

# Clinical courses following acute bacterial prostatitis

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**Purpose:** There are few studies about clinical courses following acute bacterial prostatitis (ABP). We evaluated the progression rates of chronic bacterial prostatitis (CBP) and inflammatory chronic pelvic pain syndrome (CPPS) after ABP treatment. Also evaluated the characteristics of the patients who developed CBP and inflammatory CPPS after ABP treatment.

**Methods:** Total 437 patients compatible with a confirmed diagnosis of ABP from 5 urological centers between 2001 and 2010 were enrolled to study. We defined chronic infection (CI) as a progression to CBP and inflammatory CPPS after treatment of ABP in admission periods when followed up at 3 months or more. Results were analyzed between two groups: recovered without CI (group A, n = 385) and developed to CI (group B, n = 52).

**Results:** Of the 437 ABP patients, 1.3% (6/437) progressed to CBP and 10.5% (46/437) progressed to inflammatory CPPS. The progression rate of CI was 11.8% (52/437). The patients who developed to CI were higher in alcohol consumption rate, diabetes, voiding symptoms, prior manipulation rate, enlarged prostate volume, catheterization history rate and short duration of antibiotic treatment ( $P < 0.05$ ).

**Conclusions:** The identification and characterization of these factors may accelerate the development of preventive, diagnostic and therapeutic strategies for the treatment of CI from ABP.

**Keywords:** Acute, Chronic, Bacterial prostatitis, Inflammatory chronic pelvic pain syndrome, Progression

## INTRODUCTION

Acute bacterial prostatitis (ABP) is an uncommon disease that takes only about 5% of prostatitis [1]. ABP is acute inflammation inside the prostate tissues, presenting similar symptoms to lower urinary tract infections (UTIs) of women in terms of causal bacteria and urinary virulence factors but its host response is very different from uncomplicated cystitis and its treatment process is more complex [2]. Common symptoms of ABP include fever, chill, rectal pain, lower back pain, perineal pain and increased urinary frequency and urgency as well as painful urination [3]. In severe case, the patient can show symptoms related to sepsis such as high fever, chills, cardiovascular instability and change of consciousness. The initial treatment of ABP is to administer high dose antibiot-

ics intravenously until symptoms and signs such as fever, infection and others are resolved. After symptoms improved, the medication should be changed into oral antibiotics such as fluoroquinolone and administer it for 4 weeks at least [4].

Recently, with advancement of treatment with antibiotics, most patients with ABP recover without having complications. In most studies, clinical pattern, progression and risk factors of prostatitis focus on chronic bacterial prostatitis (CBP) rather than ABP. The progression rate of acute ABP to CBP has been reported as between 4.2% to 8.1% [5,6]. However, there is no report on the progression rate from ABP to CBP and inflammatory chronic pelvic pain syndrome (CPPS). The authors defined chronic infection (CI) as post-treatment progression of ABP to CBP as well as inflammatory CPPS, and examined the progression rate to CBP as well as inflammatory

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CPPS from ABP and the characteristics of the CI patients after ABP treatment.

## MATERIALS AND METHODS

This study was conducted in 625 patients who were diagnosed with ABP and had been treated as in-patients at 5 hospitals from March of 2001 to October 2010 as a retrospective analysis. The patients who were diagnosed with prostate cancer at the time of hospitalization or during the follow-up study period for 24 months in average after being diagnosed with the infection had been excluded from this study. All patients had been diagnosed as ABP according to the clinical symptoms (fever, dysuria, painful prostate on digital rectal examination) and the laboratory findings. Those patients with symptoms of ABP and showing positive urine culture, but also those who had shown negative response to urine culture test due to the use of antibiotics but presented typical symptoms of ABP were diagnosed as ABP. When the diagnosis of ABP was not clear, those patients were excluded and so were those who had fever unrelated to UTI or who were unable to trace for follow-up study during treatment period. Finally, 437 patients who were suitable for diagnosis of ABP were included in this study.

The authors defined the case that had progressed to CBP and inflammatory CPPS after treatment follow-up of ABP over 3 months as CI. Diagnoses of CBP and inflammatory

CPPS were confirmed by the prostate massage test (Meares-Stamey four glass test).

Patients were divided into two groups; recovered without progression to CI (group A, n=385) and the group with progression to CI (group B, n=52). We evaluated the progression rate CI from ABP and also evaluated the clinical and microbiological characteristics of the patients in both groups.

