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Pelvic Pain in Men with *Mycoplasma Genitalium*

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Purpose: There are debates about *Mycoplasma genitalium* (*M. genitalium*) causing prostate infection and inducing pelvic pains. Consequently, *M. genitalium*-associated pelvic pains were characterized and their manifestation in male pelvic pain syndrome (MPPS) was evaluated through a case-control study.

Materials and Methods: The presence of *M. genitalium*-associated pelvic pains was examined in 113 *M. genitalium*-infected men, and the typical presentations of mycoplasma-associated MPPS were characterized through a case-control study involving 80 mycoplasma-infected and 234 case-matched uninfected controls. Finally, changes in symptoms following antimicrobial treatments were compared between 27 cured and 14 persistently infected cases.

Results: Pain locations from 113 men were followed as items-1a for 25.7%, 1b for 21.2%, 1c for 31%, 1d for 18.6%, 2a for 59.3%, and 2b for 23% from the Korean National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) questionnaire. In addition, the sum scores from the pain domain, voiding domain and total score were 6.68±4.75, 2.69±2.66, and 15.00±8.66, respectively. Successful antibiotic therapy significantly reduced the total score from baseline (15.148±6.798 vs. 5.357±7.025, p=0.001). From the case-control study, mycoplasma-infected men had pains more frequently during urination (1c) and on the tip of the penis (2a) (all p=0.0001) than the controls.

Conclusions: It was found that *M. genitalium* infection is associated with clinically significant male pelvic pains, which improved with adequate antimicrobial therapies. Urethral irritation symptoms without pyuria may be the typical characteristics of mycoplasma-associated pelvic pains in MPPS.

Keywords: *Mycoplasma genitalium*; Pelvic pain; Prostatitis

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INTRODUCTION

Chronic prostatitis (CP)/chronic pelvic pain syndrome (CPPS) is a common urologic disorder associated with pain or discomfort in the pelvic areas, urinary symptoms, and poor quality of life (QoL) [1]. Despite seriously impacting the QoL, the causative factors have not been thoroughly evaluated. Only 10% of patients with CP/CPPS have a clinically significant level of bacteria in their prostate based on the routine culture method [1]. Therefore, the hidden etiologies in the remaining 90% of patients must be revealed.

Mycoplasma genitalium (*M. genitalium*), the smallest-sized bacteria known with minimal DNA contents, can optimally occupy the cytoplasm of infected host cells, evade the host immunity, and take the course of a chronic infection [2,3]. Owing to its molecular characteristics, mycoplasma

infection could potentially be a causal factor for numerous uncharacterized chronic illnesses, including CP/CPPS or male pelvic pain [4].

M. genitalium causes urethritis in men and can also spread to female sexual partners, increasing the risk of chronic pelvic inflammation, cervicitis, and infertility [5,6]. *M. genitalium*-caused male urethritis can spread to the nearby epididymis [7,8]. Because of its parasitic nature in host cells, *M. genitalium* can also infect the prostate and epididymis. The precise role of cryptic bacteria, including *M. genitalium*, in the pathogenesis of CP/CPPS is unclear, causing ongoing debates about their involvement in CP and pelvic pain [9-11]. Strong evidence suggests that the specific DNA sequences of *M. genitalium* are found in the prostate in patients with chronic refractory prostatitis [12]. A case-control study revealed that *M. genitalium* infection was significantly more prevalent in the prostatitis group [9].

As the prostate is a potential reservoir for spreading various uropathogens into the urinary tract, chronic bacterial prostatitis (CBP) is characterized by prolonged or recurrent symptoms and relapsing bacteriuria [13]. Furthermore, treating CBP requires prolonged therapy with limited antimicrobials that can penetrate the prostate [13]. If *M. genitalium* infects the prostate through the urethra, its intracellular location and limited treatment options make successful eradication challenging, potentially resulting in chronic infections. Indeed, relapse or recurrent infections with the same genotype of *M. genitalium* infection were frequently observed in clinical practices after targeted antimicrobial therapies [6,14].

Urethral discharge is a unique symptom of *M. genitalium* infection, but it is not specific [6,8,11,15]. Characterizing *M. genitalium*-associated pelvic pain requires a careful evaluation of the specific symptoms of CP/CPPS using well-validated questionnaires [1,15,16]. CP/CPPS is a symptom complex characterized by genitourinary pain and voiding symptoms and is sometimes associated with sexual dysfunction [1,16]. Exposing the relationship between CP/CPPS and *M. genitalium* will require a systematic evaluation of the enrolled patients using National Institutes of Health-CP Symptom Index (NIH-CPSI) questionnaires [1,16,17]. To the best of the author's knowledge, the studies that used NIH-CPSI questionnaires for *M. genitalium*-associated pelvic pain inadequately documented and evaluated the role of this bacterium in prostate infections and their clinical characteristics.

