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Case Study

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CASE REPORT ON THE MANAGEMENT OF PROSTATIC ABSCESS CAUSED BY MULTI DRUG RESISTANT KLEBSIELLA PNEUMONIAE

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ABSTRACT

Prostatic abscess is a rare clinical entity among uropathological conditions. The diagnosis of prostatic abscess often remains difficult because of the similarity of its clinical manifestations with those of other lower urinary tract diseases. Depending on the severity of the condition, treatment options range from conservative therapy with antibiotics to surgical management. The emergence of antibiotic-resistant organisms complicates the treatment of prostatic abscess. In this case report, we are going to emphasise the management of prostatic abscesses caused by multidrug-resistant (MDR) Klebsiella pneumoniae.

KEYWORDS: Prostatic abscess, Klebsiella pneumonia, Multi Drug Resistance.

INTRODUCTION

Prostatic abscess is an infrequent condition, with an incidence of 0.5% to 2.5% of all prostatic diseases. In the modern era of antibiotics, the etiologic agent responsible for prostatic abscess is gram-negative bacteria, mainly Escherichia coli and Klebsiella pneumoniae. The risk factors contributing to the development of prostatic abscess include diabetes mellitus, immunocompromised conditions, urinary tract obstruction, indwelling catheters, etc. The diagnosis of prostatic abscess often remains difficult because of the similarity of its clinical manifestations with those of other lower urinary tract diseases. The diagnosis is made through physical examination (per rectal), specimen culture, and imaging studies. Treatment with antibiotics and surgical management are the treatment options available. The emergence of resistant organisms complicates treatment of prostatic abscesses and leads to additional complications, increasing morbidity and mortality rates.

CASE REPORT

A 69-year-old male patient with comorbidities including Type 2 diabetes mellitus, systemic hypertension, benign prostatic hypertrophy, and an old cerebrovascular accident (left hemiparesis) came to General Medicine OPD for the review of a prostatic abscess, where the etiologic agent was multidrug-resistant Klebsiella pneumoniae.

Three months ago the patient underwent a surgical procedure (proximal femoral nail in left hip) for an intertrochanteric fracture and was on Foley's catheter. A few days later, the patient presented with generalised tiredness, high-coloured urine associated with pus discharge, dribbling of urine, and decreased memory. Initial investigations revealed elevated CRP, urea, and creatinine, and the PSA value was 1.7ng/L. A routine urine test detected 45–50 micrograms of pus. Urine culture reported growth of MDR Escherichia coli and was treated with injectable piperacillin-tazobactam. Ultrasonography of the abdomen was suggestive of cholelithiasis, bilateral mildly increased renal cortical echogenicity, and prostatomegaly. Patient then developed pus discharge from the penile urethra, scrotal swelling and lower abdominal pain. A USG scrotum was done, which was suggestive of right epididymo-orchitis with funiculitis and right-sided pyocele, left epididymitis with funiculitis, an inguino-scrotal hernia, and bilateral grade II varicocele. Urine culture detected MDR Klebsiella pneumoniae. The isolated strain was sensitive to fosfomycin. Fosfomycin 3g 3 doses 3 days apart given. Pus discharge continued. Pus culture detected MDR Klebsiella pneumoniae, and the OXA-48 enzyme was detected through a rapid test for carbapenemase. The isolated strain was sensitive to Tigecycline for which Injection Tigecycline 50mg was initiated after administration of loading dose. Laboratory investigations came back within the normal range, the patient became symptomatically better, and he was discharged.

The patient was readmitted with pus discharge. Routine laboratory investigations revealed elevated total counts, CRP, and creatinine. Klebsiella pneumoniae was discovered in urine culture. The patient received Injection Ceftazidime-Avibactam. MDR Klebsiella pneumoniae grew in pus cultures. Per rectal examination revealed cystic swelling over the right lobe of the prostate. The USG KUB (Ultra Sonography Kidney Ureter Bladder) findings were suggestive of a prostatic abscess. Transurethral resection of the prostatic abscess (TURP) with abscess drainage was recommended by the Urology department but denied from the patient side. Hence, conservative management with antibiotics was provided. The patient was discharged with Ceftazidime-Avibactam for three weeks.

After a month, the patient was readmitted with similar complaints indicating recurrence which could be due to the highly resistant strain of Klebsiella pneumoniae or to non-adherence to medications caused by some patient-related factors. Pus culture revealed recurrent growth of MDR Klebsiella pneumonia, and its sensitivity report is depicted in Table 1. A carbapenem antibiotic combination of Injection Imipenem and Cilastatin was given as it had shown sensitivity to an isolated strain of multidrug-resistant Klebsiella pneumoniae. It also attains significant concentrations in the tissues of reproductive organs. With this course of antibiotics the patient became symptomatically better.

