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Infectious complications secondary to prostate biopsy

Abstract

Introduction: Prostate biopsy (PB) is a routine procedure performed by urologists in cases of suspected prostate cancer, any abnormality in the prostate-specific antigen (PSA) assay, and/or perceived by the digital rectal exam. Although this is a safe and rapid procedure, it is not without potentially serious complications, including infectious complications ranging from asymptomatic bacteriuria to acute prostatitis and even septic shock.

Materials and methods: This work reports the experience of the urology department of the Hassan II University Hospital of Fez in the study of post-biopsy prostatitis through the analysis of a retrospective series of 538 cases during the period January 2014 - December 2018.

Results: We report 11 cases of acute post-biopsy prostatitis diagnosed in the urology department of the Hassan II University Hospital in Fez. The bacteria most frequently involved in post-biopsy infections are gram-negative bacteria (Escherichia coli, Klebsiella pneumonia, Acinetobacter baumannii) although gram-positive cocci (Enterococcus faecalis and Staphylococcus saprophyticus) can also be responsible. Anaerobic bacteria are rarely found. The treatment of these post-biopsy infections is based on prolonged antibiotic therapy (3 to 6 weeks) using third-generation cephalosporins (Ceftriaxone). In our series, no death, septic shock, or prostatic abscess was found. The evolution was towards a good improvement under antibiotic treatment with discharge at home after 48 hours of apyrexia.

Conclusion: The study of infectious complications secondary to prostate biopsy makes it possible to determine the most appropriate empirical (therapeutic and prophylactic) regimens to minimize the risks. Because of the prevalence of infection by multi-resistant bacteria, particularly to quinolones, the biopsy must be performed following the rules of antibiotic prophylaxis.

Keywords: cancer, prostate, biopsy, complications, infectious

Volume 9 Issue 2 - 2021

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Received: July 14, 2021 | **Published:** August 05, 2021

Introduction

The incidence of prostate cancer is increasing worldwide at a rate of 2-3% each year.[1] In the United States of America, it is the most common type of cancer in men, with almost 250,000 new cases diagnosed each year.[2] The prostate biopsy is a daily practice of the urologist to establish the diagnosis of prostate cancer. This procedure consists of a series of multiple cores-samples taken, resulting in a true mapping of the prostate. Although there is no consensus on the ideal biopsy scheme for the diagnosis of prostate cancer,[3] the accepted standard scheme has been increased from sextant biopsies to 12-core systematic biopsies performed by transrectal or transperineal ultrasound guidance which is standar of care, but Imaging with multiparametric MRI is the most widely used way nowadays to increase the accuracy of biopsy, and has substantial evidence in the initial and the rebiopsy setting.[4] The indication for prostate biopsy is based on PSA levels and/or DRE characteristics and/or prostate imaging data.[5] Comorbidities, age, and therapeutic consequences must be taken into account before any procedure. Thus risk stratification is important to avoid unnecessary biopsies.[5] Although prostate biopsy is a safe, quick, and convenient procedure, it is not without potentially serious complications, notably infectious (acute prostatitis, prostate abscess, orchi- epididymitis, bacteremia) requiring medical or surgical management.[6] A single elevation of PSA should not lead to the immediate performance of a prostate biopsy; this level should be rechecked a few weeks later in the same laboratory under the same conditions of PSA sampling, i.e. at a distance from sexual intercourse, endoscopic manipulations, or episodes of urinary tract infection.[7] Antibiotic prophylaxis to lower the PSA level remains empirical and not currently indicated.[8] The overall morbidity reported is between 3 and 23%. Mortality is not zero but is exceptional[9] and is most often related to delayed or inappropriate management.[10] In the new era of multidrug-resistant to Escherichia coli, the aim of our study is to report the rate of infectious complications and the management from our center concerting TRUS prostate biopsy and to compare our practice and results to literature best practices.

