

Prolonged Suppression of Bacterial Growth in Urine Culture Following Fluoroquinolone Therapy in an Elderly Diabetic Patient: A Diagnostic Pitfall

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Abstract: Urine culture is the gold standard for diagnosing urinary tract infections (UTIs), but prior antibiotic therapy can cause false-negative results. Fluoroquinolones (FQs), commonly used for complicated UTIs, may cause prolonged post-antibiotic effect (PAE), particularly in high-risk patients. We report an 81-year-old diabetic woman with persistent urinary symptoms who received empirical levofloxacin (LFX) therapy. Despite adherence to treatment and repeated urine cultures showing bacteriuria on microscopy, urine cultures remained negative for 10 days following antibiotic discontinuation, and subsequently became positive for FQ-resistant *Escherichia coli*. Renal ultrasonography revealed incidental simple cysts without obstruction or acute pathology. This case highlights a diagnostic pitfall of prolonged suppression of bacterial growth in urine cultures following FQ therapy. This effect may be more pronounced in elderly patients with comorbidities. Clinicians should interpret urine cultures cautiously after FQ use in high-risk patients, and consider repeat sampling when clinical suspicion persists. As a single-case report, the findings may not be generalizable to broader patient populations and should be interpreted with caution.

Keywords: urinary tract infection, levofloxacin, fluoroquinolone, post-antibiotic effect, diabetes, drug resistance

Introduction

Urinary tract infections (UTIs) are among the most common bacterial infections in older adults with type 2 diabetes mellitus (T2DM).¹ Their proper management requires accurate microbiological diagnosis and selection of an effective antibiotic.² In clinical practice, urine culture remains the gold standard for identifying the causative pathogen and determining antibiotic susceptibility;³ however, prior antibiotic use can reduce culture sensitivity and lead to false-negative results, delaying diagnosis and treatment.⁴

Clinical guidelines generally recommend obtaining culture samples before initiating antibiotic therapy whenever possible.² Therefore, specimens should ideally be collected before antibiotic initiation or after sufficient time has elapsed to minimize residual antimicrobial effects.⁴ The inhibitory effect of antibiotics in urine may vary due to pharmacokinetic differences between agents and patients. This results in heterogeneous effects on bacterial growth and culture outcomes.⁵

FQs play a significant role in the treatment of complicated UTIs due to their favorable pharmacokinetic properties.^{6,7} These drugs also exhibit a post-antibiotic effect (PAE) on certain pathogens, including *E. coli*, which can suppress bacterial growth for several hours after drug discontinuation.⁸ In elderly patients with diabetes, pharmacokinetic changes may occur. These include reduced renal clearance and altered volume of distribution.^{9,10} In addition, weaker immune responses in diabetic patients can impair bacterial clearance and increase bacterial burden in the urinary tract.¹¹

Moreover, prior antibiotic exposure is recognized as a risk factor for antibiotic-resistant infections. Therefore, delayed microbiological diagnosis and inappropriate sampling may lead to delayed detection of resistance. This may result in selection of suboptimal therapy and potentially adverse clinical outcomes.^{12,13} Case reports have shown that the inhibitory effect of antibiotics on urine culture results can persist longer than the typically recommended washout period. These findings are

especially valuable for guiding optimal sampling timing and culture interpretation in high-risk patients, such as elderly individuals with diabetes.^{4,14} However, the duration of antibiotic-induced suppression of bacterial growth in urine cultures remains poorly defined, particularly in high-risk populations such as elderly patients with diabetes.

In this article, we report a case of an 81-year-old diabetic woman who, following treatment with LFX, had several negative urine cultures despite discontinuing antibiotics according to standard recommendations. On the tenth day after drug discontinuation, the urine culture became positive, and FQ-resistant *E. coli* was identified. This report aims to examine the phenomenon of prolonged suppression of bacterial growth in urine following FQ therapy in an elderly diabetic patient and to discuss its diagnostic and management implications.

Case Presentation

An 81-year-old Iranian woman with a history of T2DM presented with dysuria and urinary frequency. She had no fever, flank pain, or back pain. Her medications included metformin 500 mg twice daily, empagliflozin and linagliptin (25/5 mg) once daily, and carvedilol 6.25 mg once daily. Her fasting blood glucose was 93 mg/dL, HbA1c was 6.9%, and her mean blood pressure was 124/85 mmHg. Initially, LFX 500 mg once daily for 10 days was prescribed empirically without prior urine culture. Despite strict adherence to the regimen, the patient reported no improvement in urinary symptoms. Ten days after initiating LFX, she returned for further evaluation. Urine culture, laboratory tests, and renal and urinary tract ultrasonography were requested.

Because of recent antibiotic exposure, urine sampling was deferred for five days after discontinuation of LFX to minimize the risk of false-negative culture results. During this period, no additional antibiotics were administered, and urinary symptoms persisted.