Table 1: Sensitivity report of MDR Klebsiella pneumonia.

Antibiotic	Sensitivity
Amikacin	Resistant
Amoxyclav	Resistant
Cefepime	Resistant
Cefotaxime	Resistant
Cefuroxime	Resistant
Ciprofloxacin	Resistant
Cotrimoxazole	Resistant
Gentamicin	Resistant
Imipenem	Sensitive
Levofloxacin	Resistant
Meropenem	Sensitive

DISCUSSION

Prostatic abscess is a pathophysiological condition of the genitourinary system that is infrequent, with an incidence of 0.5% to 2.5% of all prostatic diseases, and is characterised by the accumulation of purulent fluid in the prostate gland. The incidence of prostatic abscess has markedly decreased in the modern era. With the widespread use of antibiotics the etiologic agent responsible for the development of prostatic abscess was changed. Formerly, it was caused by Neisseria gonorrhoeae, but now the etiologic agent has varied to other gram-negative bacteria, mainly Escherichia coli and Klebsiella pneumoniae. The mean age at diagnosis is between the fifth and sixth decades of life. The risk factors contributing to the development of prostatic abscess include diabetes mellitus, immunocompromised conditions, urinary tract obstruction, indwelling catheters, etc.[1-2] The majority of severe infections are caused by the reflux of infected urinary contents into the prostatic ducts. Since the clinical manifestations of prostatic abscess resemble those of lower urinary tract diseases, the diagnosis of prostatic abscess often remains difficult.[3] Usual symptoms include dysuria, acute urinary retention, perineal pain, and rectal tenesmus.[4] Physical examination (per rectal), specimen culture, and imaging are used to make the diagnosis. Culture reports are essential for the identification of etiological agents. Pus culture is recommended since the urine culture may be negative or the pathogen found in the urine culture may be different from that found in the pus culture. The urine culture report remains negative unless the abscess opens into the urethra or bladder.[3,5] Transrectal ultrasound screening (TRUS) remains one of the most widely used techniques for diagnosis and is also useful for aspiration and drainage. The treatment options for prostatic abscess comprise both conservative management with antibiotics and also surgical management (aspiration and drainage). The latter includes transperineal aspiration, transurethral resection of the prostatic abscess (TURP), transurethral deroofing of the prostate (TUD), and transrectal ultrasound guided needle aspiration (TRUS GA).[1] A surgical approach was selected either based on the severity of the condition or due to the failure of conservative management. The possible complications associated with surgical management include transient stress urinary incontinence, impotence due to nerve damage, retrograde ejaculation, systemic spread of organisms, and septic shock. Timely diagnosis and adequate management improve the prognosis.

Antibiotic resistance is a concerning global issue. By 2050, it is estimated that global antimicrobial resistance will have led to approximately 10 million deaths worldwide and may become another pandemic. Widespread gram-negative uropathogen resistance is also reported worldwide.[6] Multidrug-resistant (MDR) bacteria acquire nonsusceptibility to at least one antibiotic in three or more classes. It is one of the important problems that need to be addressed due to the difficulty in treating MDR microorganisms and the exponential increase in such cases.

Several **mechanisms** are involved in the development of gram-negative bacterial resistance. Some of them are: Carbapenemase production, which commonly occurs as a result of the production of KPC type (Klebsiella pneumoniae Carbapenemase), NDM type (New Delhi Metallo beta lactamase), and OXA-48 type enzymes (a class D carbapenemase according to Ambler classification); Mutation of the interacting site, Active antibiotic export via efflux pump mechanisms, Biofilm formation, etc.[7]

A prostatic abscess relapse case was discussed in this report. Initially, the patient had presented with a urinary tract infection approximately three months ago and was later diagnosed with a prostatic abscess.

