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Case Report

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Deep tissue perineal candida glabrata infection, related to sodium-glucose cotransporter 2 (SGLT-2) inhibitor dapagliflozin

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Abstract

Fournier's gangrene is a rare and serious event, primarily caused by bacteria. Candida species, mainly *Candida albicans* (C.al) are infrequently isolated, usually as a part of polymicrobial infection. Non-*C.al* Fournier's gangrene was reported in immunocompromised and diabetic patients. We report a case of a 60-year-old man with diabetes mellitus, who recently initiated treatment with SGLT-2 inhibitor presenting with perineal soft-tissue infection. Tissue cultures yielded *Candida Glabrata* as the sole pathogen. The patient received antibacterial and appropriate antifungal therapy, concurrent with surgical debridement. Yeast infection should be considered in diabetes patients under SGLT-2 therapy presenting with a deep tissue infection.

Introduction

Fournier gangrene is a type I, polymicrobial necrotizing infection caused by facultative organisms (*E. coli, Klebsiella, Enterococci*) along with anaerobes [1]. Non-albicans Candida species are rarely found as a cause of Fournier's gangrene, except in immunocompromised and diabetic patients [2,3]. Sodium-Glucose Cotransporter 2 (SGLT-2) inhibitors have an extra-pancreatic glucuretic mode of action acting in the proximal tubules of the kidneys nephron to induce urinary glucose excretion and prevent its reabsorption [4]. SGLT-2 inhibitors are associated with an increased risk of infections, mainly in the genitourinary tract [5-7]. An FDA safety announcement, issued in August 2018 the FDA, warns about rare occurrences of necrotizing fasciitis of the perineum (Fournier's gangrene) associated with SGLT-2 inhibitors [8,9]. We report a case of a Fournier's gangrene due to *Candida glabarata* in a diabetic patient under SGLT-2 inhibitors therapy.

Case report

A 60-year-old male patient, with Type II diabetes mellitus, in whom treatment with SGLT-2 inhibitor dapagliflozin 10 mg bid, was started two months ago, presented with scrotal pain, dysuria, and frequent urination. No urine culture was obtained before admission. There was no improvement after 2-weeks of treatment with oral antibiotics (Ciprofloxacin, Amoxicillin/Clavulanic acid, and Doxycycline), and the patient was admitted to our hospital. Upon admission, the patient was in severe pain (Visual Analogue Scale (VAS) - 8), with stable vital signs, a normal complete blood count, and elevated C-reactive protein of 78 mg/dL (normal range <5 mg/dL). Physical examination revealed as wollen right hemi-scrotum.

The right testis was pushed by a tender swollen 7-10 cm solid mass, at the level of right external ring, base of the penis and perineum (Figure 1).

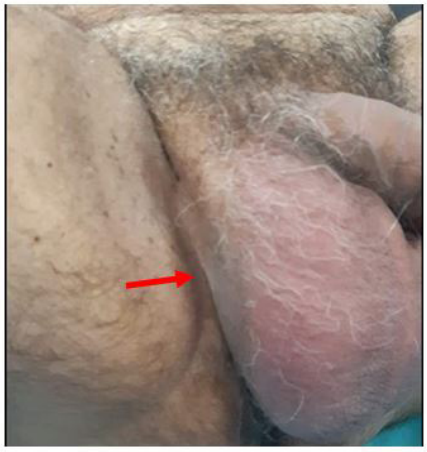

Figure 1: Swollen, erythematous, base of penis and perineum (red arrow).

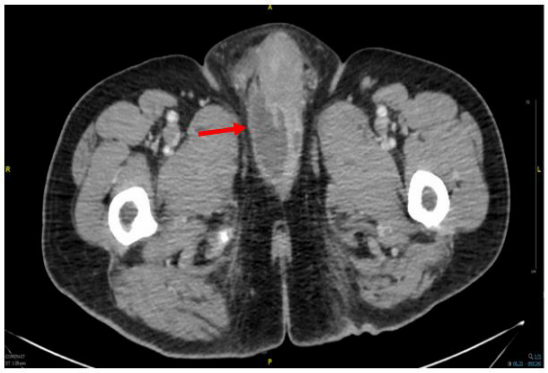

Figure 2: CT Scan: fluid collection, pressing the Corpus cavernosum (red arrow).

Ultrasound examination revealed a hypoechoic collection at the base of the penis, and apost-void residual volume of 200 ml. Computed tomography demonstrated a soft tissue infiltration with several fluid collections; the largest measured at 6.0 cm, pressing the Corpus cavernosum on the right side (Figure 2).

Empiric antibacterial treatment with ceftriaxone, metronidazole and gentamicin was initiated. Ultrasound-guided perineal exploration under general anesthesia, revealed a deep tissue abscess starting at the base of the penis on the right side up to the external ring with a minimally necrotic tissue at the site. Diagnostic cystoscopy performed due to the increased post-void volumes, revealed a severe stricture at the level of the bulbar urethra. The urethra was dilatated using an S-curved Urethral Dilator, up to 20 Fr. The prostate was found unremarkable, and the bladder had a normal appearance and capacity. The perineal incision was daily irrigated with Povidone-iodine solution and saline. Cultures from the contents of the abscess grew Candida glabrata as a solepathogen. Intravenous treatment with caspofungin was added, causing an immediate clinical improvement. The patient was discharged after 7 days of antifungal treatment. Two weeks later, the patient had a complete clinical resolution as well as improvement of bladder outlet obstruction symptoms.

