A Case of Emphysematous Cystitis in an Elderly Male Diabetic Patient with Benign Prostatic Hyperplasia treated with an SGLT2-inhibitor

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Abstract:

Emphysematous cystitis is a rare and complicated urinary tract infection associated with gas formation in the bladder wall. This is commonly associated with poorly controlled diabetes mellitus in elderly women. The case presented involves a male diagnosed with emphysematous cystitis while being treated with empagliflozin, a sodium-glucose-cotransporter-2 inhibitor (SGLT2i), for type-2 diabetes mellitus (T2DM). He was noted to have a past medical history of symptomatic benign prostatic hyperplasia, for which he was prescribed tamsulosin. Treatment was non-operative, and he fully recovered with no long-term sequelae. SGLT2i medications have been beneficial in improving glycemic control for patients with T2DM, though the risk for severe urinary tract infections remains controversial. After reviewing the literature, other cases of genitourinary infective complications have been reported.

Introduction:

Emphysematous cystitis (EC) is a gas-forming infection of the bladder wall that is most commonly caused by *Klebsiella pneumoniae* and *Escherichia coli* [1]. This most commonly afflicts elderly diabetic women, with cases approximately 2:1 women to men [2]. Type-2 diabetes mellitus is a significant risk factor, reported to include nearly 70% of patients diagnosed with EC [2]. One case reported that the average hemoglobin A1c was 9.9% or an average serum glucose level of 293 mg/dL [3]. Other significant risk factors include chronic urinary retention due to neurogenic bladder or bladder outlet obstruction and glycosuria, which provides a ripe environment for fermentation by opportunistic pathogens. EC is considered a complicated urinary tract infection (UTI) and is associated with a mortality of 3-12% [2].

Clinical Course:

A 73-year-old male with T2DM, hyperlipidemia, coronary heart disease, chronic kidney disease, cirrhosis of the liver, and benign prostatic hyperplasia (BPH), presented to the emergency department for evaluation of urinary frequency and dysuria, which developed two days before his presentation. He was prompted to report to the emergency department by his primary care provider after routine blood work revealed an acute elevation in his creatinine to 1.70 mg/dL from a baseline of 1.30 mg/dL. He was treated with tamsulosin for chronic BPH with historical nocturia, urinary frequency, hesitancy of his urinary stream, and a weakened urinary stream. His diabetes was historically treated with metformin, alogliptin, and glargine. Despite this treatment, his hemoglobin A1c continued to rise. The highest value documented was 13.2%. It was at this point

he was started on empagliflozin (an SGLT2i) 10mg by mouth daily. He continued this medication for approximately 2 months, and his hemoglobin A1c improved to 8.9% on repeated blood work. His serum creatinine was elevated on his repeated blood work at 1.70 mg/dL (baseline was 1.30 mg/dL). This, along with acutely worsened lower urinary tract symptoms, prompted his primary care physician to have him report to the emergency department.

On evaluation, he complained of reduced urinary force, urinary frequency, sensation of incomplete voiding, and dysuria for two days. He admitted to lower abdominal pressure but denied any fevers, chills, rigors, nausea, vomiting, or flank pain. On examination, his vitals revealed a temperature of 98.0°F, pulse of 98 beats per minute, respirations of 17 breaths per minute, blood pressure of 163/77 mmHg, and pulse oximetry of 99% on room air. His abdomen was soft and non-tender, though he reported suprapubic pressure with palpation. He had no costovertebral tenderness to percussion. A urine specimen was collected for urinalysis, urine culture, and sensitivity. The urinalysis revealed a specific gravity of 1.025, 2+ protein, 4+ glucose, 1+ ketones, negative nitrites, 2+ leukocyte esterase, 3+ blood, 103 WBCs on high power field (HPF), 65 RBCs on HPF, and 4+ bacteria. Other laboratory values revealed a WBC count of 17,800 mm^3 with a neutrophil count of 16,900 mm^3, hemoglobin of 14.0 g/dL, blood urea nitrogen of 37 mg/dL, creatinine of 1.69 mg/dL and serum glucose of 290 mg/dL. The working diagnosis was a urinary tract infection. He was given ceftriaxone 1g IV while in the emergency department. He was imaged with non-contrast computed tomography (CT), which revealed prostatomegaly, marked bladder distension, emphysematous changes of the bladder wall consistent with emphysematous cystitis, and bilateral perinephric streaking consistent with pyelonephritis (Figure 1A & 1B). He was unable to urinate well and had a post-void residual greater than 650 mL. He had a 3-way Foley catheter placed with 800 mL of turbid urine return. Continuous bladder irrigation was initiated to lavage the bladder. He was subsequently admitted to the hospital.

