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Chronic Bacterial Prostatitis due to *Staphylococcus haemolyticus*; Case Report

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ABSTRACT

Prostatitis causes up to 25% of male genitourinary complaint. However, due to technical restrictions in sampling, only in 10% of cases pathogens were identified. In this paper, a patient with chronic prostatitis due to *Staphylococcus haemolyticus* described. A 48-year-old man was referred with longstanding (approximately for 18 months) complaint of increased genitourinary symptoms and pain in perineum. In evaluation, moderate growth of methicillin-resistant *Staphylococcus haemolyticus* (MRSH) in post-prostatic massage voided urine and expressed prostatic secretion (EPS) was positive. Culture of urethral urine (urine or voided bladder 1; VB1), midstream urine (VB2) and post-ejaculation urine specimens were negative. Leukocyte count values in EPS and post-prostatic massage voided urine were 14 and 8 per oil immersion field respectively. PCR of urine samples was positive for *Ureaplasma urealyticum* and confirmed by repeated analysis. Based on the antimicrobial susceptibility results patient was treated with teicoplanin 400 mg intramuscularly every 12 hours for three doses followed by the daily maintenance dose of 400 mg. In addition, doxycycline 100 mg twice daily was added to cover *Ureaplasma urealyticum*. Treatment course completed in 6 weeks. Alleviation of patient's symptoms begun within the first week of treatment and this trend continued until the end of the treatment.

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Introduction

Chronic bacterial prostatitis (CBP) is defined as a long-standing (≥3 months) refractory or relapsing and remitting prostatic symptoms with proven or suspected bacterial infection. It usually presents with pain, uncomfortable feeling in genitourinary tract and may rarely accompany with systemic symptoms and sexual dysfunction (1).

Prostatitis causes up to 25% of male genitourinary complaint. However, due to technical restrictions in sampling, only in 10% of cases pathogens were identified (1, 2).

Predisposing factors for developing CBP are not clearly defined, but previous history of acute bacterial prostatitis, diabetes, smoking, presence of prostate stones, manipulation of urinary tract, and urethral anatomical abnormality may be involved (3, 4).

The gram-negative bacilli still are the most common pathogens in CBP, although the prevalence of gram-positive organisms including *Staphylococcus* and *Streptococcus* species is increasing. Coagulase negative *staphylococcus* species were occasionally reported as involved microorganisms in CBP (5, 6). In this paper, a patient with chronic prostatitis due to

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Table 1. Laboratory data of the patient.

Parameter		At admission	3 months later	6 months later
WBC (%N)		6310 (46)	6280 (49)	4550 (45)
ESR (mm/h)		10	8	8
CRP (mg/dL)		0.06	0.21	0.15
T PSA (ng/mL)		2.76	-	-
F PSA (ng/mL)		0.7	-	-
F PSA/PSA (%)		25	-	-
UA	Appearance	Clear	Clear	Clear
	Nitrite	Negative	Negative	Negative
	Leukocyte	1-2	1-2	1-2
	RBC	0-1	1-2	0-1
	Bacteria	Negative	Negative	Negative
	Yeast	Negative	Negative	Negative
Clinical data				
Fever		Negative	Negative	Negative
Dribbling		Strongly Positive	Positive	Negative
Dysuria and urgency		Positive	Negative	Negative
Perineal pain		Strongly Positive	Negative	Negative
Urinary frequency		Strongly Positive	Positive	Weakly Positive

CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, T PSA: Total Prostate-specific antigen, F PSA: Free Prostate-specific antigen, RBC: red blood cells, UA: Urine analysis, WBC: White blood cells.

Staphylococcus haemolyticus described.