The first urine sample was obtained 5 days after discontinuation of LFX: urinalysis showed abundant bacteriuria, while urine culture was negative. A second sample was collected 7 days after discontinuation, again showing persistent bacteriuria on microscopy with a negative culture. A third sample, obtained 9 days after discontinuation, showed similar findings, with persistent bacteriuria on microscopy and a negative culture. On day 10 post-discontinuation, urinalysis again demonstrated bacteriuria, and urine culture became positive, yielding FQ-resistant *E. coli*. To improve clarity, the urine culture results are summarized in a structured timeline table.

Antibiotic susceptibility testing revealed sensitivity to amikacin and nitrofurantoin, and resistance to cephalixin, cefazolin, ampicillin, ciprofloxacin, trimethoprim–sulfamethoxazole, and gentamicin.

Renal ultrasonography revealed normal kidney size and preserved cortical thickness, with no evidence of hydronephrosis or nephrolithiasis. A large, well-circumscribed exophytic cystic lesion measuring 63×72 mm was identified in the upper pole of the left kidney. Additionally, several small cortical cysts were noted in both kidneys. The urinary bladder had a normal wall thickness and contour. These findings were consistent with simple renal cysts and were not suggestive of obstructive uropathy or acute pyelonephritis.

Laboratory tests were largely unremarkable, with blood urea of 37 mg/dL and creatinine of 0.9 mg/dL. Other laboratory results are summarized in Tables 1–3, and the sequence and timing of urine culture results are summarized in Table 4. Renal ultrasonography findings are presented in Figures 1 and 2. Notably, imaging did not reveal any obstructive or inflammatory pathology that could explain the delayed culture positivity.

The patient was treated with nitrofurantoin, 100 mg orally three times daily for 7 days. Following completion of therapy, her urinary symptoms completely resolved. No bacteria were observed in the urine, and a follow-up urine culture performed approximately one week after completing nitrofurantoin therapy returned negative, confirming successful eradication of the infection.

Discussion

This case highlights an underrecognized diagnostic challenge in UTIs: prolonged suppression of bacterial growth in urine cultures following FQ therapy, particularly in elderly patients with T2DM. Despite persistent lower urinary tract symptoms and repeated microscopic evidence of bacteriuria, urine cultures remained negative until 10 days after FQ discontinuation. This duration exceeds the typical washout period recommended to minimize the risk of false-negative urine cultures following antibiotic exposure.^{2,14} To our knowledge, this case is distinguished by an unusually prolonged

Table 1 Hematology Tests. These Tests Assess the Cellular Components of Blood, Including Red and White Blood Cells, Platelets, and Indices of Red Blood Cell Size and Hemoglobin Content. ESR (Erythrocyte Sedimentation Rate) is Included as a Marker of Inflammation

Test	Result	Unit	Normal Range
WBC	7.7	$\times 10^3/\mu\text{L}$	4-10
RBC	5.2	$\times 10^6/\mu\text{L}$	3.9-5.6
Hgb	15.7	g/dL	12.0-16.5
Hct	46.7	%	36.0-47.0
MCV	90	fL	80-100
MCH	30	pg	25-32
MCHC	34	g/dL	28-40
Platelets	274	$\times 10^3/\mu\text{L}$	15-450
ESR 1 st h	5	mm/hr	Up to 20
ESR 2 nd hrs	11	mm/hr	Up to 30

Abbreviations: WBC, white blood cell; RBC, red blood cell; Hgb, hemoglobin; Hct, hematocrit; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; ESR, erythrocyte sedimentation rate.

Table 2 Blood Biochemistry Tests. These Tests Evaluate Metabolic, Renal, Hepatic, and Lipid Parameters, as Well as Long-Term Glycemic Control and Vitamin D3 Status

Test	Result	Unit	Normal Range
FBS	93	mg/dL	70-100
BUN	37	mg/dL	15-50
Creatinine	0.9	mg/dL	0.6-1.1
TG	121	mg/dL	Normal<200
HDL	36	mg/dL	>35
LDL	78	mg/dL	<130
S.G.O.T (AST)	28	IU/L	Up to 42
S.G.P.T (ALT)	21	IU/L	Up to 38
ALP	159	IU/L	64-306
HbA1c	6.9	%	Good control <7.5
Vitamin D3	62	ng/mL	Sufficient: 30-100

Abbreviations: FBS, fasting blood glucose; BUN, blood urea nitrogen; TG, triglycerides; HDL, high-density lipoprotein; LDL, low-density lipoprotein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkaline phosphatase; HbA1c, hemoglobin A1c.