This study examined *M. genitalium*-related prostatitis by examining pelvic pain in infected patients, assessing NIH-CPSI score changes post-antibiotic therapy, and identifying which NIH-CPSI items are significantly influenced by the infection in male CP/CPPS through a case-control study.

MATERIALS AND METHODS

1. Participants

This study used specimens from men who visited the Dankook University Hospital's Urogenital Infection and Prostate Diseases Clinic between September 2009 and March 2022, primarily for symptoms, such as urethral discharge, pain, pelvic pain, lower urinary tract symptoms, or due to recurrent urethritis referrals. Informed consent was obtained from all study participants, and the research protocol was approved by the Institutional Review Board of the Dankook University Hospital (202010009D). The clinical characteristics of 113 patients from 113 positive *M. genitalium* samples were analyzed to identify the associated symptoms and signs.

Forty-one patients from the 113 men enrolled who had undergone a test of cures (TOCs) were assessed to evaluate the changes in the NIH-CPSI questionnaire scores after antibiotic therapy; the infection was eradicated with the medications in 27 patients, while 14 patients still had the infection despite the antimicrobial therapies or combination therapies.

The pelvic pain associated with *M. genitalium* was examined. Eighty men without active urethral discharge or urethritis signs in their first voided urine (<5 white blood cells [WBCs] per high power field [HPF]) were selected from the 113 infected individuals as the case group [1,18]. For the controls, 234 age-matched non-mycoplasma cases from the same clinic, showing LUTs or CP/CPPS symptoms without urethritis (no active urethral discharge and <5 WBCs per HPF in first-void urine [FVU]), were selected. Only those with more than three months of CP/CPPS symptoms were classified as having pelvic pain.

2. Laboratory Tests

FVU samples from clinic visitors were collected in 15 ml tubes and frozen at -70°C; DNA was immediately extracted and analyzed using Multiplex polymerase chain reaction

Table 1. Clinical characteristics of the *Mycoplasma genitalium* infected patients

	Variable	1a. Perineum	1b. Testicles	1c. Tip of penis	1d. Below waist	2a. Pain during urination	2b. Ejaculatory pain
No. of patients	113						
Age (y)	39.38±10.87						
Urethral discharge							
Yes	32 (28.33)						
No	81 (71.67)						
WBCs in urine							
<5	80 (70.80)						
5-9	14 (12.39)						
≥10	19 (16.81)						
Pain or discomfort[a]							
No		84 (74.34)	89 (78.76)	78 (69.03)	92 (81.42)	46 (40.71)	87 (76.99)
Yes		29 (25.66)	24 (21.24)	35 (30.97)	21 (18.58)	67 (59.29)	26 (23.01)
Item[a]							
1 and 2	1.79±1.28						
3	1.77±1.40						
4	3.12±2.53						
Pain (1-4)	6.68±4.75						
5	1.33±1.58						
6	1.36±1.37						
Urinary symptoms (5, 6)	2.69±2.66						
7	0.75±1.18						
8	1.49±1.12						
Impact of symptom (7,8)	2.23±1.90						
9	3.43±1.88						
Total (from 1 to 9)	15.00±8.66						

Values are presented as mean±standard deviation or number (%).
WBC: white blood cell.
[a]Presence and severity were measured using the Korean version of the National Institutes of Health-Chronic Prostatitis Symptom Index (NIH-CPSI) questionnaire.

(PCR) with the specific primers for Chlamydia trachomatis, Neisseria gonorrhoeae, and *M. genitalium*, as described elsewhere [15,19]. Based on the PCR results, 113 *M. genitalium*-positive, gonococcal-and chlamydia-negative samples, and 234 triple-negative samples were identified. TOCs were performed three weeks later after the specific antimicrobial therapies using the Allplex II STI-7 Detection assay (Seegene).

The clinical information included the age of the participants and their symptoms according to the responses from the Korean version of the NIH-CPSI questionnaire. The results of the WBC count in the FVU samples were reviewed and classified into the following categories: <5, 5-9, and ≥10 WBCs per HPF. In the group with <5 WBCs per HPF in FVU, expressed prostatic secretion (EPS) obtained from digital rectal prostate massage was analyzed. The resulting WBC counts were classified into <10 and ≥10 WBCs per HPF.

