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The role of unusual pathogens in prostatitis syndrome

Visnja Skerk [a,*], Ivan Krhen [b], Slavko Schonwald [a], Vjeran Cajic, Leo Markovinovic [a], Srdan Roglic [a], Sime Zekan [a], Arjana Tambic Andracevic [a], Vladimira Kruzic [c]

[a] *University Hospital for Infectious Diseases, Dr Fran Mihaljevic, Mirogojska 8, 10000 Zagreb, Croatia*
[b] *Clinic for Urology, Clinical Hospital Centre Rebro, Zagreb, Croatia*
[c] *Croatian Institute of Public Health, Zagreb, Croatia*

Abstract

A total of 1442 patients with symptoms of chronic prostatitis were examined over a 4-year period at the Outpatient Department for Urogenital Infections, University Hospital for Infectious Diseases "Dr. Fran Mihaljevic", Zagreb, Croatia. An infectious aetiology was determined in 1070 (74.2%) patients. In 561 of 1070 (52.4%) patients the inflammatory finding (>10 WBC/hpf) was found in expressed prostatic secretions (EPS) or voided bladder urine (VB_3). Normal, <10 WBCs/hpf was found in 362 of 536 (67.5%) patients with symptoms of chronic prostatitis in whom *Chlamydia trachomatis* was detected in EPS or VB_3, in 51 of 151 (33.8%) patients with isolated *Trichomonas vaginalis* and in 40 of 72 (55.6%) patients with isolated *Ureaplasma urealyticum*.

Escherichia coli was the causative pathogen in 95, *Enterococcus* in 68, *Proteus mirabilis* in 37, *Klebsiella pneumoniae* in 16, *Streptococcus agalactiae* in 19, and *Pseudomonas aeruginosa* in 3 patients with chronic prostatitis. Other patients had a mixed infection. In patients with chronic bacterial prostatitis (CBP) caused by *E. coli*, *P. mirabilis*, *K. pneumoniae*, *E.* or *S. agalactiae*, an inflammatory finding was regularly found in EPS or VB_3.
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1. Introduction

Prostatitis is a disease entity diagnosed by clinical symptoms and signs, the microscopy of expressed prostatic secretion (EPS), and the culture of EPS and segmented samples [1], according to Meares and Stamey [2]. What was previously denoted prostatitis is today more frequently referred to as prostatitis syndrome. The term prostatitis syndrome refers to a number of conditions affecting the prostate and clinically manifests with urethral symptoms, prostatic symptoms, sexual dysfunction and other symptoms [1]. According to the duration of symptoms, prostatitis is described as either acute or where symptoms are present for at least 3 months, chronic [1].

The classification of prostatitis according to Drach et al. [3] differentiates between the following:

(1) *Acute bacterial prostatitis* (ABP): clinically significant infection of the prostate with acute symptoms;
(2) *Chronic bacterial prostatitis* (CBP): significant inflammation of the prostate, isolation of an aetiologically recognised organism from the prostatic fluid/urine;
(3) *Chronic abacterial prostatitis*: significant prostatic inflammation, failure to isolate an organism from the prostatic fluid/urine;
(4) *Prostatodynia*: no significant prostatic inflammation, failure to isolate an organism from the prostatic fluid/urine.

Classification of prostatitis according to the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institute of Health [4] differentiates between:

(1) acute bacterial prostatitis;
(2) chronic bacterial prostatitis;
(3) chronic pelvic pain syndrome (CPPS), inflammatory CPPS, white blood cells in semen (EPS), voided bladder urine—3 (VB_3), non-inflammatory CPPS, no white cells in semen (EPSs) (VB_3);
(4) asymptomatic inflammatory prostatitis.

* Corresponding author. Tel.: +385-1-46-03-222; fax: +385-1-46-78-244.
E-mail address: infektivna.klinika@bfm.hr (V. Skerk).

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The aim of this prospective study was to investigate the aetiology and the role of unusual pathogens in chronic prostatitis syndrome-chronic bacterial prostatitis, and inflammatory as well as non-inflammatory chronic pelvic pain syndrome.