We defined the alcohol intake as patients who drinks alcohol once or more per month and smoking history as who smoked at the time of diagnosis regardless the number of cigarettes. Patients who takes medications at the time to diagnose ABP were defined as diabetes and hypertension. The body temperature  $>37.5^{\circ}\text{C}$  was defined as fever, visual pain score  $>6$  was defined as pain, and residual urine volume exceeding 300 mL was defined as urinary retention. When the sums of voiding symptoms and storage symptoms were 7 points and 5 points respectively in accordance with the International Prostate Symptom Score, they were defined as voiding symptoms and storage symptoms. Those patients undergone prostate biopsy, Foley catheterization, urodynamic study and transurethral resection of prostate within 4 weeks prior to onset of ABP were defined as prior manipulations.

Results (frequency and percentages) were analyzed to characterize all variables using Student t test, the  $\chi^2$  tests, and multiple logistic regression analysis. Numerical data given in our data were standard deviation. *P*-value  $<0.05$  was considered

**Table 1.** Clinical characteristics of acute bacterial prostatitis patients

Characteristic	Total (n=437)	Group A (n=385)	Group B (n=52)	<i>P</i> -value
Age (yr)	56.4±13.2	56.0±14.7	56.8±12.5	0.71
Body mass index (kg/m <sup>2</sup> )	23.7±4.0	23.7±3.0	24.1±2.9	0.187
Alcohol	38.9	38.5	40.4	<0.05
Smoking	36.3	36.1	36.5	0.712
STI history	16.9	15.6	17.3	0.749
Diabetes	35.1	25.4	42.3	<0.05
Hypertension	37.4	36.1	38.6	0.142
Fever <sup>a)</sup>	73.1	71.8	75.0	0.812
Pain <sup>b)</sup>	47.9	47.2	48.0	0.693
Retention <sup>c)</sup>	17.4	17.7	17.3	0.541
Voiding symptoms <sup>d)</sup>	38.6	34.2	44.2	<0.05
Storage symptoms <sup>e)</sup>	64.1	65.2	63.4	0.691
Prior manipulation <sup>f)</sup>	41.4	21.7	53.8	<0.05
Hematuria <sup>g)</sup>	54.2	56.2	53.8	0.910
Pyuria <sup>h)</sup>	77.9	77.3	78.8	0.812
PSA (ng/mL)	20.2±34.1	19.7±33.5	21.3±25.8	0.712
Prostate volume (mL)	37.8±17.3	34.2±17.2	41.6±16.0	<0.05

Values are presented as mean ± standard deviation or %.

Group A, recovered without chronic infection; Group B, developed to chronic infection; STI, sexually transmitted infection; PSA, prostate-specific antigen.

<sup>a)</sup>Body temperature  $>37.5^{\circ}\text{C}$ . <sup>b)</sup>Visual pain score  $>6$ . <sup>c)</sup>Residual urine  $>300$  mL. <sup>d)</sup>Voiding symptom international prostate symptom score (IPSS) sum  $>7$ .

<sup>e)</sup>Storage symptom IPSS sum  $>5$ . <sup>f)</sup>Prostate biopsy, catheterization, urodynamic study, transurethral resection of prostate within 4 weeks before onset of acute bacterial prostatitis. <sup>g)</sup> $>4$  Red blood cells/high power field. <sup>h)</sup> $>4$  White blood cells/high power field.

**Table 2.** Treatment parameters of acute bacterial prostatitis patients

Parameter	Group A (n=385)	Group B (n=52)	P-value
Not doing cystostomy	49.4	73.1	<0.050
Urethral catheterization	9.6	53.8	<0.050
Duration of antibiotics (day)	36.5±10.6	27.5±13.5	<0.050
Inpatients treatment			
Quinolone	12.7	13.4	0.632
Cephalosporin+aminoglycoside	58.2	57.6	0.785
Quinolone+aminoglycoside	17.4	17.3	0.914
Others <sup>a)</sup>	11.7	11.5	0.536
Outpatients treatment			
Cephalosporin	21.8	21.1	0.792
Quinolone	67.9	67.3	0.902
Cephalosporin+quinolone	10.9	11.5	0.598

Values are presented as % or mean ± standard deviation.

Group A, recovered without chronic infection; Group B, developed to chronic infection.

<sup>a)</sup>Penicillin+aminoglycoside and penicillin+quinolone.

statistically significant.