3. Statistical Methods

The median of a dataset was recorded. Ordinal scale differences were assessed using a Student's t-test and a Mann-Whitney U test, while nominal scales were analyzed using Pearson chi-square and Fisher's exact tests. The odds ratios and 95% confidence intervals (CIs) were calculated via logistic regression, rejecting the no-difference hypotheses at $p < 0.05$, using SPSS software (version 23; SPSS).

RESULTS

1. Pelvic Pain in 113 *M. Genitalium*–Infected Cases

The average age of the 113 patients was 39.38±10.87 years, with 28.33% reporting urethral discharge and 70.80% showing low WBC counts (<5 WBCs per HPF) in FVU (Table 1). In the NIH-CPSI questionnaire, 25.66% reported pelvic pain in item-1a (perineum), 21.24% in 1b (testicles), 30.97% in 1c (tip of the penis), 18.58% in 1d (below the waist), 59.29% in 2a (pain during urination), and 23.01% in 2b (ejaculatory pain). In addition, the average scores from the pain domain, urination domain, impact of symptom, QoL, and the total score of the NIH-CPSI responses were 6.68±4.75, 2.69±2.66, 2.23±1.90, 3.43±1.88, and 15.00±8.66, respectively. In the NIH-CPSI, the average frequencies of pain (item 3) and severities (item 4) were 1.77±1.40 and 3.12±2.53, respec-

Table 2. Changes in the index scores of the NIH-CPSI questionnaire following antimicrobial treatment

	Antimicrobial treatment			Before antimicrobial treatment			After antimicrobial treatment		
	Before	After	p-value	Eradicated	Persistent	p-value	Eradicated	Persistent	p-value
No. of patients	41	41		27	14		27	14	
Age (y)	40.55±10.9	40.55±10.9	1.000	36.48±9.82	37.36±11.53	0.796	36.48±9.82	37.36±11.53	0.796
Items in the NIH-CPSI (y)									
Pain domain									
item 1	1.049±0.773	0.488±0.810	0.001	0.963±0.649	1.214±0.975	0.438	0.357±0.780	0.769±0.832	0.121
item 2	1.000±0.707	0.317±0.471	0.001	0.926±0.675	1.143±0.770	0.406	0.179±0.390	0.615±0.506	0.025
item 3	2.171±1.321	1.000±1.466	0.001	2.000±1.271	2.500±1.401	0.294	0.643±1.339	1.769±1.481	0.004
item 4	3.317±2.126	1.439±2.203	0.001	2.963±2.066	4.000±2.148	0.128	0.571±1.289	3.308±2.626	0.001
Sum of pain	7.537±4.019	3.244±4.443	0.001	6.852±3.718	8.857±4.383	0.135	1.750±3.428	6.462±4.789	0.001
Urinary domain									
item 5	1.171±1.202	0.561±0.923	0.007	1.370±1.305	0.786±0.893	0.214	0.357±0.911	1.000±0.816	0.005
item 6	1.220±1.061	0.927±1.127	0.107	1.185±1.210	1.286±0.726	0.406	0.821±10188	1.154±0.987	0.186
Sum of urination	2.390±1.935	1.463±1.885	0.008	2.556±2.190	2.071±1.328	0.776	1.143±1.957	2.154±1.573	0.006
Impact of symptoms domain									
item 7	0.585±0.741	0.488±0.978	0.242	0.593±0.797	0.571±0.646	0.881	0.393±1.100	0.692±0.630	0.041
item 8	1.488±1.075	1.171±1.283	0.111	1.481±0.975	1.500±1.286	0.968	0.750±1.143	2.077±1.115	0.001
Sum ofimpact of symptoms	2.073±1.523	1.463±1.583	0.052	2.074±1.492	2.071±1.639	1.000	0.857±1.325	2.769±1.301	0.001
Quality of life, item 9	3.659±1.938	2.341±1.957	0.003	3.667±1.941	3.643±2.134	0.924	1.607±1.618	3.923±1.706	0.001
Sum of all items	15.659±7.310	8.512±8.409	0.001	15.148±6.798	16.643±8.391	0.438	5.357±7.025	15.308±7.169	0.001

Values are presented as mean±standard deviation.
NIH-CPSI: the Korean version of the National Institutes of Health-Chronic Prostatitis Symptom Index.

tively, with a pain domain mean (items 1-4) of 6.68±4.75; 17.70% reported no pain, while 40.7% scored 4+ and 14.16% scored 7+ in item 4. The average pain domain score was 6.68±4.75 (median=7), with 71.68% of subjects scoring 4 or above and 42.48% exceeding a score of 8.