Table 3 C-Reactive Protein (CRP) Test Results. CRP Was Measured Qualitatively and Reported as Positive (+) According to the Laboratory Protocol

Test	Result	Unit	Normal Range
CRP (C-Reactive Protein)	Positive (+)	mg/L	< 5 mg/L

Abbreviation: CRP, C-Reactive Protein.

Table 4 Urine Analysis and Microbiological Findings Following Levofloxacin Discontinuation. This Table Summarizes Serial Urine Analyses and Cultures Performed After Discontinuation of Levofloxacin, Demonstrating Persistent Bacteriuria with Delayed Bacterial Growth on Urine Culture, Followed by Organism Identification and Antibiotic Susceptibility Testing

1 st Urine Analysis (5 days after Levofloxacin Discontinuation)		
Bacteria in Urine	Many	Normal: Negative
Urine Culture	No growth after 24 hrs	
2 nd Urine Analysis (7 days after levofloxacin discontinuation)		
Bacteria in Urine	Many	Normal: Negative
Urine Culture	No growth after 24 hrs	
3 rd Urine Analysis (9 days after levofloxacin discontinuation)		
Bacteria in Urine	Many	Normal: Negative
Urine Culture	No growth after 24 hrs	
4 th Urine Analysis (10 days after levofloxacin discontinuation)		
Bacteria in Urine	Many	Normal: Negative
Urine Culture	Positive after 24 hrs: >10 ⁵ CFU/mL	Neg: <10 ⁴ CFU/mL
Identified Organism	Escherichia coli (E. coli)	
Antibiotic Susceptibility Results		
Sensitive to	Amikacin, Nitrofurantoin	
Resistant to	Cephalexin, Cefazolin, Ampicillin, Ciprofloxacin, Trimethoprim–Sulfamethoxazole, Gentamicin	

Abbreviations: CFU, colony forming unit; Neg, negative.

duration of culture negativity, exceeding commonly reported intervals and highlighting a potential gap in current clinical guidance, particularly in high-risk populations. To date, there are limited data regarding the frequency or prevalence of prolonged culture suppression following FQ therapy in elderly diabetic populations. Such data are not well characterized in our local setting, highlighting the need for further investigation. Urine culture remains the reference standard for etiologic diagnosis and antimicrobial susceptibility testing in UTIs.³ However, its diagnostic sensitivity is highly dependent on appropriate timing relative to antibiotic exposure. Several studies have demonstrated that even short courses of antibiotics can significantly reduce bacterial recovery from urine cultures, leading to false-negative results and delayed diagnosis.^{4,14,15} Current clinical guidelines generally recommend obtaining cultures before antibiotic initiation or delaying sampling for several days after discontinuation, yet these recommendations are largely based on expert consensus rather than robust pharmacokinetic–microbiological data.^{7,16}

FQs are characterized by excellent oral bioavailability, extensive tissue penetration, and high urinary concentrations.¹⁷ In addition to their concentration-dependent bactericidal activity, FQs exhibit a PAE, during which bacterial growth remains suppressed after drug concentrations fall below the minimum inhibitory concentration (MIC).⁸ Although the

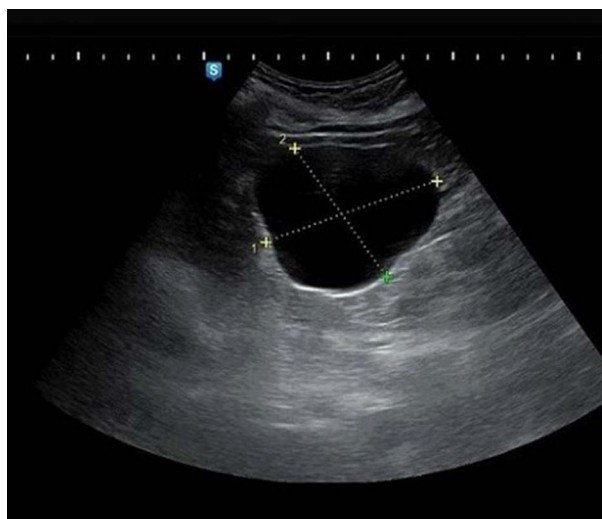


Figure 1 Renal ultrasonography of the left kidney. Gray-scale ultrasonography of the left kidney demonstrates a large, well-defined exophytic cystic lesion arising from the upper pole, measuring approximately 72×63 mm. The lesion appears anechoic with thin walls and posterior acoustic enhancement, consistent with a simple renal cyst. The surrounding renal parenchyma is preserved, with no evidence of hydronephrosis or calculi.



Figure 2 Renal ultrasonography showing additional cortical cysts. Ultrasonographic image shows small cortical cystic lesions, including a cyst measuring approximately 10.7 mm, consistent with simple cortical renal cysts. No solid components or internal septations are identified.