Materials and methods

We report on a single-center cohort of 538 prostate biopsies performed in patients in the urology department of Hassan 2 University Hospital in Morocco during the period from January 2014 to December 2018. Our study included: patients who were candidates for prostate biopsy in the urology department at the University Hospital of Fez over 5 years from January 2014 to December 2018. Patients with a justified indication for biopsy: a PSA level above 4 ng/ml or an abnormal digital rectal examination. Patients with a contraindication to prostate biopsy (uncorrected coagulation abnormality, untreated urinary tract infection, etc.) were excluded from our study. Patients with an incomplete file. All patients took an antibiotic on the morning of the biopsy session. Rectal preparation with glycerine was done in all patients. Before the biopsy, the rectum was cleaned with povidone-iodine on a case-by-case basis if there was a suspicion of infectious risk or if previous urine culture results were available. The biopsies

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performed were all transrectal ultrasound-guided biopsies. All biopsies were performed using regional anesthesia. The 12-core systematic biopsy scheme was applied to all patients. In case of visualization of suspicious areas on trans rectal-ultrasound of the prostate, additional biopsies were performed in these areas. Data were collected through an exhaustive search of the medical records and pathology reports available in the archives of the Urology Department. The following data were collected retrospectively for analysis: age, history, urinary signs, prostate weight and consistency, PSA level, creatinine level, ECBU. Ultrasound was used to estimate prostate volume, prostate appearance, post-void residual (PVR), urinary bladder, impact. All complications of the prostate biopsy were noted.

Results

We exploited 538 records over five years from January 2014 to December 2018, 11 cases were included in our study.

General characteristics

The mean age of the patients was 69.66 years, with extremes ranging from 55 to 81 years. One out of 11 patients (9%) had a history of benign prostatic hypertrophy. Two patients (18%) had had a previous biopsy. One patient out of 11 (9%) had a history of transurethral resection of the prostate. Seven out of 11 patients (64%) had a history of smoking, diabetes, and hypertension (Figure 1).

Clinical and paraclinical signs

Urinary signs were the most frequent finding with 54.5%, followed by general signs of fever and chills with 45.5%. The average weight of the prostate at RT was 52.6 grams, with a predominance of weights between 40 and 49 grams (45.5%). The prostate was indurated in 6 cases (54.5%), soft in 3 cases (27.3%), nodular in 1 patient (9.1%), and firm in 1 patient (9.1%). Of our patients, 9 had a positive cytobacteriological urinalysis, the germ isolated was Escherichia coli in 5 cases, Klebsiella pneumoniae in 2, Staphylococcus aureus, and Enterococcus faecalis with 1 case each (Figure 2). All of these patients received a 3rd generation cephalosporin-based probabilistic antibiotic therapy until it was adapted to the results of the antibiogram. The rate of susceptible bacteria is 22.3% compared to resistant strains which represent 77.7% of cases, 14.3% for extended-spectrum beta-lactamases (ESBL), 28.6% for amino-penicillins, 42.8% for Quinolone, 14.3% for Cephalosporins. The mean creatinine level was 12.42 with extremes ranging from 5 to 23 mg/l. Renal-vesicoprostatic ultrasound was performed in 66% of our patients, depending on their septic state, within 24 hours of treatment.