Case presentation

A 48-year-old man was referred to infectious diseases clinic of Imam Khomeini hospital, Tehran, Iran with longstanding (approximately for 18 months) complaint of increased genitourinary symptoms (hesitancy, dribbling, slow and narrow stream, dysuria and urgency) and pain in perineum. He did not note any special habit (smoking, alcohol drinking, or substance abuse). He was a healthy person without any baseline disease including diabetes mellitus. In his past medical history surgical procedure and manipulation of genitourinary tract were negative. Also he was sexually active but did not remember any symptom of urinary tract up to current complaints.

In his past drug history, he was treated with ciprofloxacin 500 mg twice daily and tamsulosin 0.4 mg daily for 8 weeks with suspicion of acute bacterial prostatitis following an outpatient visit about 18 months ago. The patient described wax and wane pattern for his symptoms after this treatment course.

At the clinic visit, a comprehensive work-up including physical examination, urine analysis (UA), CBC with differential, ESR, CRP, viral markers (HBV, HCV, HIV), 4-glass test, prostate specific antigen (PSA), polymerase chain reaction (PCR) of secretions were requested (Table1). Hypertrophic and tender prostate tissue was detected in digital rectal examination (DRE) in the absence of any palpable mass or nodule. These findings were confirmed in ultrasonography. In the laboratory tests, UA, serum PSA level, CBC, ESR and CRP were in the normal ranges. Also all common viral markers were negative. However, moderate growth of methicillin-resistant *Staphylococcus haemolyticus* (MRSH) in post-prostatic massage voided urine and expressed prostatic secretion (EPS) was positive. Culture of urethral urine (the first 10 ml urine or voided bladder 1; VB1), mid-stream urine (10 ml of urine after voiding 150ml; VB2) and post-ejaculation urine (collected immediately after ejaculation; VB3) specimens were negative. Leukocyte count values in EPS and post-prostatic massage voided urine were 14 and 8 per oil immersion field respectively (Table 2). PCR

Table 2. Results of the samples analysis and culture.

Item	Before treatment		After Treatment	
	Leukocyte count	Microbial culture (enriched media)	Leukocyte count	Microbial culture (enriched media)
VB1	2-3	No growth	2	No growth
VB2	1	No growth	1-2	No growth
VB3	8	moderate growth of MRSH	3	No growth
EPS	14	moderate growth of MRSH	5	No growth

EPS: expressed prostatic secretion, VB: voided bladder.

of urine samples was positive for *Ureaplasma urealyticum* and confirmed by repeated analysis (Table 3).

Based on the antimicrobial susceptibility results (Table 4) and with regard to patient preference to continue treatment at home, he was treated with teicoplanin 400 mg intramuscularly every 12 hours for three doses followed by the daily maintenance dose of 400 mg. Teicoplanin was discontinued after one week because of low patient compliance with intramuscular injections. Treatment was replaced by minocycline 100 mg twice daily which resulted in intolerable dizziness and vertigo after 4 days. Minocycline was replaced with rifampin 300 mg twice daily. In addition, doxycycline 100 mg twice daily was added to cover *Ureaplasma urealyticum*. Treatment course completed in 6 weeks. Alleviation of patient's symptoms begun within the first week of treatment and this trend continued until the end of the treatment. In next visit, repeated PCR and cultures were negative after 6 weeks. Moreover leukocyte count in EPS and VB3 samples decreased to 5 and 3 per oil immersion field. Patient was followed for 6 months and he was symptoms free.

Discussion

Approximately 25% of men experience chronic prostatitis symptoms in their lives (1). Considering duration of the symptoms and no evidence of acute infection, CBP was considered for the patient. There were no evidences of malignancy such as mass and nodules in the digital rectal examination. Treatment failure with conventional therapy is increasing due to change in the epidemiology of causative pathogens and bacterial resistance. Although fluoroquinolones are still preferred antibiotics for treatment of CBP (7, 8), the patient did not respond to 8 weeks of treatment with ciprofloxacin. Common causes of treatment failure including patient's compliance and drug-drug and food-drug interactions

Table 3. Results of urine and serum PCR.