## RESULTS

Out of 437 patients, 385 patients (88.1%) recovered without progression to CI (group A) and 52 patients (11.8%) progressed to CI (group B). Among those patients who progressed to CI, CBP were 6 patients (1.3%) and inflammatory CPPS were 46 patients (10.5%).

The mean ages of each group were 56.0±14.7 years and 56.8±12.5 years respectively. Fever (71.8% and 75.0%) and pyuria (77.3% and 78.8%) were the most common clinical symptoms in both groups. Alcohol intake (38.5% and 40.4%), diabetes (25.4% and 42.3%), urinary symptoms (34.2% and 44.2%), history of prior manipulations (21.7% and 53.8%) and prostate size (34.2±17.2 and 41.6±16 mL) were significantly higher in group B than in group A, respectively ( $P<0.05$ ) (Table 1).

Rates of cystostomy (49.4% and 73.1%), urethral catheterization (9.6% and 53.8%) and antibiotics treatment period (36.5±10.6 and 27.5±13.5 days) had shown significant differences in two groups ( $P<0.05$ ). During treatment period, the antibiotics of cephalosporin and aminoglycoside had been used most commonly, and during the treatment period as out-patient, quinolone was used most commonly, but there was no significant difference between two groups in terms of antibiotics types or used period (Table 2).

The most common bacteria among cultured pathogens was *Escherichia coli* followed by *Pseudomonas* spp and *Klebsiella* spp. There was no significant difference between two groups

**Table 3.** Microbiologic characteristics of acute bacterial prostatitis patients

Characteristic	Group A (n=385)	Group B (n=52)	P-value
<i>Escherichia coli</i>	61.3	61.5	0.941
<i>Pseudomonas</i> spp	15.1	15.3	0.749
<i>Klebsiella</i> spp	13.4	9.6	0.069
<i>Enterobacter</i> spp	7.5	7.6	0.977
<i>Streptococcus agalaciae</i>	2.7	5.7	0.412
<i>Serratia marcescens</i>	0	0	
CoNS	0	0	

Values are presented as %.

Group A, recovered without chronic infection; Group B, developed to chronic infection; CoNS, Coagulase-negative *Staphylococci*.

in types or distribution of cultured pathogens (Table 3).

## DISCUSSION

The authors implemented this study by separating the clinical prognosis of ABP into those with progression to chronic inflammation and those recovered without progression to chronic inflammation. The progression rate to chronic inflammation in 437 patients with ABP in total was 11.8%. The reason that authors had included inflammatory CPPS in chronic inflammation was because CPPS had multifactor pathological bionomics so that inflammation could be its cause. Nickel et al. [7] had reported that the triggering factors such as inflammation and dysuria cause inflammation and neurological damage to prostate and surrounding fascia, muscle and pelvic nerve and repetition of such incidences causes sensitization of peripheral tissues and other various phenomena. Patients with diabetes has much higher probability for incidence of UTI by 5 to 10 times [8]. Although it is presumed that the presence of urine glucose is related to the increase of prevalence, there is nothing scientifically verified, and UTI in patients with diabetes is considered as complicated UTI which requires treatment with antibiotics for longer period in comparison to patients without diabetes. Geerlings [9] had reported that patients with diabetes had higher prevalence of other infections such as asymptomatic bacteriuria and UTI compared to patients without diabetes. In this study, also, patients with diabetes were progressed from ABP to CI much more than those recovered without progression to CI. Given these results, it is possible to presume that diabetes has effects on the process of progression from ABP to CI and also possible to infer control of diabetes has an important role for prevention and treatment of ABP-induced chronic inflammation.

Prior manipulation such as prostate biopsy, urodynamic

study, or urethral catheterization can spread inflammation through lymphatic system or blood circulation system. Ha et al. [5] had reported that the incidences of prostatic abscess as well as chronic prostatitis were significantly higher in the group undergone procedures for lower urinary tract system before onset of ABP than in the group who did not. In this study, the percentage of those with prior history of procedures for urinary tract system and who showed progression to CI was 53.8%, presenting 2 times higher value than patients recovered without progression to CI. In comprehensive view of all these details, it is possible to infer that prior procedures for urinary tract system have effects on progression from ABP to CI thereby reduction of such procedures for lower urinary tract system would have an important role in preventing progression from ABP to CI.