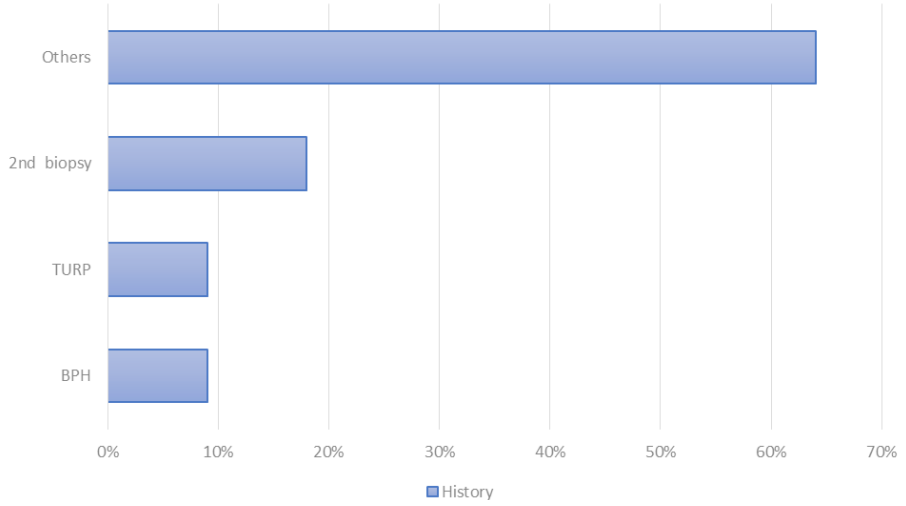

Figure 1 Different patient histories in the study population.

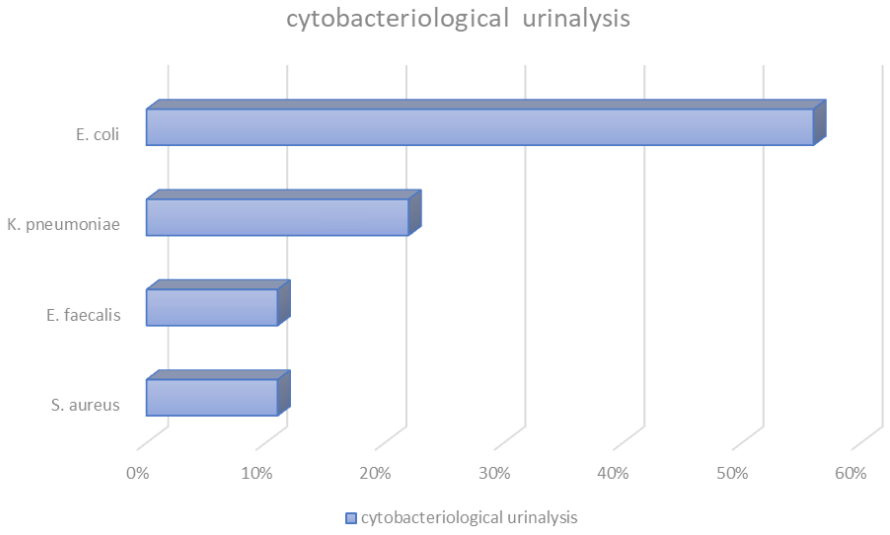

Figure 2 Isolated germs in cytobacteriological urinalysis.

Citation: Mohammed M, Dieudonné ZOJ, Ahsaini M, et al. Infectious complications secondary to prostate biopsy. *Urol Nephrol Open Access J.* 2021;9(2):47–51. DOI: 10.15406/unoaj.2021.09.00307

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Discussion

Infectious complications secondary to prostate biopsy may be limited to symptomatic urinary tract infection or low-grade febrile illness, treated with oral or intravenous antibiotics; however, post-biopsy sepsis has emerged as a risk of this procedure. The incidence of infectious complications after prostate biopsy in our study was 2%, which is in line with data from other multi-institutional studies where the incidence varies between 0.1% and 7%, depending on the prophylactic regime used.[11] In a recent study of 2184 biopsies from 1164 men. Infection was reported after 55 biopsies (2.5%), and one in five men reported any form of complication.[12] The risk of hospitalization due to infectious complications in contemporary studies varies from 0.6 to 4.1%.[12] The incidence of urinary tract infection after prostate biopsy is generally between 2% and 6%.[13] Bacteremia is sometimes accompanied by severe sepsis, which has an overall incidence of 0.1% to 2.2%.[14] Acute epididymitis is a frequent association to be routinely investigated. In addition, prostatic abscesses are rare and occur mainly in high-risk areas such as diabetes, immunodepression (human immunodeficiency virus [HIV], immunosuppressive treatments), and chronic hemodialysis.[12] In terms of repeat prostate biopsy, only 2 patients in our study had undergone a previous biopsy. Loeb et al. demonstrated that repeat biopsy was not associated with a higher risk of serious infectious or non-infectious urological complications compared to the initial biopsy.[12] In a prospective study comparing trans-perineal and routine transrectal prostate biopsy, Hara et al. found no difference in the rates of post-biopsy sepsis or fevers.[15,16]