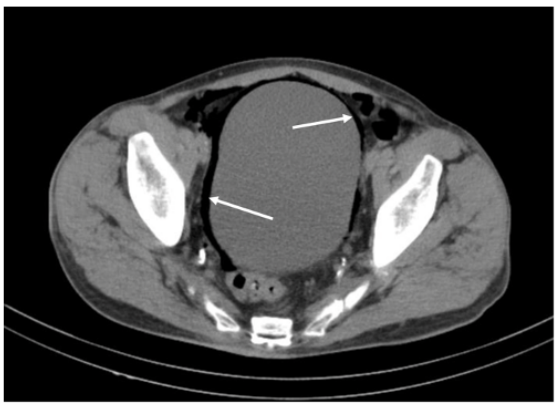

Figure 1A: The axial imaging from the initial CT scan of the abdomen and pelvis revealing emphysematous changes within the bladder wall.

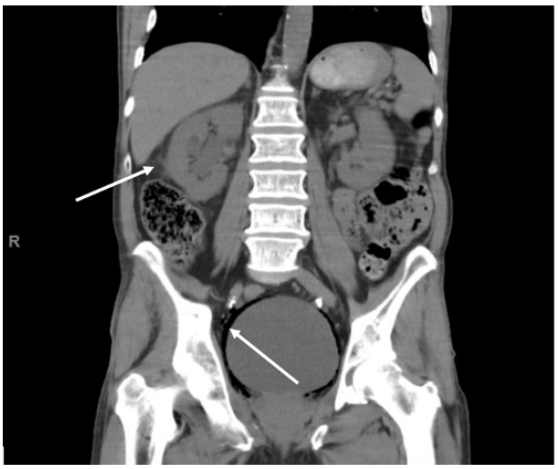

Figure 1B: The coronal imaging from the initial CT scan of the abdomen and pelvis revealing emphysematous changes within the bladder wall and perinephric fat stranding.

During his hospital stay, the urine culture grew >100,000 colonies/mL of *Klebsiella pneumoniae* which was sensitive to piperacillin-tazobactam. He was changed to piperacillin-tazobactam 3.375 g IV every six hours by the inpatient team and was continued on continuous bladder irrigation. His white blood cell count normalized over the first two days of his hospital stay. Tamsulosin was increased to 0.4mg by mouth twice daily, and finasteride 5mg by mouth daily was started to optimize the pharmacologic management of his lower urinary tract symptoms. He failed a voiding trial as an inpatient and was discharged with a Foley catheter. A non-contrast CT of the pelvis was obtained prior to discharge and revealed interval resolution of the emphysematous changes of the bladder wall (Figure 2A & 2B). On outpatient follow-up, he was liberated from the Foley catheter approximately three weeks after discharge and was continued on tamsulosin and finasteride. He recovered well without any sequelae.

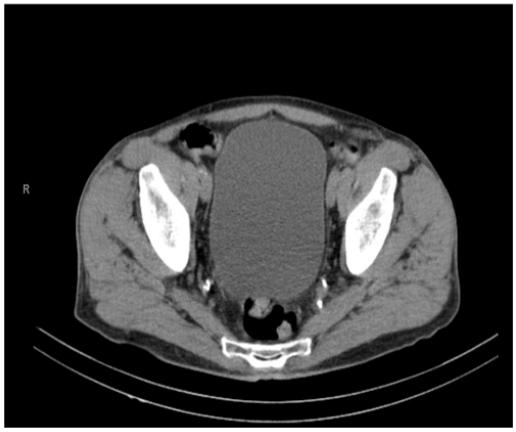

Figure 2A: Axial imaging from the repeat CT scan of the pelvis before discharge shows resolution of the surrounding emphysematous bladder wall changes.

