Multi-drug resistant E.coli urosepsis in physicians following transrectal ultrasound guided prostate biopsies – three cases including one death

William H. Carlson, MD, David G. Bell, MD, Joseph G. Lawen, MD, Ricardo A. Rendon, MD
Department of Urology, Dalhousie University, Halifax, Nova Scotia, Canada

CARLSON WH, BELL DG, LAWEN JG, RENDON RA. Multi-drug resistant *E.coli* urosepsis in physicians following transrectal ultrasound guided prostate biopsies – three cases including one death. The Canadian Journal of Urology. 2010;17(2):5135-5137

Three male physicians underwent transrectal ultrasound guided prostate biopsies for elevated prostate-specific antigen levels or irregular digital rectal exam findings. All three of these patients developed urosepsis secondary to multi-drug resistant organisms despite antibiotic prophylaxis. There are increasing reports of infectious complications following prostate biopsy caused by multi-drug resistant organisms. These cases highlight the potentially lethal risks to healthcare workers who are more likely to harbor multi-drug resistant organisms than the general population. Further research into preoperative assessment and appropriate antibiotic prophylaxis in all potentially high risk patients is warranted.

Key Words: prostate, biopsy, antibiotic resistance, urosepsis

Introduction

Prostate cancer is the second leading cause of male cancer related deaths in the United States accounting for an expected 27,360 deaths in 2009.[1] Transrectal ultrasound (TRUS) guided biopsy of the prostate is the standard of care for histological diagnosis of prostate cancer. TRUS biopsy is considered a relatively safe procedure and the risks and complications have been well described.[2-4] They include minor complications such as hematuria, hematospermia, rectal bleeding and uncomplicated urinary tract infections (UTI). Major complications such as urinary retention, significant rectal hemorrhage and bacteremia have also been described much less commonly. The rate of fever after TRUS biopsy has been reported to be 1.7%-3.5% in patients receiving antibiotic prophylaxis.

Prophylactic antibiotics have been shown to decrease postbiopsy infection rates.[5,6] Although a short course or single dose of a fluoroquinolone is often used, there is no accepted standardized antibiotic regimen. In fact, a wide range of infection prophylaxis practices amongst urologists in the United States has been observed.[7] There have been increasing reports of multi-drug resistant (MDR) bacteremia following prostate biopsy, specifically fluoroquinolone-resistant *Escherichia coli (E. coli)* worldwide.[8-10] This increase has been observed in the general population, as well as several recent reports describing this complication in healthcare workers.[11,12] Currently there are no specific recommendations for prophylaxis of healthcare workers or other potentially high risk patients. We present three cases of physicians who underwent routine TRUS biopsies and developed urosepsis secondary to MDR *E. coli.* None of the patients had any history of UTI, prostatitis, or recent antibiotic use. Two of the patients recovered with aggressive resuscitation and one patient died.

Accepted for publication February 2010

Address correspondence to Dr. Ricardo A. Rendon, Queen Elizabeth II Health Sciences Centre, Room 210, 5-South, Victoria Building, 1278 Tower Road, Halifax, Nova Scotia B3H 2Y9 Canada

Case 1

A 44-year-old physician underwent an uncomplicated 12-core TRUS prostate biopsy because of an elevated prostate-specific antigen (PSA). He received levofloxacin 500 mg orally 1 hour before the biopsy. He had immigrated to Canada approximately 6 months earlier from Central America where he worked in a hospital-based practice. His past medical history was only significant for a vasectomy and mild hypertension

that was treated. Approximately 24 hours postbiopsy the patient felt unwell and became febrile. He was brought to hospital by ambulance and admitted to the intensive care unit 36 hours after the onset of symptoms with urosepsis. There was no other suspected source of infection. Despite aggressive fluid resuscitation, vasopressors, and broad spectrum antibiotics, the patient died 10 hours later. Blood and urine cultures revealed MDR *E. coli* as the causative organism. Notably, it was resistant to ciprofloxacin, gentamicin, trimethoprim/sulfamethoxazole, ampicillin and tobramycin. It was susceptible to cefazolin and cephalexin.

Case 2

An otherwise healthy 53-year-old physician working in a hospital-based practice underwent an uncomplicated 8-core TRUS prostate biopsy because of an elevated PSA. He received ciprofloxacin 500 mg orally 1 hour before the biopsy and was given a prescription for a 3 day course. Approximately 40 hours postbiopsy he presented to the emergency room with fever and hypotension. He initially received IV fluid resuscitation and IV antibiotics – gentamicin 80 mg and ampicillin 1000 mg. Subsequently he received IV ceftriaxone 1000 mg while in the emergency department. The patient clinically improved and his vitals stabilized. The patient elected to be discharged home on oral trimethoprim/sulfamethoxazole and IV ceftriaxone as an outpatient. Approximately 8 hours after being discharged from the emergency department the patient became delirious, hypotensive, and tachycardic. He was admitted to the intensive care unit and received IV fluid resuscitation, vasopressor therapy, and IV ceftriaxone, vancomycin, and ampicillin. The patient recovered from this episode of urosepsis without long term complications. Cultures were positive for MDR *E. coli* resistant to ciprofloxacin and trimethoprim/sulfamethoxazole. It was sensitive to ampicillin, gentamicin, nitrofurantoin, and cephalexin.