Pathogens

Classification of microorganisms found in culture in the cytobacteriological examination of urine into four categories has been proposed by European researchers, according to their level of involvement in the etiology of infections.[17] A first group considered systematically pathogenic when isolated even in small microbial loads (10 CFU/ml): E. coli and Staphylococcus saprophyticus. A second group is more usually involved in nosocomial urinary tract infections when there are anatomical or iatrogenic factors that favor them: Proteus mirabilis, Klebsiella spp, Enterobacter spp, Morganella morganii, Pseudomonas aeruginosa, Enterococcus spp, and Staphylococcus aureus. A third group includes Gram-positive species (Streptococcus agalactiae, coagulase-negative staphylococci), and Gram-negative germs (Acinetobacter spp., Stenotrophomonas maltophilia) or Candida spp. Their involvement in pathology requires a level of bacteriuria/superior to 10-fold positivity and association/association with other criteria, clinical or inflammatory. A fourth group includes species considered as contaminants that usually belong to the urethral or genital flora of proximity: lactobacilli, alpha-hemolytic streptococci, Gardnerella vaginalis. Their isolation associated with the presence of urinary epithelial cells on direct examination of urine almost certainly indicates contamination during sampling. Only their isolation from a urine puncture using a suprapubic catheter could allow their pathogenic role to be evoked. Anaerobic germs are only rarely found.[17]

In our work, the germ most commonly implicated in infections secondary to prostate biopsy is E. coli, which is consistent with the literature.[18] E. coli has no natural resistance to antibiotics but acquired resistance has become a public health problem with the emergence of fluoroquinolone resistance, and the emergence of extended-spectrum beta-lactamase (ESBL) producing E. coli.[19] Fluoroquinolones, whose broad spectrum of activity covers the major part of enterobacteria, have the following properties: excellent bioavailability and tissue diffusion (particularly prostatic).[20] These characteristics make them a preferred family of antibiotics for the prevention of post-biopsy infections of the prostate,[21] unfortunately, the frequency of resistance is increasing,[19] and enterobacteria have become one of the most important causes of nosocomial and community infections. he data from our study are in line with the literature. A retrospective analysis of infectious complications in 538 prostate biopsies performed over 5 years revealed 11 complications (2%). The bacteriological analysis identified E. coli infection in 5 patients (56%). For two symptomatic patients (prostatitis), no germ could be isolated from the bacteriological samples taken.

Mode of transmission

The main mechanism of infection is probably direct inoculation of bacteria from the rectal mucosa through the biopsy needle into the prostate, blood vessels, or urinary tract. This is confirmed by high rates of bacteremia (16%-75%) and bacteriuria (36%-53%) immediately after the procedure in the absence of antibiotic prophylaxis, and the fact that most infections manifest clinically within 3 days of the prostate biopsy.[22]

