


CASE REPORT

E. coli bacterial meningitis after transrectal prostate biopsy under antibiotic prophylaxis: a case report and literature review

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Abstract

Prostate biopsy, a frequently performed procedure, is not harmless. In rare cases, life-threatening complications occur. We document a potential lethal bacterial meningitis after transrectal biopsy. In addition to our overview of all previously documented cases, we highlight the evidence of prevention of infectious complications when performing a prostate biopsy.

KEYWORDS

E. coli, meningitis, prostate biopsy

1 | INTRODUCTION

Transrectal prostate biopsy is a widely performed procedure in the diagnosis of prostate cancer. Most complications are minor and self-limiting such as hematospermia, anal blood loss, and hematuria. These are not uncommon and have an incidence up to 92%, 36.8%, and 86%, respectively.¹ Infectious complication can vary widely from asymptomatic bacteriuria to severe urinary sepsis. Hospitalization because of biopsy-related major complications ranges from 0.5% to 6.9% and has increased over time.¹ Mortality after prostate biopsy is extremely low. In a population-based study of 75190 men who underwent a transrectal biopsy between 1996 and 2005, the overall 30-day mortality rate was 0.09%.² To date, most deaths are caused by septic shock. A possible lethal bacterial meningitis after a prostate biopsy has only been described a couple of times in English literature.

2 | CASE PRESENTATION

A 55-year-old patient with a consecutive rising prostate-specific antigen (PSA) of 7.9 µg/L showed a progressive diffusion-restrictive lesion on magnetic resonance imaging (MRI; 6 mm, PI-RADS 3). The patient underwent a transrectal ultrasound-guided prostate biopsy as a further diagnosis. He had no significant medical history. He was treated with a 10 days course of ciprofloxacin 5 months before the biopsy. Antibiotics were started due to a urinary tract infection. Perioperative oral antibiotic prophylaxis (ciprofloxacin 500 mg/12 h) was started 24 h before the biopsy. Altogether, antibiotics were continued for 3 consecutive days. No additional per-operative intravenous antibiotics were given. No pre-operative urine culture was obtained.

The patient presented in our emergency department 48 h after the biopsy. He reported a high fever (>39°C), shivering, nausea, vomiting, generalized muscle pain,

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and a mild headache. Hemodynamic parameters were stable. Mean arterial blood pressure was 90 mmHg, heart rate 87 beats per minute, and oxygen saturation was 97%. Biochemical markers of infection were not elevated (WBC $5.0 \times 10^3/\mu\text{L}$, neutrophils 78%, and CRP 7.1 mg/L). Urine was not cloudy and showed 12 WBC/ μl . The abdominal ultrasound was negative. The diagnosis of bacterial prostatitis was suspected and the patient was administered to the urological ward. Empiric intravenous antibiotic treatment with $2 \times 2\text{gr}$. temocillin was started.

At first, our patient showed clinical improvement. The highest temperature registered within the first 48 h after admission was 37.3°C . After 48 h he developed a worsening pancranial headache, neck stiffness, and photophobia. The remainder of the neurological investigation was negative. Lumbar puncture yielded cloudy cerebrospinal fluid (CSF) containing 3611 WBC/ μl (91% neutrophils), 700 erythrocytes/ μl , <2 mg/dl glucose, 204 mg/dl proteins, and a high bacterial load (gram-negative). Computed tomography (CT) without contrast of the brain was negative and did not show signs of intercranial bleeding nor infarction. We note that our patient was administered his first dose of a COVID-19 Astra Zeneca vaccine 13 days before the prostate function. A CT venography was thus performed to exclude a venous thromboembolic event but was negative. Our patient was transferred to the neurological ward and antibiotics were switched to ceftriaxone $2 \times 2\text{gr}$. intravenously. The culture of the blood, urine, and the CSF showed an *Escherichia coli* resistant to amoxicillin-clavulanic acid, ciprofloxacin, trimethoprim but sensitive to temocillin, first-generation cephalosporin, amikacin, gentamycin, furadantin, and carbapenem. MRI of the brain (day 4 of ceftriaxone administration) showed enhancement of the meninges as a nonspecific sign of meningitis. No other abnormal features were noticed. Therapy with ceftriaxone was administered for 14 days intravenously and our patient recovered slowly but well. At hospital discharge, he only reported a minimal headache after severe cognitive or physical effort.