2. Patients and methods

The study was conducted at the Outpatient Department for Urogenital Infections, University Hospital for Infectious Diseases "Dr. Fran Mihaljevic", Zagreb, Croatia, between 1 March 1999 and 28 February 2003.

2.1. Patients

We examined a total of 1442 patients over 18 years of age with symptoms of chronic prostatitis and no evidence of structural or functional lower genitourinary tract abnormalities.

The inclusion criterion for chronic prostatitis is the duration of symptoms for at least 3 months.

The inclusion criteria for CBP was as follows:

- a bacterial count of 10^3 cfu/ml or more (if only Gram-positive cocci are found in EPS, a bacterial count of 10^4 cfu/ml or more is required), and 10 or more WBC/hpf (including macrophages) in EPS or VB_3,
- finding of ten or many times greater number of bacteria in EPS and urine bladder sample collected immediately after prostatic massage, than in first voided urine or midstream urine.

The inclusion criteria for chronic prostatitis caused by *Chlamydia trachomatis* was the presence of *C. trachomatis* in EPS or VB_3, absence of *T. trachomatis* in urethral swabs and absence of other possible pathogens of chronic prostatitis in EPS or VB_3.

The inclusion criteria for chronic prostatitis caused by *Ureaplasma urealyticum* or *Mycoplasma hominis* was the presence of *U. urealyticum* or *M. hominis* in EPS or VB_3, absence of *U. urealyticum* or *M. hominis* in urethral swabs and absence of other possible pathogens of chronic prostatitis in EPS or VB_3.

The inclusion criteria for nonbacterial prostatitis or inflammatory chronic pelvic pain syndrome was the presence of ten or more WBC/hpf in EPS or VB_3, the presence of *Trichomonas vaginalis* or other possible nonbacterial pathogens in EPS or VB_3.

The inclusion criteria for chronic prostatitis caused by *T. vaginalis* was the presence of *T. vaginalis* in EPS or VB_3, absence of *T. vaginalis* in urethral swabs and the absence of other possible pathogens of chronic prostatitis in EPS or VB_3.

The inclusion criteria for non-inflammatory chronic pelvic pain syndrome was the presence of clinical symptoms of prostatitis syndrome and no white cells in EPS or VB_3.

2.2. Methods

The following data were obtained for each patient: clinical history, clinical status including digitorectal examination, urethral swab specimens, selective samples of urine and EPS, according to the 4-glass localisation test (Meares and Stamey localization technique).

Urethral swab specimens were analysed for *C. trachomatis*, *T. vaginalis*, *U. urealyticum* and *M. hominis*.

In segmented samples of urine (VB_1, VB_2, VB_3) and EPS we determined the number of leukocytes and Gram-positive and Gram-negative bacteria in 1 ml sample. EPS and urine sample collected immediately after prostatic massage were examined for the presence of *C. trachomatis*, *U. urealyticum*, *M. hominis* and *T. vaginalis*.

Quantitative segmented cultures and bacterial identification in three voided urine samples and EPS were performed at the Clinical Microbiology Laboratory of the University Hospital for Infectious Diseases "Dr. Fran Mihaljevic", Zagreb by using standard microbiological methods.

Table 1
Aetiology of chronic prostatitis

Microorganism confirmed in EPS or VB_3	Patients		
	> 10 WBCs/hpf in EPS (no.)	< 10 WBCs/hpf in EPS (no.)	Total no. (%)
Chlamydia trachomatis	174	362	536 (37.2)
Trichomonas vaginalis	100	51	151 (10.5)
Ureaplasma urealyticum	32	40	72 (5.0)
Escherichia coli	90	5	95 (6.6)
Enterococcus	52	16	68 (4.7)
Proteus mirabilis	35	2	37 (2.6)
Klebsiella pneumoniae	14	2	16 (1.1)
Streptococcus agalactiae	12	7	19 (1.3)
Pseudomonas aeruginosa	2	1	3 (0.2)
Mixed infection	50	23	73 (5.1)
None	91	281	372 (25.8)
Total	652	770	1442 (100.0)

EPS: expressed prostatic secretion; VB_3: post-prostatic-massage urine.