Discussion

Fournier's gangrene due to Candida is a rare event, with few reported cases in the medical literature. The first reported case of Fournier's gangrene due to Candida also involved a man with diabetes mellitus [2]. *C. glabrata* is an emerging fungal pathogen, increasingly being recognized as a significant pathogen in superficial and systemic candidiasis, due to its inherent resistance to some antifungal drugs. Its acquisition is mostly nosocomial, and the main risk factors are the duration of the hospitalization and prior broad-spectrum antibiotic therapy [10]. To our knowledge, only threecases of Fournier's gangrene due to C. glabrata had been described [11-13]. Our case demonstrates the possible association of Fournier's gangrene due to Non-*C. al Candida* species and the use of SGLT-2 inhibitors. SGLT-2 inhibitors like dapagliflozin form a novel therapeutic approach for Diabetes mellitus type 2, which have been shown to improve cardiovascular and renal outcomes, with low hypoglycemia risk [14]. A mixed bacterial and fungal etiology could not have been ruled out, as the patient received antimicrobials prior to admission. Our patient was found to have an undiagnosed diabetic cytopathy presenting as difficulties in urination and post-void residual urine, this is likely to increase the risk of infection using SGLT-2 inhibitors, as high urinary glucose concentration and stasis facilitate the growth of bacteria and fungi. *Candida* species should be considered as apotential cause of deep tissue perineal infection, in diabetic patients receiving SGLT-2 inhibitors and thus empiric antifungal treatment might be considered pending culture results, especially in patients with a recent history of broad-spectrum antibacterial therapy. Clinical outcome in Fournier's gangrene is clearly related toprompt and appropriate medical and surgical management.

Conclusion

Our case emphasizes the importance of performing deep-tissue cultures, thorough medical history, and the assessment of lower urinary tract function when evaluating a patient presenting a deep tissue infection. It may also be advisable prior to commencing treatment with SGLT-2 inhibitors to perform a thorough urological examination and optimize urinary symptoms.

References

1. Eke N. Fournier's gangrene: A review of 1726 cases. Br J Surg. 2000; 87: 718-728.
2. Johnin K, Nakatoh M, Kadowaki T, Kushima M, Koizumi S, et al. Fournier's gangrene caused by Candida species as the primary organism. Urology. 2000; 56: 153.
3. Tayib AM, Mosli HA, Abdulwahab MH, Atwa MA. Fournier's gangrene in diabetic and renal failure patients. Saudi Med J. 2003; 24: 1105-1108. http://www.ncbi.nlm.nih.gov/pubmed/14578978. Accessed July 17, 2019.
4. Chao EC. SGLT-2 Inhibitors: A New Mechanism for Glycemic Control. Clin Diabetes. 2014; 32: 4-11.
5. Hollander P, Liu J, Hill J, et al. Ertugliflozin Compared with Glimepiride in Patients with Type 2 Diabetes Mellitus Inadequately Controlled on Metformin: The VERTIS SU Randomized Study. Diabetes Ther. 2018; 9: 193-207.

6. Bailey CJ, Gross JL, Hennicken D, Iqbal N, Mansfield TA, et al. Dapagliflozin add-on to metformin in type 2 diabetes inadequately controlled with metformin: A randomized, double-blind, placebo-controlled 102-week trial. BMC Med. 2013; 11: 43.

7. Nyirjesy P, Zhao Y, Ways K, Usiskin K. Evaluation of vulvovaginal symptoms and Candida colonization in women with type 2 diabetes mellitus treated with canagliflozin, a sodium glucose co-transporter 2 inhibitor. Curr Med Res Opin. 2012; 28: 1173-1178.

8. U.S. Food and Drug Administration. FDA warns about rare occurrences of a serious infection of the genital area with SGLT2 inhibitors for diabetes. Drug Saf Commun. 2018. https://www.fda.gov/drugs/drug-safety-and-availability/fda-warns-about-rare-occurrences-serious-infection-genital-area-sglt2-inhibitors-diabetes.

9. Bersoff-Matcha SJ, Chamberlain C, Cao C, Kortepeter C, Chong WH. Fournier Gangrene Associated With Sodium-Glucose Cotransporter-2 Inhibitors: A Review of Spontaneous Postmarketing Cases. Ann Intern Med. 2019; 170: 764.

10. Fidel PL, Vazquez JA, Sobel JD. Candida glabrata: Review of epidemiology, pathogenesis, and clinical disease with comparison to C. albicans. Clin Microbiol Rev. 1999; 12: 80-96. http://www.ncbi.nlm.nih.gov/pubmed/9880475. Accessed July 7, 2019.

11. Septimus DJ, Samo T, Fainstein V. Fournier's Gangrene Due to Candida glabrata: Case Report and Review of the Literature. Infect Dis Clin Pract. 2002; 11: 406-407.

12. Loulergue P, Mahe V, Elisabeth Bougnoux M, Poiree S, Hot A, et al. Fournier's gangrene due to Candida glabrata. Med Mycol. 2008; 46: 171-173.

13. Jensen P, Zachariae C, Grønhøj Larsen F. Necrotizing Soft Tissue Infection of the Glans Penis due to Atypical Candida Species Complicated with Fournier's Gangrene. Acta Derm Venereol. 2010; 90: 431-432.

14. Scheen AJ. Pharmacodynamics, efficacy and safety of Sodium-Glucose Co-Transporter Type 2 (SGLT2) inhibitors for the treatment of type 2 diabetes mellitus. Drugs. 2015; 75: 33-59.