3 | DISCUSSION

A bacterial infection of the leptomeninges can be caused by diverse bacteria and prompts an acute and appropriate antibacterial treatment. The predominant pathogens responsible for bacterial meningitis in adults are *Streptococcus pneumoniae* and *Neisseria meningitidis*. They account for respectively 25.1%–41.2% and 9.1%–36.2% of bacterial meningitis cases.³ Meningitis by *E. coli* happens predominantly in children aged under 3 years old, often after transmission from the childbirth channel. *E. coli* and *S. pneumoniae* are the most common pathogen in neonates in Africa.³ In

adults, on the other hand, gram-negative bacilli are an uncommon cause of meningitis. Most of the *E. coli* cases are post-trauma or following neurosurgical procedures due to dura-arachnoid disruption.⁴ Neurosurgery, a head trauma within the past month, a neurosurgical device and a CSF leak represent portals of entry in 75% of nosocomial cases.⁵ Community-acquired gram-negative meningitis in adults is very rare and counts for only 0.7%–7% of all community-acquired meningitis.⁶ A review of the literature in Marseille identified only 43 cases of community-acquired *E. coli* meningitis between 1946 and 2016. Risk factors included chronic alcoholism, cirrhosis, diabetes mellitus, disseminated strongyloidiasis, HIV, chronic obstructive pulmonary disease, and chronic organ insufficiency. Urinary tract infection was the suspected cause in 10 cases (23%).⁶

Temocillin, an old antimicrobial agent, has been rediscovered as an antibiotic to treat urinary tract infections. It is known to have excellent penetration into the urinary tract. The antibiotic is used primarily for the treatment of multiple (drug-resistant) gram-negative bacteria. Even extended-spectrum beta-lactamase producing bacteria are relatively high susceptible to temocillin. Activity for gram-positive bacteria on the other hand is limited.⁷ Attention must be given to the fact that diffusion of temocillin into the CSF is relatively low. The CSF/serum concentration ratio is estimated at approximately 10%.⁷ Therefore, in the rare case of central nervous system involvement, other antibiotic agents are strictly advised.

We performed a literature search of Pubmed, Limo, and Google Scholar to identify other cases of meningitis after prostate biopsy. Keywords included: prostate biopsy and meningitis. A total of 13 cases were identified of which eight were in English, one in German, two in French, one in Norwegian, and one in Spanish literature. All cases showed *E. coli* as the pathogenic organism and all biopsies were performed transrectally. Sandvik A. described the first case in 1982 in Norway.⁸ In 2003, a similar case of an *E. coli* acute meningitis after the transrectal biopsy was described in Heidelberg, Germany.⁹ In 2006, Diana Alecsandru reported an acute post-biopsy meningitis with a multi-resistant *E. coli* in Madrid, Spain.¹⁰ A case report from 2012 in the United States is unlike all other reports and describes meningitis with an onset 7 weeks after the prostate biopsy.¹¹ Ciprofloxacin was used as a prophylactic treatment in at least 7 cases. The time from biopsy until the development of meningitis was mostly less than 7 days. The most-reported clinical signs of meningitis included a severe headache, altered mental state, and fever. Antibiotic treatment differed but ceftriaxone was used in monotherapy in 5 cases and in combination with gentamycin in 2 other cases. There was one case of exitus letalis and one case with a persisting left hemiparesia. All other patients recovered completely. A synopsis of all cases is shown in Table 1.

TABLE 1 Clinical data of previous cases in the literature and current case of bacterial meningitis after prostate biopsy

Case no.	Date/reference	Patient age/biopsy/prophylaxis	Pathological organism	Treatment	Recovery
1	1982/ ⁸	n.a.	<i>E. coli</i>	n.a.	n.a.
2	2003/ ⁹	64 years/T.R./levofloxacin	<i>E. coli</i>	Ceftriaxone 2 × 2gr. 14 days	Completely
3	2003/ ²⁴	n.a./T.R./quinolone	<i>E. coli</i>	n.a.	n.a.
4	2005/ ²⁵	75 years/T.R./levofloxacin + metronidazole	<i>E. coli</i>	Carbapenem 3 × 1gr. 14 days	Completely
5	2006/ ¹⁰	69 years/T.R./cipprofloxacin	<i>E. coli</i>	Imipenem, Cefotaxim	Left hemiparesia
6	2007/ ²⁶	67 years/T.R./ofloxacin + metronidazole	<i>E. coli</i>	Ceftriaxone + Gentamycin	Exitus letalis
7	2008/ ²⁷	71 years/T.R./cipprofloxacin	<i>E. coli</i>	Meropenem 3 × 2gr. 21 days	Completely
8	2009/ ²⁸	60 years/T.R./cipprofloxacin	<i>E. coli</i>	Ceftriaxone 2 × 4gr. + Gentamycin 180 mg/24 h	n.a.
9	2011/ ²⁹	75/T.R./cipprofloxacin	<i>E. coli</i>	Meropenem 6gr./24 h 21 days	Completely
10 & 11	2012/ ³⁰	65 years/T.R./n.a. 69 years/T.R./n.a.	<i>E. coli</i>	Ceftriaxone 2gr./12 h Meropenem 6gr./24 h	Completely
12	2012/ ¹¹	57 years/T.R./cipprofloxacin	<i>E. coli</i>	Ceftriaxone 1 × 2gr. 14 days	Completely
13	2015/ ³¹	83 years/T.R./cipprofloxacin	<i>E. coli</i>	Ceftriaxone	n.a.
14	2021/current case	55 years/T.R./cipprofloxacin	<i>E. coli</i>	Ceftriaxone 2 × 2gr. 14 days	Completely

Abbreviations: n.a. not available; T.R. transrectal.

