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Look for Diabetes Mellitus in Chronic Fungal Urinary Tract Infection.

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ABSTRACT

Diabetes mellitus accounts for additional risk of urinary tract infection, particularly with Candida sp. The clinical presentation of diabetes mellitus varies widely and often leads to diagnostic dilemma. Owing to elevated urinary glucose level and defective host defense, diabetic patients are at risk of developing urinary tract infection by *Candida sp*. Here we describe a case of chronic urinary tract infection caused by Candida tropicalis in a patient with undiagnosed diabetes mellitus. Although the patient had no characteristic clinical features, the repeated isolation of *C. tropicalis* led to the diagnosis of diabetes. Here, we highlight the importance of laboratory investigations in proper evaluation of chronic urinary tract infections.

Keywords: Chronic urinary tract infection; *Candida tropicalis*; Diabetes mellitus

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INTRODUCTION

Urinary tract infection (UTI) is a major sequel of diabetes. High level of glucose in urine essentially favours growth of bacteria and fungi.[1] On the other hand, impaired diapedesis and phagocytic activity of neutrophil associated with increased intracellular Calcium level induced by hyperglycaemia results in breakdown of immune defence.[2] Moreover, prolonged hyperglycaemia also results in bladder neuropathy, leading to vesico-ureteric reflux and incomplete voiding of urine with unchecked multiplication of bacteria and fungi in residual urine.[2] Although bacterial pathogens account for majority of UTI episodes in diabetic patients, demonstration of *Candida spp.* in urine poses a diagnostic challenge.[3] Candiduria may represent improper sample collection, asymptomatic infection, symptomatic UTI as well as life-threatening disseminated blood stream infection. Non albicans *Candida sp.* have emerged as a important uropathogen with resistance to commonly used antifungals.[4] However, early detection and initiation of proper antifungal therapy with glycaemic control can significantly improve the outcome of *Candida* UTI in diabetic patients.

Case Report

A 60 year old male attending the urology outpatient department of our institute presented with complaints of frequency, urgency, hesitancy during micturition with reduced flow, dribbling and nocturia since several years, presenting with dysuria of 2 months duration. There was no previous history of hospital admission for these complaints, urinary catheterization or instrumentation. On examination, the patient was afebrile without signs of urinary retention, suprapubic tenderness or costovertebral angle tenderness. However, per rectal examination revealed an enlarged prostate. Abdomen was soft, without any palpable mass or tenderness. He was clinically diagnosed as having Urinary Tract Infection (UTI) with Benign Prostatic Hypertrophy (BPH) with Lower Urinary Tract Symptoms (LUTS). His urine sample was sent for culture and sensitivity. Urine microscopy, both wet mount and gram stain, revealed numerous oval budding yeast cells with pseudohyphae along with leucocytes (Figure 1a and 1b). The pseudohyphae created a diagnostic confusion as they looked similar to the arthrospores of *Geotrichum*.

We then inoculated the urine sample on to Blood agar, Cysteine Lactose Electrolyte Deficient (CLED) agar and Sabouraud Dextrose Agar. On blood agar, we observed tiny, white opaque non-haemolytic colonies. Cream coloured, soft, smooth glistening yeasty colonies were observed on SDA. Gram staining of these colonies showed gram positive oval budding ellipsoidal yeast cells. It was further identified as *C. tropicalis* by sugar fermentation tests using standard microbiological procedures. Antifungal susceptibility testing was carried out on Mueller Hinton agar with 2% dextrose and 0.5 mg/L methylene blue by disc diffusion method using Fluconazole (25µg), Voriconazole (1µg), Itraconazole (10µg) (Himedia, Mumbai, India) as per Clinical Laboratory Standards Institute (CLSI) guidelines.[5] The isolate showed sensitivity to Fluconazole and Voriconazole and resistance to Itraconazole.

We asked for a repeat urine culture from the patient to prove the aetiology along with blood culture. The second urine sample also recovered the same isolate. However, the blood culture was sterile, ruling out candidaemia.

This isolate was sent to the Mycology division, Department of Medical Microbiology, Post Graduate Institute of Medical Education and Research, Chandigarh, India for confirmation of the isolate. This national facility, supported by the Indian Council of Medical Research, has been designated as the centre for National Culture Collection of Pathogenic fungi in India.

Meanwhile, the patient was started on oral Voriconazole for 21 days. But despite therapy, the patient returned for a third time with the same symptoms. Urine culture this time too grew *C.tropicalis*.

Due to the repeated isolation of *C. tropicalis* with the same antifungal susceptibility pattern, the urologist looked for underlying co-morbidities. Investigations revealed his Random Blood sugar to be 240 mg% (13.32mmol/L) and HbA1c value to be 10%. Oral hypoglycaemic agent in adjunct to dietary modifications was prescribed for glycaemic control. Oral Voriconazole was prescribed for 21 days and patient was advised to come for outpatient follow-up. The patient showed improvement in a subsequent visit one month later and showed negative urine culture on follow up.

