Case Report

Navigating the Risks of SGLT2 Inhibitors: Dapagliflozin-Induced Pyelonephritis, Urethritis, Cystitis, and Urosepsis – A Case Report

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ABSTRACT

SGLT2 inhibitors like dapagliflozin have significantly improved the management of Type 2 Diabetes Mellitus by offering glycemic control along with cardiovascular and renal benefits. However, their use is associated with an increased risk of genitourinary infections due to increased urinary glucose excretion, which provides a suitable medium for microbial growth. In rare cases, this can escalate to serious infections.

Case Report: We present the case of a 60-year-old female with a history of Type 2 Diabetes Mellitus, Hypertension, and Ischemic Heart Disease who was on combination therapy including dapagliflozin. The patient was admitted with symptoms of fever, chills, burning micturition, vomiting, and abdominal pain. On investigation, she was diagnosed with a complicated urinary tract infection involving cystitis, urethritis, bilateral pyelonephritis, and urosepsis. Her urine analysis revealed glucose and protein positivity along with pyuria and epithelial cells. Imaging confirmed progressive renal involvement, and her laboratory investigations showed declining renal function with elevated WBC count and CRP levels. Based on clinical correlation and exclusion of other causes, dapagliflozin was identified as a contributing factor to the development of complicated UTI and urosepsis.

Conclusion: This case highlights the importance of close monitoring for urinary tract infections in patients on SGLT2 inhibitors like dapagliflozin. Clinicians should educate patients regarding early symptoms of UTI and the need for prompt reporting. Early diagnosis and withdrawal of the offending agent, along with appropriate antimicrobial therapy, can prevent progression to life-threatening urosepsis.

Keywords: Dapagliflozin, Urosepsis, Pyelonephritis, Urinary Tract Infection, SGLT2 Inhibitors, Type 2 Diabetes Mellitus, Complicated UTI.

INTRODUCTION

Dapagliflozin belongs to SGLT-2 inhibitors class. SGLT-2 inhibitors represent a recent class of antidiabetic medications that lower blood glucose levels by blocking the reabsorption of glucose in the kidneys via sodium-glucose cotransporter proteins.[1] This mechanism promotes the excretion of glucose in the urine (glycosuria) and leads to osmotic diuresis.[2,3] In addition to effective blood sugar management, these agents provide several other health benefits, such as lowering blood pressure, body weight, reducing serum uric acid levels, decreasing proteinuria, and most importantly, improving cardiovascular outcomes and minimizing the risk of hospitalization due to heart failure.[3,4,5,6]

Despite their advantages, SGLT-2 inhibitors are linked to certain side effects. These include low blood pressure, elevated potassium levels, increased risk of bone fractures, potential cancer concerns, as well as urinary and genital infections.[7]

It induces a consistent urinary glucose loss of 50–80 g/day, leading to rapid glucose-lowering effects that are independent of insulin. Although it doesn't directly affect beta cell function or insulin sensitivity, improvements in glycemic control and reduced glucose toxicity may indirectly enhance both.[3]

Its glucose-lowering efficacy depends on kidney function and diminishes as GFR declines, becoming largely ineffective below 45 ml/min/1.73 m^2.[1] While generally safe and not associated with significant cardiovascular or metabolic harm, dapagliflozin may slightly increase glucagon levels due to possible alpha cell stimulation.[8,9]

Importantly, due to its mechanism of increasing glucose in the urine, dapagliflozin is associated with a higher risk of urinary tract infections (UTIs) and genital mycotic infections, especially in individuals with a history of such infections or poor hygiene. These risks should be considered when prescribing the drug.[3]

CASE PRESENTATION

A 60-year-old female patient presented with complaints of pain in abdomen, fever with chills, burning micturition, vomiting since 3 days. She had a known complaint of Type 2 Diabetes mellitus since 4 years and on regular medication [Tab. STALIX DM (Dapagliflozin 10mg + Sitagliptin 100mg + Metformin hydrochloride extended release 500mg)] 1-0-0 and Hypertension since 4 years and on [Tab. PROLOMET T 25 (Metoprolol succinate 25 mg + Telmisartan 40 mg)] 0-0-1 and IHD (Ischemic heart disease) [Surgical procedure - PTCA (Percutaneous transluminal coronary angioplasty) done on 11/10/2024 and on Tab. Ticagrelor 90 mg 0-0-1 and Tab. Atorvastatin 40 mg 0-0-1].

