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Disseminated Trichosporonosis Presenting with Acute Emphysematous Pyelonephritis in Severely Comorbid Patient

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ABSTRACT

Trichosporon asahii is a basidiomycetous yeast, which is a rare and life-threatening pathogen and is invariably associated with disseminated trichosporonosis. Presented here is the report of a successfully treated case of a 74-year-old female with disseminated trichosporonosis who presented with acute emphysematous pyelonephritis complicated with septic plus cardiogenic shock and septic acute renal failure and heart failure stage 'C' with ischemic heart disease, diabetes mellitus type 2, hypertension. She was admitted in our hospital with complaints of high-grade fever, abdominal pain, nausea, vomiting, giddiness, burning micturition, difficulty in breathing since 1 week. CT scan KUB showed acute emphysematous pyelonephritis and blood culture and urine culture showed growth of *T. asahii.* Antifungal susceptibility testing was done and the pathogen was found sensitive to voriconazole, fluconazole and amphotericin B. Patient responded well to intravenous voriconazole and improved completely in such severely comorbid condition. Disseminated trichosporonosis is a very rare disease with mortality rate as high as 70%, especially in severely comorbid patient.

Keywords: Trichosporonosis, emphysematous pyelonephritis, antifungal, voriconazole

The genus Trichosporon is characterized by the production of septate hyphae, arthroconidia, and pseudohyphae and by yeast-like growth on culture media. There are over 50 known species of Trichosporon, 16 of them being clinically relevant. Invasive human infection is most commonly due to *Trichosporon asahii*, and less commonly with other species. Trichosporon can be found in soil, water, on plants and can colonize human mouth, gastrointestinal tract, respiratory tract, vagina, skin and urine. Over 100 cases of deep trichosporonosis have been described in literature.

Trichosporonosis represents an acute, febrile infection, which can often be fatal, with dissemination to several deep organs. It is associated with a mortality rate of about 64%. On biopsy, Trichosporon appears as a mixture of true hyphae, pseudohyphae, budding yeasts and tubular elements with square ends, called arthroconidia. Trichosporonosis is easily mistaken for candidiasis (which does not produce arthroconidia). While the pathogen grows readily on most culture media, blood cultures appear to yield positive results late in the course. Treatment with amphotericin B was recommended in the past; however, poor response and failures with this drug have been noted. These fungi are typically susceptible *in vitro* to voriconazole, as well as fluconazole, isavuconazole, itraconazole and posaconazole. Therefore, treatment should include the use of one of these azole antifungals.

Trichosporon species are being increasingly reported as an emerging pathogenic yeast-like fungi among a wide-spectrum of clinical presentations ranging from superficial involvement to disseminated invasive disease. The dissemination may occur in spleen, liver, kidney, bone marrow, brain and eye.

CASE REPORT

A 74-year-old female presented with the chief complains of severe abdominal pain, nausea, vomiting, high-grade fever, burning micturition and difficulty in breathing, associated with perspiration for the last 1 week. She

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had consulted with general practitioner and taken medication for 5 days without any improvement. She was a known case of ischemic heart disease, diabetes mellitus type 2 and hypertension. On examination, she was found to be febrile with tachycardia (PR-130/min), blood pressure - 60 mmHg systolic, respiratory rate - 30/min, oxygen saturation - 89% on room air, random blood sugar (RBS) - 287 mg/dL. Electrocardiogram (ECG) showed complete left bundle branch block (LBBB) pattern and chest X-ray showed bilateral lower zone haziness and cardiomegaly. On doing ultrasonography (USG) abdomen and KUB (kidney, ureter and bladder), changes of acute pyelonephritis were found in right kidney. Computed tomography (CT) KUB plain was done which showed bulky edematous right kidney with perinephric fat stranding, thickening of Gerota's fascia and air foci in anterior aspect of right kidney, suggestive of acute emphysematous pyelonephritis (Fig. 1).

