CASE REPORT

Radical prostatectomy in the presence of ongoing refractory ESBL *Escherichia coli* bacterial prostatitis

Louise Catherine McLoughlin, T E D McDermott, John Alan Thornhill

Tallaght Hospital, Dublin, Ireland

Correspondence to
John Alan Thornhill,
marjorie.whiteflynn@amnch.ie

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SUMMARY

A 44-year-old Indian national with a prostate-specific antigen of 5.4 ng/mL underwent 12-core transrectal ultrasound-guided prostate biopsies. Following this, he had three hospital admissions with severe urosepsis secondary to extended spectrum β lactamase (ESBL) producing *Escherichia coli*. He had recurrent sepsis immediately after discontinuation of intravenous meropenem to which the ESBL was sensitive. He proceeded to radical prostatectomy for intermediate-high risk Gleason 7 prostate cancer, while still on intravenous meropenem, 2 months after his biopsy. His prostatectomy involved a difficult dissection due to inflammatory changes and fibrosis after multiple septic episodes. He had complete resolution of infection after surgery with discontinuation of antibiotics on the third postoperative day, without any recurrence of sepsis.

BACKGROUND

This case demonstrates the significant challenge presented by the emergence of multiantibiotic resistant organisms in the setting of extended spectrum β lactamase (ESBL) producing organisms causing severe urosepsis after transrectal ultrasound (TRUS) biopsy. There is a lack of consensus in the literature about the most appropriate prophylactic antibiotic to administer prior to TRUS biopsy. This case also highlights the difficulties in treating ESBL sepsis. We were unable to discontinue intravenous antibiotics. Removing the source of sepsis, the prostate, was the only cure for ESBL urosepsis.

CASE PRESENTATION

A 44-year-old Indian man with a screening prostate-specific antigen of 5.4, no symptoms, no family history and no signs on examination underwent standard 12-core TRUS biopsy of prostate. Pathology, subsequent MRI and isotope bone scintigraphy confirmed Gleason score 7 (3+4) adenocarcinoma in moderate to high volume in 8 of 12 cores. Three of six right-sided cores had 60%, 5% and <5% tumour involvement while five of six left-sided cores had 50%, 50%, 30%, 30% and 20% tumour involvement, stage T1 N0 M0. These biopsy findings place this young man in the intermediate-high risk disease category.

The prebiopsy antibiotic prophylaxis protocol included ofloxacin 200 mg twice daily 24 h before biopsy and continuing for 3 days after. Rectal swab taken at the time of biopsy subsequently confirmed ESBL-producing *Escherichia coli*.

The patient was admitted emergently day 5 post-biopsy with severe urosepsis requiring intensive

resuscitation and intravenous antibiotic combination of meropenem and amikacin was started, after consultation with microbiology. At this time the prebiopsy rectal swab confirmed ESBL-producing *E. coli* resistant to amoxicillin, gentamicin, cefuroxime, cefotaxime, ciprofloxacin, tobramycin, augmentin, aztreonam and ceftazidime. There was intermediate sensitivity to amikacin and ceftazidime, and sensitivity to meropenem.

Despite intensive inpatient treatment and continued outpatient intravenous erapenam for 7 days, the patient was readmitted with severe urosepsis on day 9, at which time midstream urine (MSU) culture confirmed ongoing urinary infection with the same bacteria and sensitivity profile.

After further inpatient intensive intravenous meropenem and amikacin, followed by 2-week outpatient intravenous meropenem, the patient was admitted for a third time with severe urosepsis. MSU culture again confirmed ESBL-producing *E. coli* now only sensitive to meropenem.

DIFFERENTIAL DIAGNOSIS

Prostatic abscess

TREATMENT

Having ruled out a prostatic abscess or other source of sepsis in the urinary tract or elsewhere, the decision was made at a multidisciplinary meeting to proceed with radical prostatectomy as the most suitable treatment for his prostate cancer, while being aware he had ongoing ESBL *E. coli* prostatitis refractory to antibiotic treatment.

The patient underwent open radical prostatectomy with no intention of nerve sparing, 10 weeks after prostate biopsy. He had remained on intravenous meropenem throughout the preoperative and postoperative period to day 3. Radical prostatectomy was routine but note was made of significant prostatic inflammation and adhesions posteriorly.

OUTCOME AND FOLLOW-UP

The operative and postoperative courses were uncomplicated. The patient remains in complete remission from his prostate cancer and free from urinary infection at 5-month follow-up. He is continent but has erectile dysfunction.

