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Case Report

Candiduria due to Candida Glabrata in an Elderly with Diabetes on a SGLT-2 Inhibitor

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Abstract

Fungal urinary tract infections (UTI) are generally uncommon but may be seen in patients with a variety of risk factors including diabetes mellitus (DM) and immunosuppression. We present the case of an 80-year-old male with type 2 DM, chronic kidney disease, and benign prostatic hypertrophy who developed a symptomatic *Candida glabrata* infection while being treated with a Sodium Glucose Transport-2 inhibitor (SGLT2-i). The infection resolved with anti-fungal therapy and the SGLT2-i was discontinued. This case highlights the underappreciated risk of invasive fungal infections among patients treated with SGLT2-is and the need for increased awareness of this potential adverse effect.

Keywords: SGLT-2 inhibitors; Type 2 DM; Funguria; Candida Glabrata; Urinary Tract Infections

Case Presentation

Fungal urinary infection, or funguria, is relatively uncommon but may be seen in patients with risk factors such as broad-spectrum antibiotic use, urinary tract obstructions, recent surgery, immunosuppression, increased age, female sex, or Diabetes Mellitus (DM) [1]. While funguria may be asymptomatic, it may also progress to symptomatic infections requiring antifungal therapy. Candida species, especially *Candida albicans*, are the most common causative pathogens, but non-albicans species like *Candida glabrata* are responsible for 20-30% of cases of funguria and may be more resistant to Fluconazole [2].

Since their introduction in 2013, Sodium-Glucose Transport-2 inhibitors (SGLT2-is) have become a cornerstone of treatment for DM. Inducing urinary glucose excretion, these antihyperglycemic agents offer myriad benefits beyond simple glycemic control and are now recommended for the treatment of congestive heart failure (CHF) and chronic kidney disease (CKD) [3,4]. The glycosuria induced by SGLT-2is alters the urinary microenvironment and may promote fungal growth [5-7]. While studies have not definitively associated SGLT-2i use with funguria, they have demonstrated a three-fold increased risk of external genital mycotic infections [8,9].

An 80-year-old male with a history of Type 2 DM, CKD Stage 3a, benign prostatic hypertrophy (BPH), asymptomatic candiduria the year prior, and a recently diagnosed hepatic abscess presented to the emergency department (ED) in August of 2024 with dysuria and nausea. In June of 2024, his hepatic abscess, thought secondary to a prior Whipple procedure, had been treated with Piperacillin-Tazobactam. He had been discharged home with a three-week course of Amoxicillin-Clavulanate and follow-up imaging had suggested that his abscess was resolving.

Seven days prior to his August admission, he had presented to a urology clinic with urethralgia, urge incontinence, and pyuria. He had been diagnosed with acute bacterial prostatitis and prescribed a 10-day course of Levofloxacin. Despite treatment, his dysuria had persisted and been accompanied by nausea, and these symptoms had prompted his ED visit. At the time of presentation, his outpatient medication regimen had included Glyxambi, a combination medication containing both a dipeptidyl peptidase-4 inhibitor and an SGLT2-i.

Upon arrival in the ED, he was afebrile and hemodynamically stable with a blood pressure of 110/58 and a pulse of 71 beats per minute. His physical exam revealed right upper quadrant and left costovertebral angle tenderness without peritoneal signs.

Laboratory findings were notable for leukocytosis (WBC 12.4) and elevated creatinine (2.65 mg/dL from a baseline of 1.35 mg/dL). His urinalysis showed pyuria (>100 WBCs) and 3+ leukocyte esterase. A CT scan of the abdomen and pelvis revealed a hypodense lesion in the right hepatic lobe, consistent with his known resolving abscess. It also demonstrated a 2 mm calculus in the upper pole of the right kidney.

The patient was admitted to the Internal Medicine service and treated for presumed prerenal acute kidney injury (AKI) and a resistant UTI with intravenous fluids and Piperacillin/ Tazobactam. The urine culture obtained in the ED showed fungal growth, and intravenous Fluconazole was added to the treatment regimen. Follow-up urine cultures identified *Candida glabrata*, so the Infectious Disease consultant recommended switching from Fluconazole to Micafungin. The patient's AKI, dysuria, and nausea improved, and

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he was discharged on hospital day 11 with outpatient follow-up. He continued to feel well, and one week later, his outpatient team discontinued his Glyxambi. The patient remained well and without urinary symptoms at a five-month outpatient follow-up appointment.

Discussion

This case describes an instance of funguria in an elderly male with multiple predisposing risk factors who was being treated with an SGLT-2i. His risk factors—including T2DM and urinary obstruction from BPH—in conjunction with recent antibiotic use for a hepatic abscess, likely disrupted normal urinary defenses, creating an environment conducive to fungal colonization. Broad-spectrum antibiotics can disturb urinary tract flora—allowing opportunistic fungi like Candida to thrive [2,10]. Additionally, urinary stasis from BPH can limit pathogen clearance. Although many cases of candiduria are asymptomatic, this patient developed symptoms requiring anti-fungal treatment.

Glyxambi, a combination medication containing the SGLT-2i Empagliflozin, inhibits glucose reabsorption in the proximal renal tubules. The resulting glycosuria facilitates fungal colonization of the urinary tract both by disrupting the normal urinary microbiome and impairing innate immune responses [11,12]. SGLT-2is may cause diuresis, and volume depletion can impair mucosal barrier function and local immunity [13].

While Glyxambi has demonstrated statistically significant benefits in lowering hemoglobin A1C compared to monotherapy, its safety profile includes warnings about bacterial urosepsis, pyelonephritis, and external genital mycotic infections [11,12]. Numerous studies have shown a higher incidence of UTIs for patients on Glyxambi or Empagliflozin monotherapy compared to placebo and Linagliptin alone, however, these trials do not differentiate between bacterial and fungal infections [11,12]. Some studies have reported an increased risk of external mycotic genital infections with SGLT-2is, and two case reports have described candidemia secondary to Empagliflozin use, however, no trials have definitively linked SGLT-2is with invasive fungal infection [14,15].

Given the increased use of SGLT2-is for Type 2 DM, CHF, and CKD, clinicians should be vigilant in monitoring for fungal UTIs, particularly in elderly individuals with risk factors for candiduria. They should also consider evaluation for fungal infections in such people presenting with symptoms of UTI or whose infections do not respond to antibiotic treatment.

Conclusion

This case underscores the possibility that fungal UTIs, particularly those due to *Candida glabrata*, may be under-reported and under-appreciated in patients being treated with SGLT2-is. Clinicians should be aware of this potential adverse effect--especially in older adults with risk factors for funguria--and maintain a high index of suspicion when evaluating patients with urinary symptoms who are taking SGLT2-is. Further research is needed to determine the incidence of funguria and invasive fungal infections among individuals being treated with SGLT2-is and how best to mitigate their risk.

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