The laboratory findings at the time of admission were hemoglobin (Hb) - 13, white blood cell (WBC) count - 17,000/mm^3 out of which neutrophils - 83%, lymphocytes - 10%, eosinophils 3%, platelets - 1,05,000/mm^3, blood urea - 119 mg/dL, serum creatinine - 2.47 mg/dL, serum Na - 129 mEq/L, serum potassium - 5.0 mEq/L, S Cl - 97 mEq/L, total protein - 6.3 g/dL, serum albumin - 3.3 g/dL, RBS - 287 mg/dL, total bilirubin - 1.2 (direct-0.4, indirect-0.8), serum glutamic pyruvic transaminase (SGPT) - 19 IU/L, serum glutamic oxaloacetic transaminase (SGOT) - 20 IU/L, troponin I - negative, C-reactive protein (CRP) - 73.6 mg/L, erythrocyte sedimentation rate (ESR) - 80 mm/hr, serum procalcitonin - 22.93 ng/mL, NT-proBNP - 34,768 pg/mL, D-dimer - 2,410 ng/mL; urine analysis - albumin ++ (100 mg/dL), sugar ++ (500 mg/dL), pus cells - 10-12, red blood cell (RBC) - 15-18.

After admission, urine culture was sent which showed growth of budding yeast cells with colony count of 50,000 CFU/mL; blood culture of three bottle sample showed *T. asahii*. Figure 2 shows hyphae and rectangular arthrospores of *T. asahii* and Figure 3 shows cream-colored, wrinkled, yeast-like colonies of *T. asahii* on Sabouraud dextrose-agar (SDA).

Echocardiography showed ischemic dilated cardiomyopathy with ejection fraction 30%, severe systolic dysfunction, moderate MR and TR, Grade 1 diastolic dysfunction. Patient's urine output was 300 mL in 24 hours.

After reviewing the history, examinations and investigations, it was found that the patient was suffering from disseminated trichosporonosis which presented with the acute emphysematous pyelonephritis and was complicated with septic plus cardiogenic shock and septic acute renal failure and heart failure and unstable angina. The patient was already a known case of ischemic heart disease, dilated cardiomyopathy, hypertension and type 2 diabetes mellitus.