Case 3

An otherwise healthy 64-year-old recently retired physician underwent an uncomplicated 6-core TRUS prostate biopsy because of an irregular digital rectal exam. He received ciprofloxacin 500 mg orally 1 hour before the biopsy. Approximately 16 hours postbiopsy the patient developed fevers, malaise and headache and he went to the emergency department. The patient was pan-cultured, fluid resuscitated and started on IV ceftriaxone. He remained in hospital for 4 days and recovered completely. Urine cultures were positive for MDR *E. coli* resistant to ciprofloxacin and ampicillin. It was susceptible to gentamicin, cephalexin, nitrofurantoin and trimethoprim/sulfamethoxazole.

Comment

An estimated 192,280 new cases of prostate cancer were diagnosed in the United States in 2009.[1] The vast majority of these cases were diagnosed by TRUS prostate biopsy. Infectious complications of this procedure have been previously shown to occur in 1.7%-3.5% of patients.[2-4] Although the use of prophylactic antibiotics has significantly decreased infectious complications, the emergence of MDR organisms is increasing the frequency and severity of postbiopsy infections.[8-10] In response, the challenge is to identify patients who are at increased risk for harboring MDR organisms and to provide appropriate prophylaxis.

Patients who have had previous fluoroquinolone exposure or recent hospitalization are at an increased risk of having MDR organisms.[13] A recent study involving hospitalized patients revealed 11.5% were colonized with fluoroquinolone-resistant *E.* coli.[14] Healthcare workers are exposed to this environment and are known to frequently harbor MDR organisms.[15,16] Kamdar and colleagues reported three cases of hospital employees or relatives of hospital employees with postbiopsy fluorquinolone-resistant *E. coli* bacteremia.[11] These three patients required hospitalization, fluid resuscitation, and IV antibiotics. There were no fatalities reported in the study. A near-fatal case of postbiopsy fluoroquinolone-resistant *E.coli* bacteremia was also reported in a physician who primarily worked in an oncology unit.[12] This patient had been exposed to ciprofloxacin twice in the previous 2 years, however the *E.coli* was also resistant to gentamicin, trimethoprim/sulfamethoxazole, cephalothin, and ampicillin. Although healthcare workers are frequently exposed to MDR organisms, specifically fluoroquinolone-resistant *E.coli*, there is little literature investigating whether they have higher rates of colonization than the general population. The lack of research in this area is likely secondary to potential liability issues and work place restrictions if workers were to test positive.

One development which may aid in identifying high risk patients is prebiopsy rectal cultures. Recent research described a technique in which stool on the glove following digital rectal exam was cultured. Yoshitsugu and colleagues were able to isolate *E.coli* in 77% of samples obtained.[17] Once *E.coli* was isolated, fluoroquinolone-resistant strains were identified. Although this technique is likely not practical or necessary for every patient undergoing TRUS prostate biopsy, it potentially could be very useful for high risk patients such as healthcare workers or those with previous fluoroquinolone exposure.

With the growing body of literature demonstrating MDR organisms, the identification of high risk patients is imperative. However, currently the optimal prophylaxis regimen is still controversial and may vary depending on individual and local resistance patterns. Feliciano and colleagues recently reported 79% of patients with positive blood and/or urine cultures following TRUS biopsy had fluoroquinolone-resistant organisms.[9] Of the fluoroquinolone-resistant *E. coli*, 100% were susceptible to any generation of cephalosporin except cephalexin which was 91% susceptible. Gentamicin was susceptible in only 77% of these cases. The authors recommended empirical treatment with a third generation cephalosporin or amikacin when suspecting bacteremia following prostate biopsy. Even if the ideal prophylaxis were known for high risk patients, administering IV or intramuscular antibiotics in an outpatient setting can be logistically challenging.

In the cases described above, another factor identified to be contributing to the severity of infection was the patients' resistance to seek immediate medical attention when their symptoms first appeared. All of our patients undergoing TRUS prostate biopsies are instructed to go immediately to the emergency department if they develop fever, chills, malaise, lower urinary tract symptoms or any other signs of infection. In case 1, the patient delayed medical attention approximately 36 hours after the onset of fever and malaise. By the time he presented he had altered level of consciousness and was in septic shock. In case 2, the patient had a sensation of "perineal fullness" and malaise approximately 30 hours after his biopsy, but he did not seek medical attention until he had fever and hypotension the next morning. Additionally, after initial resuscitation the patient elected to return home on oral antibiotics and wait for culture results. Based on this information, we hypothesize that healthcare workers, more specifically physicians, may delay seeking medical attention and put themselves at further risk.