Most of ABP is assumed as originated by ascending infection of urinary tract and it is presumed to incur by reflux of infected urine into ejaculatory duct or prostatic tube passing through posterior urinary tract. The ascending infection of urinary tract can also onset by procedures for bladder and urinary tract such as urethral catheterization [10]. Lindert et al. [11] had reported urethral catheterization is a causative factor of prostatic infection. Meanwhile, as cystostomy can reduce the internal pressure of prostatic tube and prevent intraprostatic tube reflux of infected urine, sprapubic cystostomy is being accepted as the best treatment for ABP. In this study, 53.8 % of patients with progression to CI had history of urethral catheterization and cystostomy was higher percentage in patient without progression to CI. So it is possible to infer that not doing urethral catheterization or cystostomy may be related to the progression from ABP to CI. Therefore, restraining urethral catheterization and performing cystostomy can be helpful for preventing progression to CI in patients with ABP.

There is a report that many of patients diagnosed with prostatitis were also diagnosed with prostatic hypertrophy [12,13]. This condition makes patients more susceptible to inflammation of bladder or prostate as the inflammation either accelerates enlargement of prostate gland itself or such enlargement induces incomplete urination. Linear mass growth can increase intraprostatic tube reflux and internal pressure of prostate theoretically. Such conditions elevate bacterial infection rate of prostate and decrease the treatment rate [14]. In this study, the prostatic volume of the group with progression to CI was larger than that of the group without progression CI. Therefore reduction of prostatic volume can be helpful for preventing progression from ABP to CI by reducing voiding pressure.

Approach to the treatment of ABP is determined by the

clinical symptoms of patient. In most cases, the treatment period of ABP in use of antibiotics is 2 weeks at minimum and sometimes there are cases requiring 4 to 6 weeks as well [15,16]. Fluoroquinolone can be prescribed for 10 days in cases determined as having no accompanying complications and even if there is any but determined as minor [17]. Even though there had been no agreement on the best treatment method so far due to various factors including the needs of considering antibiotic resistance in specific regions, concomitant use of fluoroquinolone and aminoglycoside together in addition to inclusion or exclusion of penicillin or the 2nd and the 3rd generation cephalosporin are recommended to the patients with ABP being treated as in-patients [18]. When the patient is clinically stabilized, has no fever, no urine retention and responds as negative to blood and urine culture tests, orally taking antibiotics can be initiated for use. In this study, the treatment period of in-patients as well as out-patients whose ABP had progressed to CI in use of antibiotics was  $27.5 \pm 13.5$  days whereas the treatment period of patients recovered without progression to CI in use of antibiotics was  $36.5 \pm 10.6$  days. In case of in-patients at all ages, the combined therapy of cephalosporin and aminoglycoside was used most frequently, while in case of out-patients, quinolone was most commonly prescribed.

The period of antibiotics administration to prevent progression from acute prostatitis to chronic prostatitis is recommended as two to three weeks administration by Chronic Prostatitis Collaborative Research Network Guidelines and in general, it is common to administer for about 1 month [19]. In this study, antibiotics had been used in the group with progression to chronic inflammation for  $27.5 \pm 13.5$  days and in the group without progression to chronic inflammation for  $36.5 \pm 10.6$  days, presenting sufficient quantity of antibiotics had been used in both groups. Of course, the timing to make determination on progression to chronic inflammation could not be 3 months after always but the authors had implemented this study by designating 3 months after treatment of acute prostatitis as the basis of progression or not according to clinical experiences.

Millan-Rodriguez et al. [20] had reported that gram-negative bacteria of Enterobacteriaceae group was most commonly detected in patients with ABP (87%) and gram-negative bacteria among isolated microorganisms was 10%, as reported such as *Proteus mirabilis*, *Pseudomonas aeruginosa*, *Klebsiella*, *Enterococcus* spp., and *Serratia* spp., and *Enterococcus* spp. were detected. In this study, *E. coli* was detected as the most common bacterium that caused ABP.

In this study, progression rate of CBP and inflammatory

CPPS was 1.3% and 10.5%, respectively and the progression rate of CI was 11.8% from ABP treatment. The patients who developed to CI were higher in alcohol consumption rate, diabetes, voiding symptoms, prior manipulation rate, enlarged prostate volume, catheterization history rate and short duration of antibiotic treatment. Identification of these factors in patients with ABP can be helpful for establishing preventive, diagnostic and therapeutic strategies against progression to CI.

## CONFLICT OF INTEREST

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

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