Extended-spectrum beta-lactamase gram-negative sepsis following prostate biopsy: implications for use of fluoroquinolone prophylaxis

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Extended-spectrum beta-lactamase (ESBL) producing organisms are resistant to penicillins, cephalosporins, aminoglycosides, trimethoprim-sulfamethoxazole, aztreonam, and most fluoroquinolones. We report a case of a 72-year old man who developed septic shock with an ESBL organism after a transrectal ultrasound (TRUS)-guided prostate biopsy despite having received fluoroquinolone prophylaxis. The patient recovered with intravenous ertapenem. Fluoroquinolone resistant bacteria are increasing in prevalence. This needs to be recognized when the antibiotic choice for pre-procedure prophylaxis is made.

Key Words: prostate, biopsy, needle, beta-lactamases, urinary tract infections, prevention and control

Introduction

Antibiotic prophylaxis has been utilized for many years in patients undergoing urological procedures. Fluoroquinolone antibiotics, such as ciprofloxacin and levofloxacin, have proven to be ideal antibiotics for such prophylaxis because of their broad spectrum of antibiotic activity, their ability to achieve high urinary tract concentrations, and their good safety profile. However, a variety of bacteria have now been detected which are resistant to fluoroquinolones. The advent of resistance has the potential to jeopardize the effectiveness of fluoroquinolones in antibiotic prophylaxis. We report a case in which a patient developed sepsis due to multiresistant bacteria, despite the use of fluoroquinolone prophylaxis.

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Case report

A 72-year old man with history of diabetes mellitus and orthotopic liver transplantation for hemochromatosis had a right above the knee amputation and a prolonged hospital stay. Postoperatively he developed urinary retention and was performing clean intermittent catheterization. At that time his urine culture was positive for vancomycin-resistant *Enterococcus.* There were no symptoms or signs of infection (fever, pyuria) and therefore this was felt to more likely represent colonization than infection and was not treated. On physical examination he was discovered to have several hard prostate nodules. His PSA was 0.8 ng/mL.

The patient was scheduled for a transrectal ultrasound-guided prostate biopsy. He was prescribed a 3-day course of levofloxacin which he began taking the day prior to the procedures. The prostate biopsy was uncomplicated with 12 cores taken. The pathology revealed benign prostatic tissue with mild acute inflammation.

The next day the patient presented with fever of 39.6∞C, chills, tachycardia, and hypotension. A provisional diagnosis of septic shock complicating urinary tract infection was made. He was admitted to the hospital and started on intravenous ampicillin/sulbactam. Blood cultures and urine culture subsequently revealed > 100000 colonies *Escherichia coli* producing extended-spectrum beta-lactamase which was sensitive only to carbapenems. A 3-week course of ertapenem was then started. Toward the end of the 3 weeks he developed mental status changes that were deemed possibly secondary to ertapenem and it was discontinued. Urine culture at that time revealed 40000 colonies of ampicillin resistant, vancomycin sensitive *Enterococcus faecalis*. He then underwent a 2-week course of vancomycin and a repeat urine culture was negative.

Discussion

Transrectal ultrasound (TRUS) guided prostate biopsies have been associated with infective complications, including asymptomatic bacteriuria, urinary tract infection, and septicemia. Bacteria are introduced into the urine and blood from the rectum via the biopsy needle. Technological advances in biopsy technique such as smaller gauge spring loaded needles and ultrasound guidance, as well as the use of bowel preparations and prophylactic antibiotics have led to a reduction in the incidence of infectious complications.

Fluoroquinolones are widely used for pre-biopsy prophylaxis due to coverage of common colorectal and urinary flora, high concentration within prostatic tissue, and ease of oral administration. Kapoor et al reported that a single pre-biopsy oral dose of ciprofloxacin 500 mg can reduce post biopsy bacteriuria and clinical urinary tract infection (UTI) rates.[1] However, disagreements over the prophylactic agent used as well as the duration of therapy exist. Sabbagh et al found neither clinical nor statistical difference between 1 day and 3 day regimens for patients undergoing TRUS guided biopsies.[2] In addition, there have been concerning cases reported in which patients developed post biopsy urosepsis despite ciprofloxacin prophylaxis.[3]

Resistant organisms present a growing problem in health care practice today. Over the past 30 years, multiple bacterial species have developed extended spectrum beta-lactamases (ESBL), a heterogenous group of plasmid and integron encoded enzymes responsible for resistance to penicillins, cephalosporins, aminoglycosides, trimethoprim-sulfamethoxazole, aztreonam, and most fluoroquinolones. This mechanism of resistance is of growing importance and this is the first report of an ESBL infection following prostate biopsy. Hyle et al reported an increasing resistance to flouroquinolones and trimethoprim-sulfamazole, as high as 57.6% and 77.6% respectively, in multi-drug resistant (MDR) ESBL producing *Escherichia coli* and *Klebsiella* species.[4] While beta-lactamases such as ESBLs do not directly affect non beta-lactam antibiotics, genes encoding resistance to non-beta-lactams may be present on the same plasmid as genes encoding the ESBLs. In vitro and observational studies strongly suggest that carbapenems should be regarded as the therapeutic choice for serious infections caused by ESBL-producing organisms.[5] Reliance on carbapenems for empiric treatment has resulted in concern regarding development of carbepenem resistance which has been observed in ESBL organisms.[6] With resistance to a growing number of antibiotic classes, treating ESBL infections poses a significant therapeutic challenge, and there is a growing association with ESBL producing infections and negative clinical outcomes.[6]

Risk factors for ESBL organism infection include recent total exposure antimicrobial use[5] and hospital exposure.[4,7] Paterson et al showed that ESBL infections were less prevalent at institutions that implemented contact isolation for ESBL patients.[8] Greater emphasis on early identification of ESBL isolates by active infection control surveillance may decrease the nosocomial spread of these organisms. Increased clinical suspicion for the presence of resistant organisms is necessary in patients with multiple risk factors.

The advent of organisms resistant to fluoroquinolones, such as ESBL producing organisms has the potential to greatly impact the use of fluoroquinolones as prophylaxis for urological procedures. Patients at risk for fluoroquinolone resistant organisms include patients with prolonged hospitalization (such as the patient in this case report), nursing home residents, and patients with recent use of fluoroquinolones. In our complicated patient, a second urine culture prior to the biopsy may have revealed the ESBL organism and prompted directed antimicrobial treatment prior to the procedure.

In our opinion, urologists should review the prior microbiology of patients about to undergo urological procedures and avoid the use of fluoroquinolones in patients with prior urinary tract colonization or infection with fluoroquinolone resistant organisms. The choice of prophylaxis in such patients can be difficult. However, it would appear logical to choose an antibiotic for prophylaxis that has neither been used by the patient recently nor have demonstrated resistance to that antibiotic. Consultation with and infectious disease specialist may be necessary to use intravenous agents such as ertapenem as prophylaxis if no other suitable agents are available. □

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