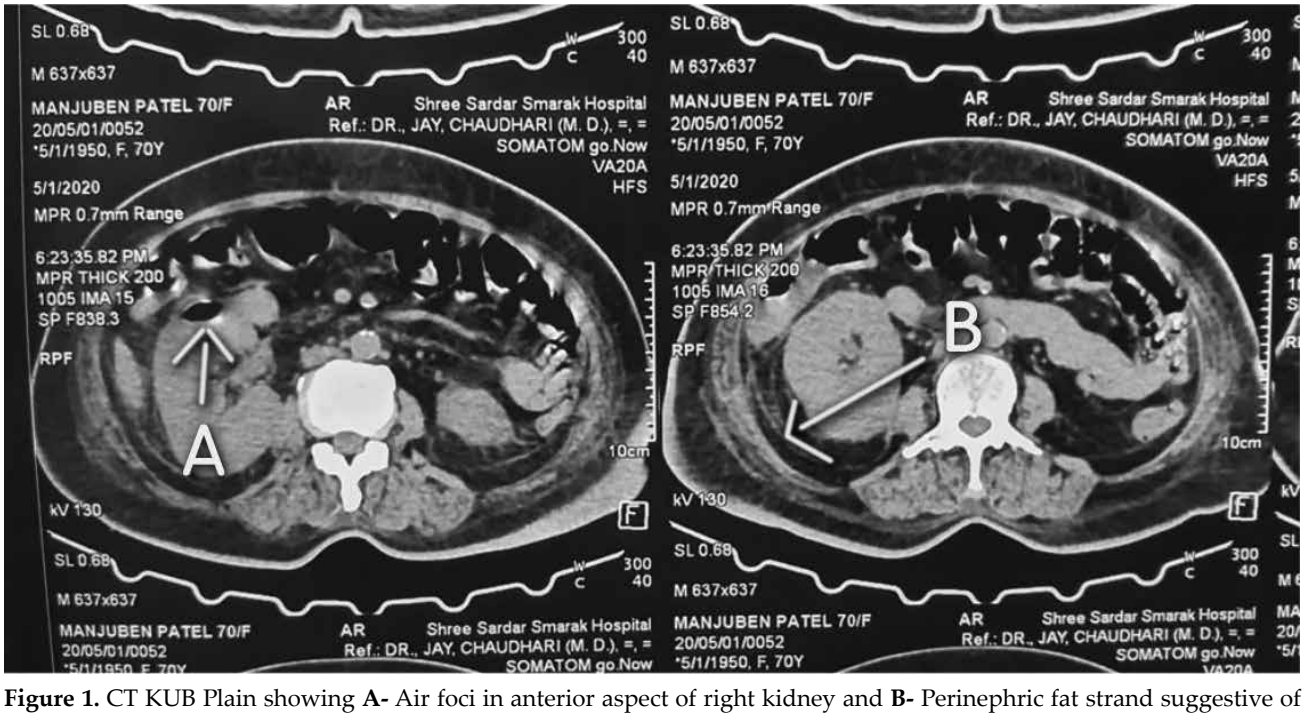

Figure 1. CT KUB Plain showing **A-** Air foci in anterior aspect of right kidney and **B-** Perinephric fat strand suggestive of emphysematous pyelonephritis.

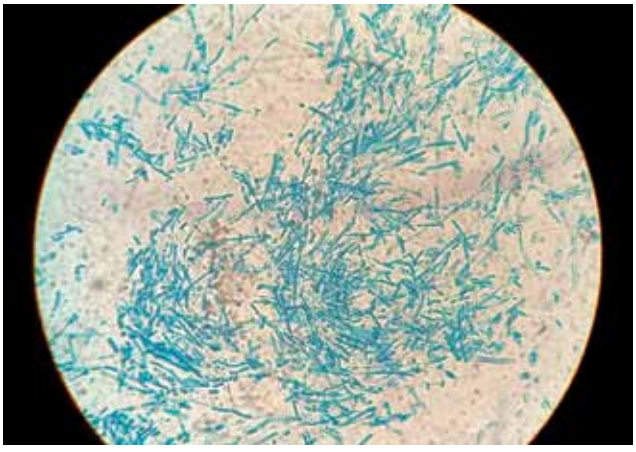

Figure 2. Hyphae and rectangular arthrospores of *T. asahii.*

Figure 3. Cream-colored, wrinkled, yeast-like colonies of *T. asahii* on SDA.

Treatment

After admission, patient was put on broad-spectrum injectable antibiotic meropenem loaded with 1 g, then 500 mg 8 hourly, in divided doses, along with vasopressor support to counteract the septic shock, and oxygen support. On receiving the culture sensitivity report which was showing sensitivity to voriconazole, fluconazole and amphotericin B, patient was put on one broad-spectrum antibiotic meropenem and added antifungal from azole group injectable voriconazole (200 mg) 12 hourly, as voriconazole appears to be the antifungal agent of choice. After 4-5 days, the patient started responding to the treatment, with blood pressure raising to the normal level, urine output increasing gradually, patient was afebrile and relieved from all symptoms after 1 week. On reviewing blood

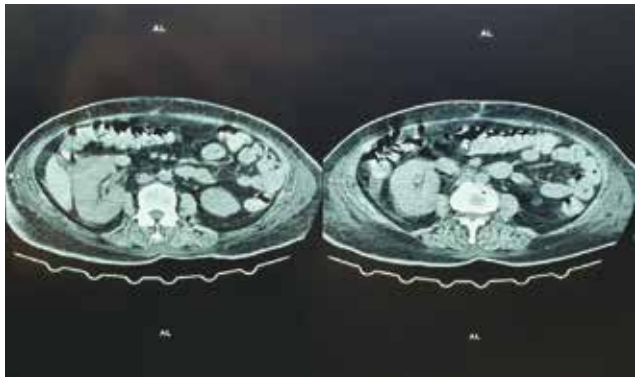

Figure 4. Repeat CT KUB Plain after treatment showing absence of air foci and resolution.

investigation during the course of treatment, it was noted that total WBC count, platelet count, creatinine, urea, procalcitonin started to normalize. Blood culture and urine culture drawn on 10th day became sterile. Repeat CT KUB showed resolution and complete absence of air foci in right kidney compared to previous CT KUB (Fig. 4).