Pathogen	Result
HSV 1&2	Negative
HPV6	Positive
HPV11	Negative
Neisseria gonorrhea	Negative
Treponemapallidum	Negative
Chlamydia trachomatis	Negative
Ureaplasmurealyticum	Positive
Ureaplasmaparvum	Negative
Mycoplasma hominis	Negative
Mycoplasma genitalium	Negative
Trichomonasvaginalis	Negative

HSV: herpes simplex virus, HPV: Human papillomavirus.

Table 4. Antimicrobial susceptibility pattern of isolated *Staphylococcus hemolyticus* (Standard Disk Diffusion Method, CLSI 2015).

Susceptible	Minocyclin,Nitrofurantoin,Rifampin
Resistant	Cefoxetin/Oxacilllin, Penicillin, Ceftriaxone, Azithromycin, Ofloxacin, Ciprofloxacin, Levofloxacin, Doxycyclin, Tetracycline, Co-Trimoxazole

were evaluated and ruled out by a clinical pharmacist. Therefore, the possibility of infection with a less-common isolate was suspected.

Approximately 47 species of *Staphylococcus* have been identified. Although *Staphylococcus haemolyticus* was less isolated previously (9), its frequency is increasing now (10). A great clinical challenge about this microorganism is differentiating contamination from true infection. The patient was educated about sampling procedures and the samples were collected under supervision of a pathologist. Moreover, microorganism was isolated from the EPS and VB3. Therefore, contamination seems unlikely. Moreover, the results of urine PCR revealed *Ureaplasm urealyticum* as a contributing microorganism.

Biofilm formation by *Staphylococcus haemolyticus* has an important role in the virulence and resistance to conventional antibiotic therapy. In addition to antimicrobial susceptibility, permeability of antibiotics into infected prostate tissue should be taken into account in selection of appropriate treatment regimen (1, 6). An antibiotic with high lipid solubility, low protein binding, low degree of ionization, high dissociation constant (pKa), high serum concentration, and low molecular weight is considered as an agent with sufficient penetration to prostate tissue (11). Treatment of MRSA prostatic abscess was promising with vancomycin (12-18). Wang et al., showed that administration of vancomycin in the tail vein of the rats led to prostatic concentrations that were equal to or greater than that of the serum. Additionally, improvement in pathology of prostate and bacterial burden reduction were remarkable (19).We did not find any published clinical study on administration of teicoplanin in CBP and penetration of teicoplanin in to prostate tissue remains unknown. Considering similar structure of vancomycin and teicoplanin, similar penetration would be anticipated for teicoplanin. Improvement of patient's symptoms in the first week of treatment supported this theory.

Considering the patient's noncompliance with teicoplanin injections, alternative options were explored. With respect to antimicrobial susceptibility results, the isolated *Staphylococcus haemolyticus* was resistant to tetracycline and doxycycline, but susceptible to minocycline. According to Performance Standards for Antimicrobial Susceptibility Testing by Clinical and Laboratory Standards Institute (CLSI), there is no cross-resistance among tetracycline in *Staphylococcus spp.* (20) which justifies susceptibility to minocycline despite resistance to doxycycline and tetracycline. Minocycline and doxycycline reached to at least 40% of their serum concentrations in prostate tissue (1). Since minocycline is active against both isolated microorganisms, it was initiated for the patient. After developing intolerable dizziness with this agent, treatment course was continued with the combination of doxycycline and rifampin to cover *Ureaplasma* and *Staphylococcus,* respectively. Successful treatments of prostatitis with rifampin were reported in previous studies (21, 22) which indicates sufficient prostatic penetration.

In conclusion, resolution of patient's symptoms within the first week of treatment with teicoplanin, implies its acceptable prostatic penetration. Besides suitable penetration, ease of teicoplanin administration in outpatient setting and satisfactory antimicrobial activity against methicillin-resistant *Staphylococcus,* make it a reasonable option in treatment of CBP caused by this microorganism.

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