DISCUSSION

TRUS-guided biopsy is the 'gold standard' for obtaining a histological diagnosis of prostate cancer (European Association of Urology Guidelines on Prostate Cancer 2013). There has been a noticeable rise in recent years in the rate of TRUS biopsy

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sepsis, along with an increasing prevalence of multiresistant organisms.^{1–3} Over 5% of men have a symptomatic urinary tract infection after TRUS biopsy which results in serious morbidity in 70% of cases (systemic symptoms and admission to hospital).² A Canadian study reported a significant rise in the readmission rate after TRUS biopsy from 0.6% to 3.6% between 1996 and 2005.³ In a New Zealand study, 10% of men readmitted for TRUS biopsy infection required admission to an intensive care unit.⁴ The commonest pathogen implicated in post-TRUS biopsy sepsis is *E. coli*, accounting for 75–90% of infectious complications.⁵

ESBL and quinolone-resistant bacteria are increasingly prevalent in rectal flora.^{5–6} ESBL-producing *E. coli* has been increasingly identified in post-TRUS biopsy infections.⁵ Level 1 evidence confirms that antibiotic prophylaxis reduces the rate of bacteriuria after TRUS biopsy.⁷ This evidence is based on the use of fluoroquinolones and trimethoprim/sulfamethoxazole as appropriate antibiotics for prophylaxis.⁸ However, the routine use of fluoroquinolones is now becoming less effective, and may actually be accelerating the development of antibiotic resistance, as the preceding use of fluoroquinolones is a significant risk factor for the development of subsequent ESBL-producing *E. coli* infection.^{5–9} Broad-spectrum carbapenems are currently one of the last lines of antibiotic defence against such bacteria, and are increasingly used in the prophylaxis and treatment of TRUS biopsy sepsis.⁹ Adjunctive measures to antibiotic prophylaxis have been described but remain controversial. Prebiopsy rectal enemas to reduce the rectal microbial burden prebiopsy did not show significant benefit.¹⁰

There has been one report of a patient undergoing a laparoscopic radical retropubic prostatectomy a short interval after a hospital admission for fluoroquinolone-resistant *E. coli* sepsis after a TRUS biopsy. In that case, antibiotics had been discontinued 1 month before surgery. Severe adhesions of the prostate were noted intraoperatively in this Korean report, resulting in difficult dissection of the prostate from the endopelvic fascia. This patient also had no recurrence of sepsis after his prostatectomy.¹¹ In our case open surgery was chosen over laparoscopic or robotic-assisted techniques. With the potential for intraoperative adhesions, it was felt that open surgery would delineate surgical planes with more ease and safety. Considering biopsy pathology and risk category, this patient was deemed unsuitable for nerve sparing. Preoperatively it was also considered that nerve sparing would potentially not be feasible, again due to the presence of intraoperative adhesions and inflammation from repeated infection.

There are no standard guidelines for the management of TRUS biopsy sepsis, but broader-spectrum antimicrobials should be considered.¹² Individual risk factors should be considered when deciding on empiric treatment, such as prior exposure to fluoroquinolones and a history of recent travel to areas endemic for resistant organisms.^{4–13} Our patient is of Asian ethnicity, and did not have a history of foreign travel, but it could be postulated that Asian travel, even by proxy, is a risk factor to ESBL colonisation. At the time of this case our protocol of ofloxacin 200 mg starting 24 h before prostate biopsy was based on a large prospective trial.⁹ Our antibiotic practice is also directed by another large retrospective series documenting antibiotic resistance in our catchment area.¹⁴ We have now adopted a policy of prebiopsy rectal swab to detect ESBL. The swab is performed at the initial consultation when TRUS biopsy is booked.

There are no recommendations in the literature about the optimal timing of radical prostatectomy, if it is indicated, after TRUS biopsy sepsis. It is well recognised that relatively few

antibiotics reach therapeutic levels in prostatic tissue with either oral or intravenous administration. Our antibiotic prioritisation is therefore decided with a consultant microbiologist and considering our published local antibiotic resistance patterns. If the patient is refractory to intravenous antibiotic treatment, as in our patient, we suggest that surgery should be expedited. However, with this approach one can expect less distinct dissection planes in an inflamed and fibrotic surgical field, precluding successful nerve sparing technique, and potentially increasing incontinence rates. The relative young age and biopsy pathology results (moderate-to-high risk prostate cancer category) made the decision to proceed with a non-nerve sparing radical prostatectomy relatively straightforward. If this patient had been older, had a lower risk tumour or limited life expectancy, then management options including surveillance, radiotherapy or watchful waiting could be appropriate from a cancer viewpoint. The decision to proceed with radical prostatectomy because of infection would have been more difficult. We hope this paper adds to the literature to facilitate such decision-making in this clinical scenario.

Learning points

- ▶ The complete resolution of symptoms after prostatectomy indicates that this is a potential treatment for recurrent sepsis in severe cases refractory to intravenous antibiotic treatment as in our patient.
- ▶ There are no guidelines for the optimal interval for radical prostatectomy after prostate biopsy sepsis. In this case, the prostatectomy was performed while the patient was still on antibiotics.
- ▶ Expediting surgery in cases with ongoing prostatitis will potentially preclude successful nerve sparing technique and increase incontinence rates.

Contributors LCM was involved in case review and drafting of manuscript. TEDM and JAT were involved in editing manuscript.

Competing interests None.

Patient consent Obtained.

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