


Case Report: Urinary Tract Infection in a Diabetic Postmenopausal Woman With Multiple Episodes of Recurrence: An Antimicrobial Susceptibility dispute

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ABSTRACT: Urinary tract infection (UTI) is caused by bacteria growing in urine and affect kidneys, bladder, ureters, and urethra. Women with diabetes are at high risk of developing UTI. This is a case of a 60-year-old postmenopausal woman with uncontrolled type-1 diabetes mellitus and hypertension, who presented with an acute onset of dysuria, burning micturition, and increased frequency. This case highlights the shortfall in the preliminary management plan of performing imperative clinical laboratory investigations including urine detailed report (DR), urine culture and sensitivity(C/S), and plasma glucose testing to initiate antimicrobial treatment. UTI requires to be treated precisely in diabetic patients with the help of a comprehensive diagnosis for signs of dysuria, frequent urination, and pelvic pain. The treatment of UTIs should always begin with culture and sensitivity analysis while the patient is symptomatic, to initiate antimicrobial treatment. Comorbidities should be managed appropriately during treatment to achieve desired therapeutic outcomes.

KEYWORDS: Urinary tract infection, postmenopausal, diabetes mellitus, and culture sensitivity

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Introduction

The frequency of UTIs increases with growing age in women, about 10% to 15% of women aged between 65 and 70 years and 15% to 20% of women aged ≥ 80 years suffered from bacteriuria.¹ Among the various risk factors in postmenopausal women, decreased level of estrogenic hormones seems to modify the urogenital epithelium and microbiome responsible mainly for recurrent UTIs.² Additionally, postmenopausal women with diabetes have been noticed to encounter UTIs more frequently than non-diabetic ones. Elevated glucose levels in urine offer a platform for bacterial multiplication, facilitating bacterial colonization by providing immense microbial nutrients, resulting in moderate to severe urinary infection. The consequences of diabetes-related urinary infections could prolong the hospital stay and relapse, bloodstream infection, septic shock, and other renal complications may occur.³ Diabetes in certain conditions can affect the urogenital system as well thus bringing damage to the respective organs and ultimately leading to pyelonephritis. Such kind of infection is about 15-fold more likely to be observed in diabetic individuals, accentuating the need for timely diagnosis of UTI with appropriate treatment.⁴

Patient Information

We report the case of a 60-year-old postmenopausal woman from Karachi, Pakistan, who presented to an outpatient department (OPD) of renal disease in a tertiary care hospital setting. The patient has taken her first consultation with a nephrologist,

reporting a 1-week history of an acute febrile illness with painful and burning micturition (dysuria). The patient was in a usual state of health and perfectly managing household chores. One week before the onset of symptoms, she developed a steady fever with slight lower abdominal pain associated with dysuria. The painful urination started gradually accompanied with increased frequency to urinate. Past medical history was significant for hypertension and diabetes mellitus for 15 years. She has been taking sitagliptin + metformin (50/500 mg) BD and glimepiride 2 mg OD for the management of diabetes.

Diagnostic Assessment and Therapeutic Intervention

The nephrologist ordered an Ultrasound of the Kidneys, Ureters and Bladder (U/S KUB) pre and post-void (Table 1). The findings revealed that the urinary bladder has normal walls. Pre and post-void volume was 674 and 146 ml respectively with no mass or calculus within the urinary bladder. The left kidney measured 10.2 cm and its cortical thickness was 2.0 cm. A simple cyst was seen at the lower pole measuring 1.9×1.8 cm. The presence of a simple kidney cyst usually requires no treatment but rarely causes complications in the normal urine flow due to urine obstruction. This may lead to swelling of the kidney (hydronephrosis). The prescribed medications included tablet vaccinium macrocarpon 475 mg for 1 month and conjugated estrogen cream L/A for 2 to 3 weeks. The symptoms relieved mildly, and sudden relapse occurred after 2 months.

The severity of symptoms in this recurrence worsened to severe pain in the lower pelvic area and extreme dysuria.



Table 1. Summary of Laboratory investigations and Medication management approach.

NO. OF CONSULTATIONS	MEDICAL PRACTITIONER	LAB INVESTIGATIONS	MEDICATION MANAGEMENT
1	Nephrologist	U/S KUB (Pre & Post void)	Premarin (conjugated estrogen) cream L/A for 2 wk + Tab. Vaccinium macrocarpon 475 mg BD for 1 mo.
2	Urologist	Sr. creatinine, FBS, HbA1c, Uric acid, Urine DR, U/S urinary bladder (pre & post void), Urine C/S	Tab. Baclofen ½ BD + Cap. Tamsulosin 0.4 mg OD HS + Cap. Cholecalciferol 50000IU OD + Tab. Candesartan 16 mg OD Continues for 4 wk. After Recurrence: Piperacillin + Tazobactam 4.5 g IV BD for 5 d.
3	General Physician	Urine C/S & DR	Tab. Fosfomycin 500 mg q8h for 3 mo + Tab. Amlodipine 10 mg OD + Tab. Candesartan 16 mg OD HS. Based on previous HbA1c report: Humalog Mix 50/50 30 units before breakfast and 35 units before an evening meal.