In this case, apart from fungemia, the most challenging aspect was that the patient was also in cardiac failure and cardiogenic shock, which was managed with injectable diuretics (furosemide 20 mg 8 hourly according to permissible level of blood pressure >100 mmHg), oral beta-blocker (metoprolol 25 mg b.i.d.), antiplatelet drugs (aspirin 75 mg, clopidogrel 75 mg, atorvastatin 20 mg), injection nicorandil as continuous infusion as patient was repeatedly facing anginal episode, injectable low molecular weight heparin (LMWH), nebulization and uncontrolled diabetes was managed with bolus of regular insulin. Patient repeatedly went into atrial fibrillation which was successfully managed using amiodarone infusion 600 mg in 2 mL/hr infusion for 24 hours; thereafter maintenance with oral amiodarone 200 mg t.d.s. Patient responded very well and came out of the shock, symptoms of cardiac failure relieved and episode of atrial fibrillation also reduced.

DISCUSSION

T. asahii is a universal yeast-like fungi which is present in the soil; however, it may also be present in human skin and gastrointestinal tract and is an emerging fungal pathogen seen in the immunocompromised host. In this patient, the urinary tract may be the portal of entry as the patient is diabetic, which leads to the development of bulky edematous kidney with air locule inside, with perinephric fat stranding, which lead to acute emphysematous pyelonephritis. *T. asahii* was isolated in blood culture suggesting that it was

the causative agent. Trichosporon species is susceptible *in vitro* to voriconazole, fluconazole, isavuconazole, itraconazole and posaconazole. Therefore, treatment should include the use of one of these azole antifungals. Trichosporon species is resistant to echinocandins but appears to respond clinically to treatment with voriconazole. Azoles are shown to be more effective in the treatment of trichosporonosis than amphotericin B. Voriconazole appears to be the antifungal agent of choice in disseminated trichosporonosis. The mortality rate for disseminated Trichosporon infection has been as high as 70% but is decreasing with the use of newer azoles, such as voriconazole.

CONCLUSION

In the present case, *T. asahii* was sensitive to voriconazole, fluconazole and amphotericin B and the patient responded well to voriconazole therapy. Isolation of same yeast in two consecutive blood and urine culture samples and isolation of no bacteria concluded *T. asahii* as the etiological agent of the infection in this patient. There was absence of growth of fungus in urine and blood culture with complete recovery of the patient following antifungal treatment. This strongly validates *T. asahii* as the cause of disseminated infection in this case.

SUGGESTED READING

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No Increase in Death Risk with Immune Checkpoint Inhibitors for COVID-19 Cancer Patients

Use of immune checkpoint inhibitors was not associated with an increased mortality risk from COVID-19 in patients with cancer, reported an international observational study.

The study included 113 cancer patients with laboratory-confirmed COVID-19 within 12 months of receiving immune checkpoint inhibitor treatment. The patients did not receive chemotherapy within 3 months of testing positive for COVID-19. Thirty-three patients were admitted to the hospital, including 6 admitted to the ICU; 9 patients died. This represents a mortality rate of 8%, which is in the middle of the rates reported previously for cancer patients in general (7.6-12%). COVID-19 represented the primary cause of death in 7 of the patients, including 3 of those admitted to the ICU. The findings were presented at the AACR virtual meeting: COVID-19 and Cancer… (*Medscape*)

Only 16 Volunteers to Take Part in Coronavirus Vaccine Trials at AIIMS-Delhi

New Delhi: The COVID-19 vaccine trial at AIIMS-Delhi will include only 16 volunteers in the first phase. While it was initially planned to include 100 volunteers for the trial, the number was reduced as several locals who intended to participate were found to have antibodies against the virus.

The target of 375 volunteers for the trial of India's indigenously developed Covaxin has been met already. A senior doctor involved in the trials at Delhi's premier hospital stated that besides AIIMS-Delhi, 11 other centers are conducting vaccine trials and that they have already enrolled enough people to test the vaccine… (*ET Healthworld – TNN*)