PAE is typically short, residual antimicrobial effects may persist longer in certain patients, notably in high-risk populations.^{8,18}

Advanced age is associated with significant pharmacokinetic variability, including reduced renal drug clearance, altered hepatic metabolism, and changes in body composition that affect drug distribution.⁹ Importantly, serum creatinine alone may underestimate reduced renal function in elderly individuals due to decreased muscle mass, potentially leading to prolonged drug exposure despite “normal” laboratory values.¹⁹ Diabetes mellitus further complicates this scenario by causing immune dysregulation, impaired neutrophil function, and altered urinary tract host defenses, all of which can influence bacterial persistence and response to antimicrobial therapy.^{20,21}

In the present case, repeated urinalyses consistently demonstrated abundant bacteria, while cultures remained negative until day 10 after LFX discontinuation. This discordance strongly suggests ongoing bacterial presence with suppressed culturability rather than true microbiological eradication. Similar discrepancies between microscopy and culture have been

described following antibiotic exposure and may reflect sublethal bacterial injury or temporary growth inhibition rather than sterilization of the urinary tract.^{14,15}

Alternative explanations for the discrepancy between persistent bacteriuria on microscopy and negative culture results should also be considered. These include infection with fastidious or slow-growing organisms, prior partial antibiotic treatment, or technical factors related to specimen collection, transport, or laboratory processing. However, the eventual growth of *E. coli* in culture, along with persistent microscopic bacteriuria and clinical symptoms, makes these alternative explanations less likely in the present case.

The eventual isolation of FQ-resistant *E. coli* is clinically significant. Prior exposure to FQs is a well-established risk factor for the selection of resistant uropathogens, particularly in older adults and patients with recurrent or complicated UTIs.^{2,12} In this context, empirical FQ therapy not only failed to improve symptoms but also obscured microbiological diagnosis, delayed recognition of resistance, and ultimately prolonged the duration of treatment.

Imaging studies excluded obstructive uropathy, nephrolithiasis, and acute pyelonephritis, and the renal cystic findings were consistent with incidental simple cysts. Thus, structural abnormalities were unlikely to explain either symptom persistence or delayed culture positivity, further supporting the role of prolonged antimicrobial suppression as the primary mechanism.

This study has several limitations. First, direct susceptibility testing for LFX was not performed. Although ciprofloxacin was used as a representative FQ in the antibiogram, the absence of LFX-specific susceptibility data should be considered when interpreting the findings. Importantly, resistance to ciprofloxacin does not invariably indicate resistance to LFX in *E. coli*, as cross-resistance among FQs may vary.²² Second, the follow-up urine culture after completion of nitrofurantoin therapy was not obtained at a standardized interval comparable to the initial 10-day observation period. These factors may limit direct comparison of bacterial clearance dynamics and should be taken into account when interpreting the results. In addition, no pharmacokinetic measurements (eg., serum or urinary drug concentrations) were available to directly support prolonged antimicrobial exposure, and therefore the proposed mechanism remains inferential. Finally, as a single-case report, the findings may not be generalizable to broader patient populations.

Taken together, this case underscores the potential limitations of standard washout intervals for urine culture following antibiotic exposure. In high-risk patients, particularly elderly individuals with diabetes, persistent discordance between clinical symptoms, urinalysis findings, and negative culture results may indicate ongoing infection despite apparently negative cultures. In such scenarios, clinicians should be aware that a single negative urine culture obtained shortly after FQ therapy may not reliably exclude infection. Repeat urine culture after a longer interval (eg., ≥ 7 –10 days), with careful correlation to clinical and urinalysis findings, may assist in clinical interpretation. In selected cases with persistent diagnostic uncertainty, additional diagnostic approaches may also be considered.²³ These findings are derived from a single case and should be interpreted in this context. Further studies are needed to better define the optimal timing of urine culture after FQ exposure in high-risk populations.

Conclusion

This case highlights that negative urine cultures obtained shortly after FQ therapy may not reliably exclude active infection, particularly in elderly patients with T2DM. In the presence of persistent urinary symptoms and bacteriuria on microscopy, clinicians should interpret negative culture results with caution. In such high-risk patients, delayed or repeated urine cultures, along with close clinical correlation, are essential to avoid missed or delayed diagnosis. Increased awareness of this diagnostic limitation may improve clinical decision-making, reduce inappropriate reassurance from false-negative results, and support more effective management of complicated UTIs.

Declaration of AI Assistance

This study used generative AI- and AI-assisted technologies to paraphrase and rewrite certain sections to improve clarity and readability. The content was generated based on the original text, while ensuring accuracy and maintaining scientific integrity.

Ethics Statements

Ethics approval by the local ethics committee was not required, as this is a case report with anonymized details. Written informed consent was obtained from the patient for publication of any potentially identifiable images or data contained in this article.

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Disclosure

The author declares no conflicts of interest in this work.

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