2. Changes in the Index Scores of the NIH-CPSI Questionnaire after Antimicrobial Treatment

As shown in Table 2, some scores in the NIH-CPSI questionnaire decreased significantly after treatment (items 1, 2, 3, 4, 5, and 9) (all $p<0.05$), whereas the scores from items 6, 7, and 8 did not improve significantly (all $p>0.05$). Consequently, the total score of the NIH-CPSI also decreased from 15.659±7.310 to 8.512±8.409 (p=0.001).

The individual scores in the different items were similar in the cure and persistent groups before treatment (all items $p>0.05$). Except for the score in the voiding item (item-6), the final scores of each item in the NIH-CPSI questionnaire decreased more specifically in the eradicated group than the persistent group. The final total score of the NIH-CPSI questionnaire of the eradicated and persistent groups was 5.357±7.025 and 15.308±7.169, respectively, after antimicrobial treatment (p=0.001).

3. Typical Pelvic Pain in *M. Genitalium* Infected Men

Of the 113 *M. genitalium*-infected cases, 33 were excluded because of potential urethritis (5 WBCs or more per HPF in the FVU). The mean age±standard deviation of the remaining cases was 40.95±10.88 years. Although 62 cases (77.5%) reported pain or discomfort in the pelvic area (items 1 and 2), 18 cases (22.5%) did not report any pain or discomfort according to the responses from items 1 and 2. The 234 age and case-matched controls (mean age; 41.81±10.11 years) were selected, with 181 cases (77.35%) reporting pain or discomfort in the pelvic area (items 1 and 2) and 53 cases (22.65%) showing no symptoms in items 1 and 2.

The WBC counts in EPS were significantly different in the two groups; 36.2% of *M. genitalium*-infected cases revealed ≥10 WBCs per HPF in the EPS, whereas 16.2% of the non-infected controls had an equivalent level (p=0.004). The scores in items 1a, 1b, 2b, 3, 4, 5, 8, and 9 of the NIH-CPSI questionnaire were not similar in the two groups (all $p>0.05$). Pain below the waist (item-1d) was reported more commonly in the controls. The scores in voiding symptoms (item 6) and the impact of the symptoms (item 7) were significantly higher in the control group than in the case group. Compared to the non-infected persons with CP/CPPS, the typical pelvic pain reported by the *M. genitalium*-infected patients with CP/CPPS included pain or discomfort on the tip of the penis (item-1c) and pain during urination (item-2a). Multivariate analysis showed that an *M. genitalium* infection significantly increased the risk of having pain on the tip of the penis (adjusted odd ratio [OR], 3.105; 95% CI, 1.463-6.589; p=0.0001) and the risk of having pain during urination (adjOR, 3.375; 95% CI, 1.903-5.986; p=0.0001) than the

Table 3. Typical pelvic pain in the *Mycoplasma genitalium*-infected cases

Variable	*Mycoplasma genitalium*		p-value	OR (95% CI)	
	Infected	Non-infected		Univariable	Mutivariable
No. of patients	80	234			
Age (y)	40.95±10.88	41.81±10.11	0.519	Not included	Not included
WBCs in urine					
<5	80 (100)	234 (100)			
≥5	0 (0.0)	0 (0.0)			
WBCs in EPS					
<10	30 (63.8)	196 (83.8)	0.004	1	Not included
≥10	17 (36.2)	38 (16.2)		2.923 (1.467-5.821)	
Not taken	33	8			
Pain or discomfort (No)					
1a. Perineum					
No	61 (76.3)	185 (79.1)	0.638	1	0.878 (0.433-1.781)
Yes	19 (23.8)	49 (20.9)		1.176 (0.643-2.150)	
1b. Testicles					
No	62 (77.5)	182 (77.8)	1.000	1	0.850 (0.426-1.697)
Yes	18 (22.5)	52 (22.2)		1.016 (0.553-1.867)	
1c. Tip of penis					
No	57 (71.3)	215 (91.9)	0.0001	1	3.105 (1.463-6.589)
Yes	23 (28.7)	19 (8.1)		4.566 (2.327-8.960)	
1d. Below waist					
No	70 (87.5)	173 (73.9)	0.013	1	0.431 (0.192-0.968)
Yes	10 (12.5)	61 (26.1)		0.405 (0.196-0.836)	
2a. Pain during urination					
No	36 (45.0)	178 (76.0)	0.0001	1	3.375 (1.903-5.986)
Yes	44 (55.0)	56 (24.0)		3.863 (2.267-6.584)	
2b. Ejaculatory pain					
No	61 (76.3)	188 (80.3)	0.430	1	1.107 (0.560-2.186)
Yes	19 (23.8)	46 (19.7)		1.266 (0.690-2.325)	
3	1.60±1.37	1.67±1.51	0.7		
4	2.95±2.53	3.22±2.68	0.434		
Sum of pain scores	6.21±4.66	6.08±4.49	0.829		
5	1.16±1.34	1.53±1.58	0.06		
6	1.16±1.09	1.80±1.47	0.0001		
Sum of voiding scores	2.33±2.07	3.33±2.62	0.005		
7	0.65±0.86	0.99±0.97	0.005		
8	1.48±1.14	1.52±0.97	0.749		
Sum of QoL	2.13±1.75	2.51±1.78	0.096		