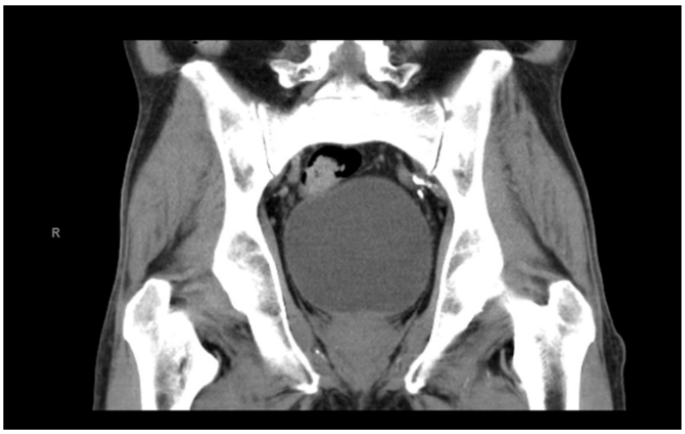

Figure 2B: A coronal image from the repeat CT scan of the pelvis before discharge shows resolution of the surrounding emphysematous changes of the bladder wall.

Discussion:

EC is a rare and complicated urinary tract infection, and if not appropriately identified and treated, it may be fatal [4,5]. The presenting clinical scenario is variable, ranging from incidental diagnosis from abdominal imaging studies to severe sepsis and even septic shock [6]. For those patients who present without symptoms, a diagnosis is made on imaging results alone [7,8]. Many cases have been diagnosed incidentally based on radiographic results. Though EC may be identified on plain radiography, typically showing a translucent ring around the bladder, CT has been generally accepted as the gold standard for diagnosis [9]. The value of a CT scan for initial diagnosis has been noted in the literature [7-9]. While most cases of emphysematous cystitis are treated medically, there are instances where the infection progresses, and surgical intervention is necessary [9].

Symptomatic patients typically report irritative voiding symptoms, including urinary frequency, urgency, and dysuria [6,9]. Pneumaturia has been documented, though the literature notes this as an increasingly rare symptom [7]. A trifecta of occurrences thought necessary for EC was previously described as the presence of gas-forming bacteria, high glucose content of the local tissues, and impaired tissue perfusion [8]. This was thought to provide the perfect environment

for EC to develop. Conditions that are significant risk factors include recurrent UTIs, retained urine due to bladder outlet obstruction, chronic urinary catheter use, immunosuppression, and diabetes mellitus [5,6,9].

SGLT2i medications have been associated with a higher risk of urinary tract infections in patients with diabetes mellitus in some literature, though this remains controversial [10,11]. Through meta-analysis, Li et al. found that a higher risk of complicated UTIs is associated with canagliflozin, dapagliflozin, and empagliflozin compared to placebo [12]. Recurrent UTIs, and even a case of Fournier's gangrene, have been reported after the addition of empagliflozin for improved diabetic control [13,14]. In contrast, studies have shown a low risk of urinary tract infections with the addition of an SGLT2i medication to help improve diabetic control [15,16]. Research has shown improved cardiorenal risk in patients with T2DM [17,18]. One study even reports that empagliflozin slows the progression of end-stage renal disease [19]. When considering clinical guidelines for diabetes management, SGLT2i medications are now indicated for those patients who have concurrent comorbidities of established atherosclerotic cardiovascular disease, heart failure with reduced or preserved ejection fraction, and/or chronic kidney disease (defined as GFR < 60 mL/minute) [20].

In this case, the patient's hemoglobin A1c improved after adding the SGLT2i medication. However, due to his complication of emphysematous cystitis, this was stopped. One similar case was discovered during the literature review [21]. Though SGLT2i medications have proved efficacious for improving T2DM and the associated cardiorenal impacts, it remains uncertain as to the degree of caution needed to be exercised in patients with a history of benign prostatic hyperplasia with lower urinary tract symptoms (LUTS).

Conclusion:

The case presented documents a case of symptomatic acute urinary retention and EC in a male with T2DM with a history of BPH with LUTS who was initiated on empagliflozin. His treatment was nonoperative. He ultimately had no sequelae after successful medical treatment of EC upon follow-up at three months post-discharge. Overall, the literature favoring SGLT2i medications outweighs the noted risks in the reviewed and presented cases. Clinicians may exercise caution and have an informed discussion with patients when contemplating initiation of an SGLT2i medication with symptomatic BPH or a history of UTIs. Appropriate patient education and close follow-up with these patients is recommended.

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