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EMPHYSEMATOUS CYSTITIS: YET ANOTHER LETHAL OUTCOME FOLLOWING REPEATED ADMINISTRATION OF SGLT2 INHIBITOR

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INTRODUCTION

Emphysematous cystitis is a rare complication of urinary tract infection characterized by gas in the lumen and/or the wall of the bladder.[1] Risk factors include female sex, diabetes, neurogenic bladder, bladder outlet obstruction, and recurrent UTI.[1] Herein we describe a patient with Diabetes Mellitus who succumbed to septic shock induced by emphysematous cystitis following continued administration of SGLT 2 inhibitor despite multiple recurrent episodes of urinary tract infection.

CASE REPORT

55-year-old female presented to primary care clinic with fever with chills, dysuria, right sided flank pain radiating to pelvis and hematuria of a week duration. Past medical history included type 2 DM managed with insulin Glargine, liraglutide, empagliflozin, and glimepiride, neuropathy treated with gabapentin, hepatic cirrhosis with lactulose, hypothyroidism with levothyroxine, depression with amitriptyline and duloxetine, and hypertension with lisinopril. On physical examination, patient was alert, oriented but hyperventilating though without acute distress. Significant positive findings included fever, 102°F, pulse 110/min, blood pressure 90/60 mm Hg and respiratory rate 24/minute as well as right costovertebral angle tenderness. Rest of the examination including, heart, lungs, abdomen was essentially unremarkable. Neurological examination was intact without focal deficit. Urinalysis confirmed hematuria as well presence of infection including gm negative bacteriuria. Diagnosis of acute pyelonephritis was entertained and the patient was referred to emergency

room of a local community hospital. Laboratory testing was significant for leukocytosis with a left shift, serum creatinine, 1.7 mg/dl, serum urea nitrogen, 46 mg/dl and glucose 286 mg/dl without anion gap. Liver enzymes, and rest of chemistry panel all were within normal ranges. Hemoglobin A1C was 11.3%. Urinalysis showed hematuria and glycosuria >1000 mg/dL without leukocytes, nitrites, or protein. Patient was admitted and started on Zosyn (Piperacillin/tazobactam) 3.375 g every six hours with Foley catheter placement. Further evaluation with X-ray of abdomen and pelvis showed air in the urinary bladder wall. Abdominal CT scan documented extensive air within the bladder wall and bladder lumen, confirming the diagnosis of emphysematous cystitis. Urine culture grew >100,000 CFUs of Klebsiella pneumoniae, with negative blood culture. Sensitivity was noted for both Zosyn as well as for antibiotic Augmetin (Amoxicillin/Clavulanate). Urology was consulted and determined that surgery was not indicated at that time as the patient became afebrile after two days of IV Zosyn administration. At this juncture, IV Zosyn was replaced with oral Augmentin 500 mg every 8 hours and patient was discharged with instructions to continue the course of oral Augmentin 500 mg every 8 hours for 12 days and pre-hospitalization medications including Empagliflozin with a follow up clinic visit in 2 weeks. During the follow up visit, patient appeared to have recovered claiming to be asymptomatic and with unremarkable physical examination. However, 3 weeks after hospitalization, the patient presented to the Emergency room with altered mental status and slurred speech. Apparently, she had missed several doses of lactulose and thus, diagnosis of hepatic encephalopathy was considered. Physical examination revealed pulmonary edema. Soon, she lapsed into hypoxemia and was started on respiratory support with BiPAP and nitroglycerin was administered to treat flash pulmonary edema. CXR showed possible early infiltrate vs. atelectasis in both lower lung fields. Head CT without contrast showed no acute intracranial abnormalities. EKG showed normal sinus rhythm with right bundle branch block. Ammonia was markedly elevated at 236 µmol/L (11 to 32 µmol/L). Lactic acid was elevated at 5.1 mmol/L (0.5-1.9). UA showed glycosuria with glucose >1000 mg/dL, proteinuria with 200 mg/dL, and hematuria with moderate blood indicating possible UTI. Soon the patient became hypotensive with blood pressure, 60/40 mm Hg. Resuscitation was initiated with administration of Levophed and patient was transferred to the ICU with diagnosis of septic shock. Repeated abdominal CT scan showed extension of air from within the bladder wall noted previously to adjacent intra and extra peritoneal recesses confirming progression of emphysematous cystitis or probable ruptured urinary bladder. Urologist deemed patient to be too unstable for surgical intervention. Patient manifested episode of ventricular tachycardia

followed by several seizures and lapsed into coma. Resuscitation maneuvers were futile and patient expired.

DISCUSSION

The use of SGLT2 inhibitors is well established to contribute to an increased risk of UTI.[2-9] Moreover, several instances of acute pyelonephritis culminating in urosepsis have been attributed to use of these agents.[2-5] Finally, occasional fatality secondary to urosepsis following administration of these agents has been reported as well.[2-4]

This case report describes 'emphysematous cystitis' with leakage of air into peritoneal and subcutaneous spaces resulting in a lethal outcome following continued administration of SGLT2 inhibitor despite occurrence of recurrent urinary tract infections. We believe that persistent glycosuria induced by SGLT 2 inhibitor was responsible for promoting recurrent urinary tract infection leading to progression to emphysematous cystitis and urosepsis and death. Thus, this case report may be the first documented case of emphysematous cystitis, yet another lethal complication following administration of SGLT2 inhibitor.

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