Values are presented as mean±standard deviation or number (%).
Pain characteristics were measured by using the Korean version of the National Institutes of Health-Chronic Prostatitis Symptom Index (CPSI) questionnaire.
WBC: white blood cell, EPS: expressed prostatic secretion, QoL: quality of life, OR: odds ratio, CI: confidence interval.

controls (Table 3).

DISCUSSION

Mycoplasma spp. can elicit chronic infection in the host cells of various organs, making them a potent candidate for some of the enigmatic diseases reported. As they incorporate themselves intracellularly, *Mycoplasma* spp. may gain dormant survival in the cytoplasm, and their intraprostatic presence may act as a trigger for chronic or recurrent pelvic pain [2,3,12]. Of the 113 patients with *M. genitalium* infection, symptoms of urethral discharge were notified in 32 patients (28.33%), and pyuria was found in 19 patients (16.81%). Such subacute or chronic characteristics could be from the parasitic nature of *M. genitalium* in the infected host cells [2,3,8,11].

The development and validation of the NIH-CPSI questionnaire by the NIH CP Collaborative Research Network enhances the evaluation of prostate infections, with pain or discomfort being a primary defining characteristic of CP/CPPS patients [16]. The NIH-CPSI questionnaire has become the primary tool for evaluating CP/CPPS symptom severity and treatment responses. Their consistent outcome has greatly aided in understanding the treatment responses [1,16,20,21]. Discomfort or pain is frequently found in cases of *M. genitalium* infections. A six-point decline in the NIH-CPSI total score after specific treatments is accepted as the optimal cut point for clinically significant

improvement in patients with CP/CPPS [22]. In addition, the NIH-CPSI total score, pain, and QoL scores can be used as responsive criteria for improvements in the clinical trials for CP/CPPS. In contrast, the NIH-CPSI urinary score is not generally considered a primary endpoint after treatment [22]. This study revealed that pain on the tip of the penis and pain or burning during urination are two typical symptoms associated with the infection. In addition to the two manifestations, one in four infected persons complained of pain from various pelvic locations. On the other hand, if associated pelvic pain occurred, three in four infected people were troubled with significant pelvic pain, and close to half of the infected persons suffered from moderate to severe pelvic pain.

The hypothesis was that if an *M. genitalium* infection is associated with pelvic pain, the group successful in treatment should show improved scores in their final NIH-CPSI questionnaire, while the group unresponsive to treatment should have similar final scores. Therefore, 41 patients took TOCs and serial NIH-CPSIs after their respective antimicrobial therapy (Table 2). Each item in the NIH-CPSI questionnaire was similar in the scores of 113 patients (Table 1) and 41 patients (Table 2). With the antimicrobial therapy, 27 patients achieved the eradicated status, while the infection was not eradicated in 14 patients despite using various antimicrobials. The initial scores of all items in the questionnaire were similar in the two groups (all $p>0.05$).

Only the eradicated group showed improved scores with treatment; the infection-persistent group revealed similar final scores to the initial scores. The ordinal scales in the items in the NIH-CPSI have generally improved, but the scores for obstructive symptoms (item 6) did not change even after medication use. An approximate ten-point decline in the NIH-CPSI total score following antimicrobial treatments in the eradicated group confirms that *M. genitalium* may be associated with CP/CPPS. Finally, based on the results from the study on the 113 men and on TOC, it could be presumed that an *M. genitalium* infection in urogenital organs may induce male pelvic pain and aggravate their QoL.