E. coli meningitis stays a rare and poorly described condition. Available knowledge is only based on case reports. The presumed mechanism regarding etiology is a hematogenous bacterial spread. Possible options are an arterial route of entry but also venous spreading seems plausible. This assumption stands because of the direct vascular connection between the periprostatic venous plexus and the lumbar vertebral venous plexus. Retrograde flow through this plexus during periods of high intra-abdominal pressure has been postulated to allow the spread of infection from the pelvic organs.¹²

Prostate biopsy still is the best, and most widely used, diagnostic tool in detecting prostate cancer. Toleration is well with mostly minor complications such as hematospermia, hematuria, or minor rectal bleeding.¹ Historically urologists are more familiar with the transrectal procedure. One reason is the presumed requirement of general anesthetics during a transperineal approach. Recent publications show a benefit in favor of this transperineal approach. This method has been associated with a lower infection rate because of the passage of the biopsy needle through an easily sterilized skin surface. A systematic review including 165 studies described a sepsis rate of 0.1% and 0.9% for transperineal versus transrectal biopsies, respectively.¹³ This was confirmed by another study showing a lower readmission rate due to sepsis after the transperineal approach (1.0%) versus the transrectal approach (1.4%).¹⁴

To reduce the risk of infection during the transrectal biopsy, several measurements have been described. Rectal preparation with povidone-iodine resulted in a significantly lower rate of infections.¹⁵ Prophylactic administration of antibiotics has shown to significantly reduce infectious complications.¹⁶ Traditionally fluoroquinolones were the main source of single empirical prophylaxis. However, since resistance rates are rising, the indication for quinolone perioperative antibiotic prophylaxis has been suspended in March 2019 by the European Commission. An exception has been made if local fluoroquinolone resistance rates are low. But until today, no resistance threshold for this issue has been set.¹⁷ Two randomized controlled trials investigated the single use of aminoglycosides and the single use of cephalosporines as a prophylactic treatment. These two agents showed comparable results to quinolones regarding infectious complications.¹⁶ Therefore, cephalosporins or aminoglycosides can be used as individual prophylactic agents. The use of fosfomycin as a single prophylactic stays controversial. A meta-analysis from 2018 representing 3112 patients comparing fosfomycin to fluoroquinolone, showed a significantly lower infection rate in the fosfomycin group.¹⁸ In contrast, results from a large Canadian cohort in 2019 concluded inferior

effectiveness of fosfomycin in preventing urinary sepsis.¹⁹ Targeted prophylaxis, based on rectal swap or stool culture, was originally introduced to administer alternative antibiotics in cases of fluoroquinolone resistance. This antimicrobial prophylaxis method achieved a low rate of infectious complications, with only a 0.6% sepsis rate.²⁰ A meta-analysis from fifteen studies (eight retrospective and seven prospective) representing 12 320 participants showed lower infectious complications and morbidity when targeted prophylaxis was administered.²¹ All studies compared targeted prophylaxis to a quinolone baseline and the type, dosage, and duration of the alternative antibiotic agent usually remained unclear. Another option is empirical augmented prophylaxis based on 2 classes of antibiotics. In most cases, fluoroquinolone is used in combination with an aminoglycoside or a cephalosporin to broaden the spectrum. A large retrospective study of 15 236 transrectal prostate biopsy cases showed that augmented empirical prophylaxis was statistically superior to single-agent empirical and targeted prophylaxis. It must be noted that even during broad-spectrum augmented prophylaxis, sepsis developed in a significant amount (0.29%) of patients.²² Furthermore, we would like to highlight that no randomized control trials are available until today it is not proven that augmented prophylaxis is superior to monoprophyllaxis. A more detailed overview of the pathophysiology, epidemiology, causative organisms, and protective measures of infectious complications after prostate biopsy, has been reported in a review by Derin et al.²³

The most effective step to reduce infections stays the implementation of transperineal biopsies. This was confirmed in a meta-analysis published in March 2021. The study showed a significantly lower rate of infectious complications after a transperineal prostate biopsy compared to a transrectal biopsy with a relative risk of 0.55.¹⁵

4 | CONCLUSION

We described a new case of acute *E. coli* meningitis after a transrectal biopsy. Consideration should be given to all available evidence highlighting the benefit of a transperineal biopsy. If infectious complications do occur, attention must be given to neurological symptoms. This prompts an urgent administration of antibiotics with a high penetration through the blood–brain barrier.

AUTHOR CONTRIBUTIONS

TV: conceptualization, investigation, resources, writing-original draft. KV: reviewing and editing, supervision. SD: reviewing and editing, supervision. EW: reviewing and

editing, supervision. PV: reviewing and editing, supervision. DO: reviewing and editing, supervision.

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CONFLICT OF INTEREST

There is no conflict of interest.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Not applicable.

CLINICAL TRIAL REGISTRATION

Not applicable.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this published article.

ETHICAL APPROVAL

Not applicable.

CONSENT

Written consent to publish was obtained from the patient.

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