Table 2
Age of patients with chronic prostatitis syndrome

Age (years)	Patients infected with									
	CT	TV	UU	EC	PM; KP	E	BHS-B; P. aer	Mixed infection	Undetermined	All
18–19	5	2	1	0	–	0	0	5	5	7
20–29	107	45	15	15	2	14	2	21	25	110
30–39	202	52	22	17	6	35	6	13	38	167
40–49	85	21	17	26	5	9	6	15	69	105
50–59	96	16	15	19	14	8	5	9	70	90
60–69	31	12	1	7	15	2	–	8	62	36
>70	10	3	1	11	11	0	–	2	103	21
Total	536	151	72	95	53	68	19	73	372	1442

CT: *C. trachomatis*; TV: *T. vaginalis*; UU: *U. urealyticum*; EC: *E. coli*; PM: *P. mirabilis*; KP: *K. pneumoniae*; E: *Enterococci*; BHS-B: *S. agalactiae*; P. aer: *P. aeruginosa*.

The diagnosis of urogenital mycoplasma was confirmed by semiquantitative culturing and antimicrobial susceptibility test Mycoplasma duo 62740 Sanofi, Diagnostic Pasteur. The diagnosis of *T. vaginalis* was confirmed by culturing on DIAMOND modified medium.

C. trachomatis was examined in EPS/urine sample collected immediately after prostatic massage by using McCoy cells and Lugol stain or by using DNA/RNA DIGENE hybridisation method.

Urethral swab specimens were analysed by using McCoy cells and Lugol stain for the detection of *C. trachomatis*.

The isolation of *C. trachomatis* was performed at the Croatian Institute for Public Health, Zagreb, Croatia. Laboratory testing for viruses or fungus was not performed.

3. Results

Of 1442 patients with symptoms of chronic prostatitis, 652 had 10 or more WBCs/hpf, including macrophages, in EPS or in voided bladder collected immediately after prostatic massage. An infectious aetiology was determined in 1070 (74.2%) patients. *C. trachomatis*, *T. vaginalis* and *U urealyticum* were the causative pathogens in half of our patients with chronic prostatitis syndrome (Table 1).

In patients with chronic bacterial prostatitis caused by *Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae, Enterococcus or Streptococcus agalactiae*, inflammatory finding was regularly found in EPS or VB_3. Patients with symptoms of chronic prostatitis syndrome, in whom *C. trachomatis*, *U. urealyticum* or *T*. vaginalis were detected as the only possible pathogens of prostatitis, often had normal WBC_s/hpf findings in EPS or VB_3.

The occurrence of these organisms related to the age of patients with chronic prostatitis syndrome is shown in Table 2.

4. Discussion

The results of our 4-year study, which evaluated 1442 patients with chronic prostatitis syndrome, suggest that many patients with inflammatory as well as non-inflammatory pelvic pain syndrome may have unusual pathogens in their prostate. The aetiological organisms of prostatitis syndrome suggested as important in the literature include *C. trachomatis*, *U. urealyticum*, *M. hominis* and *T. vaginalis* [5–9]. *C. trachomatis* may originate in the prostate in an unknown percentage of patients with prostatitis syndrome [10,11].

In our study, an infectious aetiology in patients with chronic prostatitis syndrome was determined in 74.2% of patients. In 52.4% of these patients, the inflammatory finding (>10 WBCs/hpf) was found in EPS or VB_3. Normal WBCs/hpf (<10) was found in 67.5% patients with symptoms of chronic prostatitis in whom *C. trachomatis* was detected in EPS or VB_3, in 33.8% of patients in whom *T. vaginalis* was isolated, and in 55.6% of 72 patients in whom *U. urealyticum* was isolated.

These results encouraged discussions about current classification of prostatitis syndrome and criteria for certain categories, especially when taking into consideration the fact that *C. trachomatis* and urogenital mycoplasma are classified as bacteria, and consequently cause bacterial prostatitis and not nonbacterial prostatitis [12].

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