Abbreviations: Cap., capsule; C/S, culture sensitivity; DR, detailed report; FBS, fasting blood sugar; HbA1c, glycated hemoglobin; KUB, kidney, urinary bladder; L/A, local application; Sr., serum; Tab, tablet; U/S, ultrasound.

This time patient approached to a urologist for second consultation. The lab investigations were further ordered for progressive diagnosis, showing the following results: Serum creatinine = 1.48 mg/dl, Fasting blood sugar (FBS) = 96 mg/dl, HbA1c = 7.98%, Uric acid = 6.07 mg/dl. Urine detailed report (DR) = pus cells (0-1), epithelial cells⁶⁻⁸ and bacteria (few), U/S urinary bladder (pre & post void) = urinary bladder has normal walls. No mass or calculus within the urinary bladder. Pre void volume = 494 ml and post void volume = 48.6 ml. (Remarks: normal scan of the urinary bladder, insignificant post-void residue seen). Based on the lab findings the urologist prescribed her tablet baclofen ½ BD + capsule tamsulosin 0.4 mg OD HS + capsule cholecalciferol 50000IU OD + tablet candesartan 16 mg OD for 1 month. The symptoms of urge incontinence and overflow incontinence were relieved but after the discontinuation of treatment, subsequently, a brief period of 2 months recurrence occurred with high-grade fever recorded as 101°F/38.33°C. On the next visit, the patient was advised to perform a urine C/S test. The report-I showed >100 000 CFU/ml of *Flavobacterium species* susceptible to ciprofloxacin, cotrimoxazole, and piperacillin + tazobactam (combination) while gentamicin was found to be resistant. The patient was admitted to daycare for 5 days to initiate antibacterial treatment with piperacillin + tazobactam 4.5 g IV BD for 5 days and was advised to repeat U/S pre and post-void afterward. The results of the repeated scan were found to be pre void volume = 498.4 ml and post void volume = 316 ml for which Urine DR correlation was advised. After reviewing the reports, the urologist recommended cystoscopy, due to significant postvoid residual urine volume, to investigate the cause of incontinence, overactive bladder, and persistent dysuria. The patient refused this diagnostic procedure ultimately.

Eventually, the patient decided to take third consultation from a general physician (GP). The GP simply asked to perform urine culture C/S and considered previously performed

investigations. The second C/S test was again repeated after few months, growth of *Enterococcus species* >100 000 CFU/ml was observed susceptible against nitrofurantoin, fosfomycin, and ampicillin. The outcome of the therapeutic approach from C/S analysis showed complete relief of all the signs and symptoms, which did not relapse.

The Clinical and Laboratory Standards Institute (CLSI) guidelines proposed by the US-FDA was used for antimicrobial susceptibility testing. Gram Staining method was performed on bacterial culture for identification and Colony Forming Unit (CFU) method was used for the quantification of bacteria. Multiplex PCR (BIO-RAD) method was used for the detection of causative pathogen. Antibiotic susceptibility was determined by the Disk Diffusion Method.

Discussion

We report the case of a patient from a category of the simple housewife of postmenopausal age presented with an acute febrile illness with severe dysuria, urge and overflow incontinence. On OPD treatment, she had clinical signs suggestive of uncomplicated UTI. Urine analysis confirmed the presence of UTI with culture results. Furthermore, elevated HbA1c (7.98%) suggested a higher risk of diabetes-associated complications, whereas serum creatinine is also slightly higher (1.48 mg/dl) that may be a suspected sign of chronic renal failure.

The UTI is most instigated when normal flora of the periurethral zone is substituted with pathogenic bacteria that may escalate to further renal complexities extending from bacterial cystitis to bacterial pyelonephritis. Upsurge in the intensity of infection is alleged to be caused by the degree of bacterial pathogenicity that empowers them to attain immunoevasion, colonization and move in and out of the host cell and obtain nutrition from the host cells. Some of the common uropathogens are *Escherichia coli*, *Staphylococcus saprophyticus*, *Klebsiella pneumoniae*, and *Proteus mirabilis*.⁵ The diagnostic work-up

must begin with documentation of the symptoms stated by the patient and laboratory results.⁶ Additionally, a thorough pelvic examination should be performed to rule out any structural or functional abnormalities of the urinary tract—a sign of complicated UTI. Generally, the postvoid residual volume is the non-compulsory test in postmenopausal women. However, clinical investigations related to urinary tract abnormalities might be suggestive of complicated UTI.⁷ Presently, the patient has undergone repeated KUB ultrasounds for pre and post-void residual volume. Based on high post-void volume (316 ml) the urologist recommended the cystoscopy while the patient refused to do so. The structural scan seemed to be normal. The need to perform cystoscopy at once for recurrent UTI did not prove from past studies due to the low prevalence of structural abnormalities (0%–15%).⁸