Potential risk factors for biopsy infections

Recent studies on prostate biopsies have noted that there are specific risk factors for patients, namely the existence of comorbidities and a recent hospital stay.[14] In one study, it was observed that patients who had been hospitalized within 1 month before prostate biopsy[23] had a very high risk of developing severe infectious complications compared with patients who had no history of hospitalization (odds 8.63; 95% confidence interval [CI], 1.48-50.4; P = .02). A history of urological pathology would be an associated risk for the occurrence of post-biopsy infectious complications. Thus, patients with urethral catheters are at greater risk of complications after prostate biopsy than patients without catheters (19.2% versus 3.06%; P < 0.0001).[24] Previous biopsy history has not been definitively shown to increase the risk of post-biopsy infection. Although there is some evidence to suggest that the number of previous biopsies increases the risk of harboring fluoroquinolone-resistant organisms,[25] studies have shown that the rate of infection increases after the first diagnostic biopsy (2.3%), rising to 2.6% and 3.8% at the first and second biopsies, respectively, after which it decreases to 1.2% for three more repeat biopsies.[12] In terms of repeat prostate biopsy, only two patients in our study had had a previous biopsy and experienced infectious complications. However, repeat biopsy per se was not a risk factor, which was also the case in a large database study.[26]

Antibiotic prophylaxis

The learned societies have all indicated the benefit of pre-prostate biopsy antibiotic therapy. Quinolones are the prophylaxis of choice, with ciprofloxacin being superior to ofloxacin.[27] Three days of antibiotic therapy has not shown any greater benefit than a single dose of prophylaxis.[28] Increased resistance to quinolones is associated with an increase in severe post-biopsy infection.[26] Resistance to fluoroquinolones, on the other hand, is thought to be the cause of infectious complications. Factors leading to resistance include previous transrectal biopsies, indwelling urinary catheters, episodes of urogenital infection, and a history of foreign residence or hospitalization in the previous six months. Patients with these risk factors should receive targeted antibiotic therapy after culture and detection of the infectious germ during rectal swabbing.[29] Rectal disinfection with povidone-iodine may be recommended before any prostate biopsy.[29] However, a systematic review study [29] found no

Citation: Mohammed M, Dieudonné ZOJ, Ahsaini M, et al. Infectious complications secondary to prostate biopsy. *Urol Nephrol Open Access J.* 2021;9(2):47–51. DOI: 10.15406/unoaj.2021.09.00307

significant difference between Trans-perineal biopsies in terms of infectious risk compared to transrectal prostate biopsy but in contrast, a more recent meta-analysis comparing seven studies found twice the infectious risk in patients after Trans-perineal biopsies compared to transrectal biopsies with an RR of 0.26 (0.14-0.48).[30]

Clinical aspects

The clinical manifestations of post-biopsy infectious complications vary in nature and intensity depending on the terrain. Infectious complications are more serious, usually in the form of acute prostatitis. This is manifested by a febrile syndrome with a sudden onset: fever of 40°C, chills, headaches, myalgias; associated with urination symptoms: pollakiuria, burning, difficult or impossible urination. The micturition signs localise the urinary infection.[31] They can be very discreet and go unnoticed, with the disease being mistaken for influenza syndrome.

Para-spinal myalgia is often confused with renal pain and the diagnosis of pyelonephritis is wrongly made. The rectal examination is painful and reveals a warm, oedematous, sensitive prostate, but it may be normal.[11] Pelvic, perineal, urethral, penile, and sometimes rectal pain are also suggestive of acute prostatitis. A febrile urinary tract infection in men should be the first indication for a diagnosis of acute prostatitis. There may be a discharge of pus from the urethral meatus. The urine is cloudy and foul-smelling.[32]

Conclusion

Prostate biopsy is one of the most common urological procedures performed by urologists. It is a relatively safe procedure and the risk of severe complications is low, but the incidence of infectious complications has recently increased. Escherichia coli is the most common pathogen in post-biopsy infectious complications. Fluoroquinolones are the antibiotics used for prophylaxis. However, antibiotic resistance worldwide is increasing, and post-biopsy infectious complications from fluoroquinolone-resistant organisms are also increasing. Thus, the performance of prostate biopsy should follow recommendations regarding indications and techniques, although targeted antibiotic prophylaxis should be considered to decrease the risk of complications.

Statement of ethics

Subject has given their written consent to publish his case (including publication of images).

Funding sources

The authors have no funding sources to declare.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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