trichosporon* can be associated with superficial skin and subcutaneous infections such as white Piedra or it can progress to a devastating invasive infection in immunocompromised hosts, such as cancer, AIDS, and prolonged neutropenia, and require the use of corticosteroids [1]. The majority of cases of *Trichosporon*osis have been North American (33.9%), followed by cases in Europe (27.6%) and Asia (23.3%) [5], disseminated cases of *Trichosporon* have been reported in immunocompetent patients from China, India, and the USA [2-4]. Invasive *Trichosporon* cases from Saudi Arabia are rare. However, Alhedaihy et al. reported up to 3.2% non-*Candida* related fungemia secondary to *Trichosporon begeli* [12]. There have been two reports of successful treatment with amphotericin of cavitating pneumonia secondary to *Trichosporon begeli* in acute myeloid leukemia [13,14].

Herein, we are reporting a rare presentation of invasive fungal infection secondary to *Trichosporon* spp. in a young, critically ill female with advanced SLE. She had presented with an acute abdomen that necessitated sigmoid resection with a colostomy. This presentation was initially attributed to vasculitis related bowel ischemia. However, the histopathological result revealed elements of invasive fungal infection, although this was inconclusive. Based on the clinical presentation, mucormycosis was considered owing to its angioinvasion pathogenicity which results in severe intestinal bleeding, as was the case in our patient. Ambisome had been started on day one of the clinical suspension. Thereafter, PCR had shown evidence of *Trichosporon asahii*. Nevertheless, the patient was continued on ambisome which treats mucormycosis and exhibits variable *in vitro* susceptibility to *Trichosporon* as a few reported cases have responded to amphotericin B monotherapy or in combination with flucytosine [3]. During the surveillance of multi drug resistant organisms (MDRO) in the ICU, the patient was found to have *Trichosporon asahii*, detected from a rectal swab and from blood culture. This was sensitive to voriconazole, fluconazole, itraconazole, amphotericin B and resistant to all echinocandines. Triazoles exhibit better *in vitro* and *in vivo* antifungal activities against *Trichosporon* spp. than amphotericin B [5]. Owing to excessive bleeding, oral voriconazole could not be started nor was an intravascular route used as the patient suffering acute kidney injury [15]. Therefore, the patient was kept on ambisome combination therapy with caspofungin pending a full yeast identification result which was verified after the patient's death. Notably, a combination of echinocandin with amphotericin B or azoles have demonstrated some *in vitro* and *in vivo* synergistic antifungal effects [16-19].

To the best of our knowledge, a *Trichosporon* invasive infection in SLE has been reported in only one patient from Thailand, who was suffering from fungaemia secondary to central line [18]. Our patient is likely to be the second case. The uncertainty of the diagnosis due to the initial histology in our patient addresses another highly critical IFI, which is that mucormycosis, particularly with a correlating clinical presentation, may have forfeited the opportunity to offer the best available therapy earlier in the course for disseminated *Trichosporon*. The definitive microbiological isolates were only identified postmortem. The overall prognosis of *Trichosporon*osis is very poor, even with appropriate antifungal treatment, which is usually voriconazole or ambisome in combination with flucytosine or fluconazole. Mortality varies from 60% to 80%, especially in the presence of neutropenia [20].

## CONCLUSION

*Trichosporon* is an opportunistic fungal infection that requires a high index of clinical suspicion. Molecular diagnosis is a rapid and highly sensitive reliable diagnostic tool that can play a crucial role in speeding up the diagnosis. Treatment should be offered promptly and, based *in vitro* and retrospective clinical data should consist of an appropriate anti-fungal therapy such as voriconazole.

Outweighing the benefits and risks of providing voriconazole in the event of acute renal impairment is the substantial impact of the treatment on a disease with extremely high mortality.

## CONFLICT OF INTEREST

We declare no conflict of interest for the authors

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