Routinely, the bacterial growth in a urine culture is a positive indicator of UTI.⁹ Currently, 2 urine C/S tests of the patient were performed at an interval of 5 months to select an appropriate anti-microbial agent. So far, the genus *Flavobacterium* has endured extensive taxonomic amendment and being rare opportunistic pathogens having low virulence may occasionally be involved in severe infections.¹⁰ Piperacillin + Tazobactam was selected earlier and later fosfomycin. *Enterococcus* bacterial species are gram-positive and normally reside in the gut and may lead to antibiotic-resistant UTIs.¹¹ The recurrent UTI refers to ≥ 2 infections in 6 months or ≥ 3 infections in 1 year.¹² In case of symptomatic patient, urine C/S analysis is recommended at least once as this may eliminate recurrent UTIs due to irrational drug treatment.

According to a study, 8% to 26% of asymptomatic bacteriuria have been observed in diabetic women with a projected incidence of 2 to 3 times higher than non-diabetic women.¹³ A cohort study was conducted for over 6000 patients with diabetes mellitus registered for 10 clinical trials of diabetes therapies. The prevalence of urine infection was found to be 91.5/1000 for women and 28.2/1000 for men, with the cumulative risk of 3.5% and 1.1%, respectively in females and males over 6 months period.¹⁴ A strong correlation between diabetes and UTI, emphasized critical considerations toward metabolic alterations characterized by hyper/hypoglycemia, HbA1c levels, insulin resistance, and glycosuria. The patient's HbA1c level was found to be 7.98% which was addressed during third consultation with the GP.

For consultation, it was reported that general physicians should be the first choice for the effective treatment of recurrent uncomplicated UTI.¹⁵ They then proceed with specialist referral, either for nephrologist or urologist, in case of identification of any potential risk factors for complicated UTI or in a case where surgical intervention is required to rectify the cause of UTI. These referrals can also be used to diagnose the cause of recurrence for lower UTI. Nonetheless, before progressing for referrals, urine culture of the symptomatic period and after sensitivity-adjustment treatment should be performed for

diagnostic confirmation of UTI and assist experts in further evaluation and management.¹⁶ Our patient showed an overdue response to this method of treatment consultation.

Our patient has used vaccinium macrocarpon for 1 month as prescribed by a nephrologist and showed only mild improvements in the symptoms. The use of vaccinium macrocarpon to prevent UTI as the first choice of management is contradictory, and no sanction can be made for its efficacy or inefficacy. Recently, cranberry is recommended as a non-antibiotic preventive option to avoid recurrent UTIs in women. This agent is thought to be anti-adherent and prevent pathogens' sticking to uroepithelial cell receptors, consequently reducing the pathogenesis.¹⁷ Few studies, however contradicting the role of the cranberry in UTIs as insignificant responses were recorded.¹⁸

Our patient has also been prescribed a topical application of estrogen hormones for vaginal dryness, burning, and irritation. The use of vaginal estrogens prophylactically for UTI in postmenopausal women is proved to be an effective option.² The topical estrogen cream contains *Estriol* 0.5 mg recommended to be applied vaginally every night for 2 weeks, then twice a week for 8 months.¹⁶ The choice of antibiotics for recurrent UTI must be based on the urine culture and antimicrobial susceptibility testing. The ideal agents for empiric therapy of acute simple cystitis are fosfomycin, nitrofurantoin, trimethoprim/sulfamethoxazole, and pivmecillinam.¹⁹ In case of allergies and resistance to the first-line antibiotics, oral-beta lactams are suitable to use and if beta-lactams cannot be used fluoroquinolone (such as levofloxacin, ciprofloxacin) can be used.²⁰ Our patient was prescribed Piperacillin + Tazobactam 4.5 g IV BD for 5 days based on culture and susceptibility report-I. After the recurrence, Fosfomycin 500 mg q8h was given for 3 months, based on culture report-II.

The combined treatment with insulin to sustain good glycaemic control and sufficient hydration along with the Fosfomycin for 3 months, made our patient show good recovery from the recurring episodes of UTI. It was found that diabetic females are more susceptible to UTIs and because of the potential complications UTIs must be appropriately managed.

Author Contributions

F.K.: Concept, design and interpretation of data for the article, R.B.: Critical revision for important information and approval for case report version to be published, S.G.: Responsible for integrity and accuracy of any part of the work.

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