The patient denied any history of drug allergies. Her personal history includes mixed diet, disturbed sleep, regular bowel movements, decreased appetite and no addictions.

On physical examination the patient was moderately built and nourished. Pallor was positive, no signs of icterus, clubbing, cyanosis, koilonychia, lymphadenopathy, edema. She is conscious and well oriented to time, place and person. Her vitals were found to be stable.

Table 1: Trend of Biochemical and Hematological Parameters (15/01/25 – 27/01/25)

DATES	15/01/25	20/01/25	22/01/25	23/01/25	24/01/25	25/01/25	26/01/25	27/01/25
TESTS								
Sr. Creatinine (0.6-1.2 mg/dl)	1.47	3.6	3.9	4.5	4.3	4.2	3.7	3.3
Blood urea (10-45 mg/dl)		56	72	77	79	71	62	55
Sodium (135-155 mmol/L)		131	128	132	131	131	130	
Sr. Total protein (6.60-8.30 g/dl)		5.6						5.7
Sr. Albumin (3.4-5 g/dl)		2.6						2.8
Alkaline phosphatase (0-115 U/L)		200						244
GGT (0-55 U/L)		79						198
CRP (0-10mg/L)		222.5			122.9			
Platelets (1.4-4.4 lakhs/cumm)	7.81	4.62		2.99		2.94		
PCV (34-48%)	30.8	24.2		21.5		31.2		
Hb (11.5-16g/dl)	10.2	8.1		7.1		10		9.6
WBC (4000-11000 cells/cumm)	14770	18560		19320		18570		14000
Neutrophils (40-75%)		90		88		84		62.9
Lymphocytes (40-20%)		6		10		8.3		22

INVESTIGATIONS:

USG and OTHER FINDINGS: -

15/01/25

- Grade I fatty liver
- Cystitis with bilateral minimal hydro-ureteronephrosis
- Gall bladder sludge

20/01/25

ECG: Probable sinus tachycardia

Anterior T wave abnormality is borderline for age and gender borderline ECG

Urine culture:

Biochemical examination: glucose and protein (positive)

Urine Microscopy:

Pus cells: 6-8 cells/hpf

Epithelial cells: 5-6 cells/hpf

22/01/25

- Features of early pyelonephritis, bilateral pyelitis and urethritis.
- Cholelithiasis with no features of cholecystitis.

Peripheral smear:

Normocytic Normochromic Anemia with Neutrophilic Leukocytosis.

27/01/25

- Bulky bilateral kidneys with mild perinephric and peri-ureteric fat stranding-S/o bilateral pyelonephritis.
- Cholelithiasis with no features of cholecystitis.

DISCUSSION

Dapagliflozin, an SGLT2 inhibitor, reduces blood glucose by promoting urinary glucose excretion. While beneficial, this mechanism increases urinary glucose levels and can lead to a higher risk of urinary tract infections (UTIs), especially in women, elderly patients, and those with underlying conditions like diabetes or renal impairment.

In this case, the patient was on a fixed-dose combination of dapagliflozin, sitagliptin, and metformin for T2DM management. She presented with symptoms suggestive of a complicated UTI, and investigations revealed features consistent with cystitis, urethritis, pyelonephritis, and urosepsis. Lab reports showed elevated creatinine and

blood urea levels, rising CRP, leukocytosis, and imaging confirmed extensive renal and urinary tract involvement. The progression to urosepsis underlines the potential severity of genitourinary side effects associated with dapagliflozin.

Urosepsis is a systemic response to a UTI that has spread to the bloodstream, posing a life-threatening risk if not promptly treated. In this case, early diagnosis and supportive management, along with discontinuation of dapagliflozin, led to clinical improvement.

Clinicians should consider the risk-benefit ratio of continuing SGLT2 inhibitors in patients with recurrent UTIs or when signs of systemic infection appear. Patient education regarding the recognition of UTI symptoms and the importance of hydration and hygiene is essential during SGLT2 inhibitor therapy.

CONCLUSION

This case report emphasizes that while dapagliflozin and other SGLT2 inhibitors provide excellent glycemic and cardio-renal benefits, they may pose a risk for serious urinary tract infections leading to complications such as pyelonephritis and urosepsis. Early recognition, prompt treatment, and discontinuation of the offending agent are crucial. Patient counseling about symptoms of UTIs and the risks of untreated infections must be part of routine practice when prescribing SGLT2 inhibitors.

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