Although rare, post-TRUS prostate biopsy infection with a MDR organism can be severe and potentially lethal. Healthcare workers are increasingly exposed to MDR organisms and at increased risk of colonization. It is important to identify healthcare workers, specifically those with previous fluoroquinolone exposure, before undergoing prostate biopsy although appropriate prophylaxis remains unclear. Further research into the value of preoperative culturing and appropriate antibiotic prophylaxis in healthcare workers and other high risk patients is warranted. It is imperative to inform all patients of the signs and symptoms of infection and the dangers of delaying medical attention when they occur. □

References

1. Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, Thun MJ. Cancer Statistics, 2009. *CA Cancer J Clin* 2009;59:225-249.
2. Raajimakers R, Kirkels WJ, Roobol MJ, Wildhagen MF, Schroder FH. Complication rates and risk factors of 5802 transrectal ultrasound-guided sextant biopsies of the prostate within a population-based program. *Urology* 2002;60(5):826-830.
3. Rodriguez L, Terris M. Risks and complications of transrectal ultrasound guided prostate needle biopsy: a prospective study and review of literature. *J Urol* 1998;160(6 Pt 1):2115-2120.
4. Enlund A, Varenhorst E. Morbidity of ultrasound-guided trans-rectal core biopsy of the prostate without prophylactic antibiotic therapy: a prospective study in 415 cases. *Br J Urol* 1997;79(5):777-780.
5. Kapoor DA, Klimberg IW, Malek GH, Wegenke JD, Cox CE, Patterson AL, Graham E, Echols RM, Whalen E, Kowalsky SF. Single-dose oral ciprofloxacin versus placebo for prophylaxis during transrectal prostate biopsy. *Urology* 1998;52(4):552-558.
6. Aron M, Rajeev TP, Gupta NP. Antibiotic prophylaxis for transrectal needle biopsy of the prostate: a randomized controlled study. *BJU Int* 2000;85(6):682-685.
7. Shandera K, Thibault G, Deshon G. Variability in patient preparation for prostate biopsy among American urologists. *Urology* 1998;52(4):644-646.
8. Miura T, Tanaka K, Shigemura K, Nakano Y, Takenaka A, Fujisawa M. Levofloxacin resistant *Escherichia coli* sepsis following an ultrasound-guided transrectal prostate biopsy: report of four cases and review of the literature. *Int J Urol* 2008;15(5):457-459.
9. Feliciano J, Teper E, Ferrandino M, Macchia RJ, Blank W, Grunberger I, Colon I. The incidence of fluoroquinolone resistant infections after prostate biopsy – are fluoroquinolones still effective prophylaxis? *J Urol* 2008;179(3):952-955.
10. Young J, Liss M, Szabo R. Sepsis due to fluoroquinolone-resistant *Escherichia coli* after transrectal ultrasound-guided prostate needle biopsy. *J Urol* 2008;74(2):332-338.
11. Kamdar C, Mooppan UM, Gulmi FA, Kim H. Multi-drug-resistant bacteremia after transrectal ultrasound guided prostate biopsies in hospital employees and their relatives. *J Urol* 2008;72(1):34-36.
12. Weber B, Saliken J, Jadavji T, Gray RR, Moore R. A near-fatal case of sepsis with an antibiotic-resistant organism complicating a routine transrectal prostate biopsy in a health care worker. *CUAJ* 2008;2(5):543-545.
13. Shigehara K, Uchibayashi T, Maeda E, Namiki M. Detection of drug-resistant Escherichia coli in patients with complicated cystitis: analysis of risk factors. *Int J Urol* 2009;16(10):808-812.
14. Lautenbach E, Metlay JP, Weiner MG, Biker WB, Tolomeo P, Mao X, Nachamkin I, Fishman NO. Gastrointestinal tract colonization with fluoroquinolone-resistant *Escherichia coli* in hospitalized patients: changes over time in risk factors for resistance. *Infect Control Hosp Epidemiol* 2009;30(1):18-24.
15. Jones R. Resistance patterns among nosocomial pathogens: trends over the past few years. *Chest* 2001;119(2 Suppl):397-404.
16. Solberg C. Spread of Staphylococcus aureus in hospitals: causes and prevention. *Scand J Infect Dis* 2000;32(6):587-595.
17. Yoshitsugu N, Miyabi I et al. Rectal swab cultures can assess for alternations in microbial flora; rectal colonization of fluoroquinolone resistant Escherichia coli among transrectal ultrasonography guided prostate biopsy patients. *J Urol* 2009; 181(4 Suppl):66.