A lower urinary tract localization test, such as the Meares-Stamey 4-glass test, remains the reference standard for men with CP/CPPS symptoms [1]. In such lower urinary tract localization tests, the WBC counts and ordinary culture from VB1 can be used to evaluate the possibility of urethral contamination [1]. Unfortunately, almost all cryptic microbes that could cause urethritis can only be diagnosed using PCR. Wet smear and ordinary culture methods from VB1 are limited to evaluating the cryptic organisms [15,19]. Furthermore, urologists do not usually pay attention to these sexually transmitted infections (STIs) because urethritis caused by the STIs is usually mildly symptomatic or asymptomatic without evidence of pyuria in the urine samples. Finally, urologists have clinically excluded patients with urethritis as potential subjects of CP/CPPS if they had active signs or symptoms of urethritis and if their symptoms were less than three months [1]. Therefore, certain cryptic organisms that are not cultivated on ordinary culture methods and are asymptomatic or mild symptomatic could not receive attention for causal etiologies of CP/CPPS.

Urethritis can be defined if the Gram stain of urethral discharge is two or more WBCs per oil immersion field or if the sediment of the first-voided urine is 10 or more WBCs/hpf. Certain non-gonococcal STIs, such as *M. genitalium*, usually reveal cryptic characteristics in infected persons. In such cases, five or more WBCs/hpf in FVU may be acceptable for the definition of urethritis [18]. Therefore, the 33 cases with active urethral discharge or ≥5 WBCs per HPF in FVU were excluded. The remaining 80 infected cases, who were thought to be less influenced by urethral infections, were included in the CP/CPPS study population.

EPS is commonly used in urology and has become the gold standard for prostatic inflammation in urological patients [1]. The significant EPS threshold for inflammatory CP/CPPS was set at 10 WBCs/hpf or higher to reduce the risk of contamination. Because of a higher standard of the WBC counts in EPS than the standard without urethritis (<5 WBCs/hpf), this study suggests that *M. genitalium*-associated CP/CPPS was closer to inflammatory CP/CPPS in this case-control study than non-inflammatory CP/CPPS. Accordingly, the WBC counts in EPS were significantly higher in the *M. genitalium*-infected group than in the non-infected controls, providing further evidence of prostate inflammation by *M. genitalium*.

The case-control study showed that pain or discomfort on the tip of the penis (item 1c) and pain during urination (item 2a) are typical symptoms of *M. genitalium*-associated pelvic pain. In contrast, the controls scored higher in item 1d and obstructive symptoms in items 6 and 7. Higher scores in the urinary symptom domain in the controls could be

attributed to their characteristics because the control group was recruited from those who visited the same clinics with lower urinary tract symptoms, CP/CPPS-like symptoms, and annual prostate check-ups.

The urethral irritation symptoms without pyuria in patients with mycoplasma-associated pelvic pain may result from minimal urethral inflammation caused by a subacute urethral infection or urethral irritation by CP/CPPS. Discriminating between the urethra and prostate is very important in samples from separated organs to exclude urethral contamination. Unfortunately, separating samples is not practical in clinical practice.

Finally, *M. genitalium* is rarely reported in the general population. To enroll enough cases for this rarely reported disease, large numbers of patients are usually required for adequate data analysis. A case-control risk-matching method was used to reduce statistical errors and bias [23]. Initially, known *M. genitalium* infected cases were collected, followed by the selection of controls matching the age parameter and CP/CPPS case from the patient pool.

A limitation of this study was the lack of differentiation between prostatic and urethral mycoplasma infections. Some items from the NIH-CPSI questionnaire may be affected by the inevitable combined symptoms or signs of urethritis. In addition, all clinical characteristics of the patients in this study must be understood at the tertiary levels of care because antimicrobial therapy in primary care clinics may alleviate their initial acute characteristics of infection. Nevertheless, the enrollment and systematic evaluation of many *M. genitalium* patients in the male pelvic pain syndrome (MPPS) study likely addressed some of the limitations.

CONCLUSIONS

This study characterized *M. genitalium*-associated male pelvic pain. An *M. genitalium* infection is associated with clinically significant male pelvic pain, which was improved by adequate antimicrobial therapy. The typical pelvic pain in MPPS by *M. genitalium* was reported on the tip of the penis and pain or burning during urination.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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