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However, the patient was symptomatic a year later and the urine culture sent again grew *C. tropicalis* with the same antifungal susceptibility pattern. Subsequent blood investigations revealed poor glycaemic control, with HbA1c value of 11%.

Figure 1a. Wet mount of Urine showing yeast cells with pseudohyphae and pus cells.

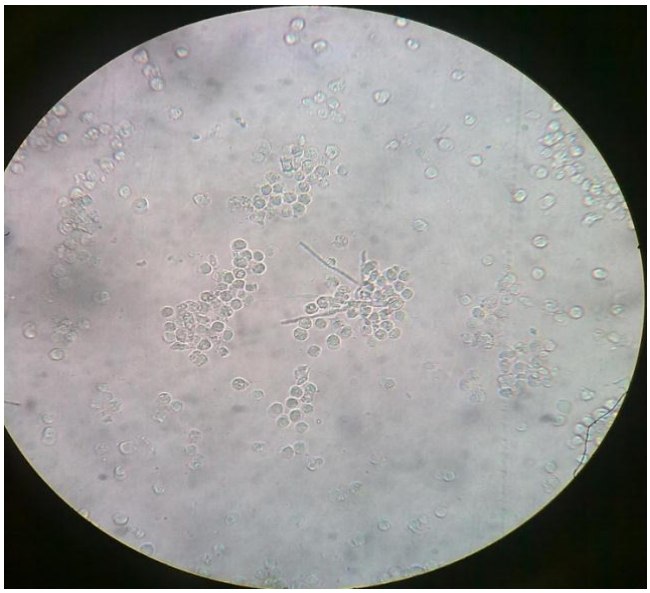
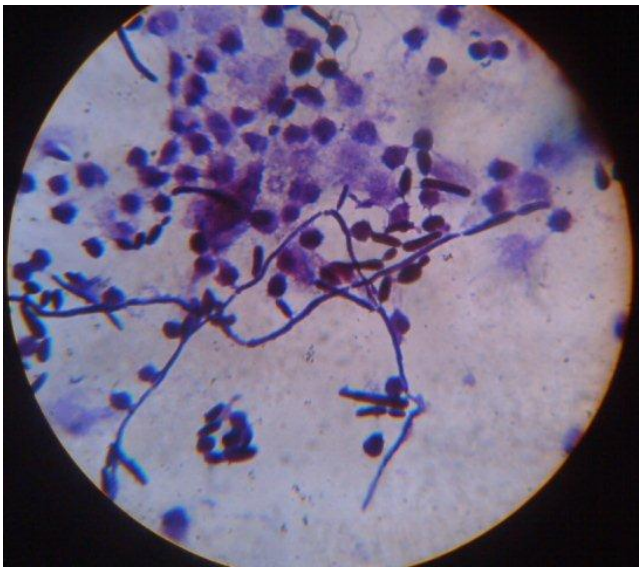


Figure 1b. Gram staining of Urine showing gram positive ellipsoidal yeast cells with pseudohyphae and pus cells.



DISCUSSION

C. tropicalis is the most common non albicans *Candida sp.* associated with human infection.[6] The worldwide increase in patients with impaired immune defence mechanisms associated with diabetes, HIV infection, prolonged anti-cancer, immunosuppressive, steroid or antibiotic therapy, and chronic debilitated illness and resistance to common antifungals are the main factors attributing to its pathogenic potential.[6] Conversely, recurrent or chronic *C. tropicalis* infection with appropriate therapeutic measures may indirectly indicate the presence of these predisposing factors as an underlying co-morbidity. In this case, the patient had no typical signs and symptoms suggestive of diabetes at the first presentation (except nocturia). The persistence of *C. tropicalis* urinary infection despite Voriconazole therapy was the clinical clue to identify undiagnosed diabetes mellitus.

Chronic/recurrent UTI by *C. tropicalis* is an infrequent finding. It has been reported in *C. albicans, C. lipolytica* and *C. utilis*.[7-9] In comparison to males, recurring episodes of UTI are more common in females and mainly attributed to sexual activity and presence of vaginal candidiasis.[10] In general, along with prostatic secretions with fungistatic properties, normal urinary flora also suppress the growth of *Candida* species on urinary mucous membranes.[11] Although *C. tropicalis* balanoposthitis may be the source of candiduria in males,[6] it was not detected in this patient. The significance of species level identification and antifungal susceptibility pattern is invaluable in treating non albicans *Candida sp.* infections. In addition to it, microbiology laboratory may provide vital evidences to revisit the clinical condition and identify unrecognized co-morbidities, as in this case.

In conclusion, we have reported a case of *C. tropicalis* UTI, where repeated recovery of same isolate was the key to identifying underlying diabetes.

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