Fosfomycin, a phosphoenolpyruvate analogue with bactericidal activity, was prescribed (3g 3 doses 3 days apart). It has excellent activity against various bacteria, including MDR gram-negative microorganisms. It acts irreversibly by inhibiting the cell wall synthesis, thereby blocking the first step involved in the synthesis of uridine diphosphate N-acetylglucosamine (UDP-GlcNAc) enolpyruvyl transferase. It shows significant activity against gram-negative bacteria. Resistance may develop when mutations occur to the chromosomal gene involved in the uptake system mediating the entry of fosfomycin into the bacteria.[8]

Later pus cultures revealed MDR Klebsiella pneumoniae growth, and OXA-48 was identified through a rapid test for carbapenamase. For the same reason, the patient was administered **Tigecycline**. Tigecycline is a glycylcyline antimicrobial agent. It binds to the bacterial 30S ribosome, thereby preventing protein synthesis and bacterial growth. It has shown a bacteriostatic effect against Klebsiella pneumoniae. The molecular mechanisms involved in Tigecycline resistance include upregulation of resistance nodulation division efflux pumps and structural alteration of the 30S ribosomal subunit protein S10 resulting in target site modifications.[9]

Later, the patient was readmitted with complaints of pus discharge. The TRUS done was suggestive of a prostatic abscess. The culture of the pus reported the growth of MDR Klebsiella pneumoniae, for which **Ceftazidime-Avibactam** was given, which is a combination of the antipseudomonal cephalosporin and the novel beta-lactamase inhibitor. The resistance mechanism of Klebsiella pneumoniae includes the production of carbapenamases. Avibactam has the potential to inhibit Ambler class A and class D carbapenamases and restore the antibacterial activity of ceftazidime. The ceftazidime/avibactam combination is considered a preferred treatment option for MDR gram-negative bacteria.[10,11] The patient was discharged with instructions to continue the antibiotic course for three weeks.

After a month, the patient was readmitted with similar complaints, indicating recurrence, which could be due to the highly resistant strain of Klebsiella pneumoniae or to non-adherence to medications caused by some patient-related factors. A carbapenem antibiotic combination of **Imipenem and Cilastatin** was provided. It has shown sensitivity to an isolated strain of multidrug-resistant Klebsiella pneumoniae. Imipenem inhibits bacterial cell wall synthesis, and cilastatin prevents the renal inactivation of imipenem by dehydropeptidase. Imipenem also displays potent activity against biofilms, which can be formed by clinical isolates of Klebsiella pneumoniae. It also attains significant concentrations in the tissues of reproductive organs.[12] With the course of antibiotics, the patient improved symptomatically and was thus discharged.

Table 2: Antibiotics and their penetration into the prostate.[13]

Antibiotics	Penetration
Norfloxacin	Good
Ciprofloxacin	Good
Levofloxcin	Good
Penicillin	Poor
Nitrofurantoin	Intermediate
Gentamicin	Poor
Trimethoprim-Sulfamethoxazole	Good
Tetracycline	Good
Imipenem	Good

Due to the lack of proper guidelines for the management of prostatic abscess, treatment regimens may vary and depend on the empirical therapy and the sensitivity of the isolated pathogen.[14] Early diagnosis is important for a better prognosis. Based on the severity of the condition, treatment options include conservative management with antibiotics and surgical management. Empiric therapy should cover mainly gram-negative organisms.[15] Antibiotics and their penetration into the prostate is depicted in Table 2. The first-line agents include levofloxacin and beta-lactam antibiotics for a course of two to four weeks for complete resolution. Serial monitoring is required to confirm the same. In the scenario of emerging resistant organisms, the management becomes complicated and involves the use of third-generation cephalosporins, aztreonam, carbapenem, trimethoprim-sulfamethoxazole, fluoroquinolone antibiotics, etc. In an environment of increasing resistance among gram-negative bacteria, the above-mentioned antibiotics have been positioned as an option in treating infections by these bacterial strain due to their susceptibility to these antibiotics, their pharmacokinetic properties, and their activity against biofilms.[16]

In this case, the multidrug-resistant Klebsiella pneumoniae was successfully treated in a stepwise manner with appropriate antibiotics, resulting in a better prognosis.

CONCLUSION

Prostatic abscess is an uncommon urological condition characterised by the accumulation of pus within the prostate gland. With the advent of antibiotics in the modern era, the incidence rate has reduced, and the etiologic agent has changed from Neisseria gonorrhoea to Escherichia coli and Klebsiella pneumonia. Treatment with antibiotics and surgical management are the treatment options. Empirical therapy with antibiotics should target mainly gram-negative organisms. The emergence of resistant organisms further complicates the

condition, resulting in increased morbidity and mortality. Meticulous diagnosis and early and adequate management of the prostatic abscess will result in a better prognosis.

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ABBREVIATIONS
MDR – Multi Drug Resistant
OPD – Out Patient Department
USG – Ultra Sonography Kidney Ureter Bladder
TURP - Transurethral resection of the prostatic abscess
TRUS - Transrectal ultrasound screening
TUD - Transurethral deroofing of the prostate
TRUS GA - Transrectal ultrasound guided needle aspiration

CONFLICT OF INTEREST
The authors declared that there is no conflict of interest.

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