

# Procalcitonin as an indicator of urosepsis

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**Background:** Procalcitonin has been advocated as a marker of bacterial infection, so this study was carried out to determine the usefulness of serum procalcitonin in the early diagnosis of urosepsis.

**Methods:** The subjects were 37 febrile patients with urinary tract infection in whom we examined the serum procalcitonin concentration at the start of treatment.

**Results:** Thirty patients had acute pyelonephritis (16 simple, 14 complex), one had emphysematous pyelonephritis, five had acute prostatitis, and one had acute epididymitis. The procalcitonin level was  $<0.5$  ng/mL in 18 patients,  $\geq 0.5$  ng/mL in one patient,  $\geq 2$  ng/mL in seven patients, and  $\geq 10$  ng/mL in 11 patients. Five of the 11 patients with procalcitonin levels  $\geq 10$  ng/mL had disseminated intravascular coagulation. All patients with urinary tract obstruction and disseminated intravascular coagulation had procalcitonin levels  $\geq 10$  ng/mL.

**Conclusion:** Although this retrospective study comprised a small number of patients, we found that procalcitonin was a useful marker for urinary tract infection.

**Keywords:** procalcitonin, urosepsis, urinary tract infection, urology

## Introduction

Blood culture is a very specific method for detection and confirmation of septicemia, but test results are available only after 24 hours. C-reactive protein is an acute-phase protein produced by the liver in response to tissue injury or infection. However, the C-reactive protein level can also be very high in nonseptic states, eg, postoperatively and in inflammatory disease.<sup>1,2</sup> However, a definite correlation between infection and changes in C-reactive protein has not been documented as yet.

Procalcitonin is a 13 kDa, 116-amino acid prohormone of calcitonin. In 1993, Assicot et al<sup>3</sup> reported increased procalcitonin levels in patients with sepsis and infection. Further clinical studies indicated that bacterial inflammation and sepsis, but not viral infections or autoimmune disorders, could induce high concentrations of serum procalcitonin.<sup>3-7</sup> In this study, we evaluated the relationship between urosepsis and procalcitonin.

## Materials and methods

From January 2008 to October 2010, 37 patients with febrile urinary tract infection (UTI) had their procalcitonin levels measured and were evaluated for the severity of UTI at our hospital. Our criteria for UTI were febrile symptoms (ie, dysuria, low back pain) and a core body temperature more than 38°C.

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All patients provided a urine sample for culture before treatment with antibiotics. If patients needed to be hospitalized, blood culture was performed at least twice before administration of antibiotics. Blood culture was confirmed to be positive if the same organism was found in urine culture.

The BRAHMS PCT-Q (Thermo Fisher Scientific, Waltham, MA, USA) is an immunochromatographic test for semiquantitative detection of procalcitonin, and is used for diagnosing and monitoring the effects of treatment for severe bacterial infection and sepsis. The BRAHMS PCT-Q test system requires an incubation period of only 30 minutes, is not apparatus-dependent, and does not need calibrating. The test uses a monoclonal mouse anticatalcalcin antibody conjugated with colloidal gold and a polyclonal sheep calcitonin antibody.

A procalcitonin level  $< 0.5$  ng/mL indicates the possibility of local bacterial infection;  $\geq 0.5$  ng/mL indicates that a systemic infection (sepsis) is unlikely;  $\geq 2$  ng/mL suggests the possibility of a systemic infection (sepsis), although various other conditions are also known to induce procalcitonin; and  $\geq 10$  ng/mL indicates the likelihood of sepsis, unless other causes for a high procalcitonin level are known. It is important to note that a systemic inflammatory response is almost exclusively due to severe bacterial sepsis or septic shock.<sup>8</sup>

Comparisons between groups were performed using the Mann–Whitney *U* test and Kruskal–Wallis nonparametric analysis of variance.

## Results

Thirty patients had acute pyelonephritis (16 without and 14 with resistant-organ acute pyelonephritis), one had emphysematous pyelonephritis, five had acute prostatitis, and one patient had acute epididymitis. The procalcitonin level was  $< 0.5$  ng/mL in 18 patients,  $\geq 0.5$  ng/mL in one patient,  $\geq 2$  ng/mL in seven patients, and  $\geq 10$  ng/mL in 11 patients.

All patients had positive urine cultures. The principal bacterium was *Escherichia coli* (Table 1). As shown in Table 2, 16 of 20 patients had a positive blood culture, and the procalcitonin level was  $< 0.5$  ng/mL in 2/5 patients (40%),  $\geq 2$  ng/mL in 6/6 patients (100%), and  $\geq 10$  ng/mL in 8/9 patients (88.9%). There was only one patient with procalcitonin  $\geq 0.5$  ng/mL, so we excluded this case from the statistical analysis.

No significant differences were observed between procalcitonin and C-reactive proteins levels or between

**Table 1** Results of urine culture

Bacteria	Number
<i>Escherichia coli</i>	18
<i>Enterococcus faecalis</i>	4
<i>Pseudomonas aeruginosa</i>	2
<i>Klebsiella oxytoca</i>	2
<i>Klebsiella pneumoniae</i>	2
<i>Enterobacter cloacae</i>	2
Methicillin-resistant <i>Staphylococcus aureus</i>	2
<i>Staphylococcus aureus</i>	2
<i>Proteus mirabilis</i>	1
<i>Acinetobacter lwoffii</i>	1
<i>Escherichia coli</i> , ESBL-producing	1

procalcitonin and white blood cell levels. Eleven patients had procalcitonin levels  $\geq 10$  ng/mL. Eight of these patients required drainage and five had disseminated intravascular coagulation. All patients with urinary tract obstruction and disseminated intravascular coagulation had procalcitonin levels  $\geq 10$  ng/mL (Table 3).

## Discussion

UTI is a disease commonly encountered in the clinical setting, and sepsis resulting from UTI is a serious condition that can affect the prognosis. It has been reported that the mortality rate due to urosepsis is 16.1%.<sup>9</sup> It has also been reported that 78% of cases of urosepsis are due to urinary tract obstruction.<sup>10</sup>

C-reactive protein is generally regarded as a useful marker for the diagnosis of sepsis and is used along with blood culture. However, such methods are sometimes inadequate for diagnosing sepsis, and a testing method enabling more rapid and efficient diagnosis has long been considered necessary.

Procalcitonin is considered a useful marker for rapid differential diagnosis of bacterial sepsis and evaluation of its severity.<sup>11–13</sup> In a report comparing blood culture and procalcitonin, diagnostic sensitivity was 42.6% for blood culture and 70.2% for procalcitonin, and the diagnostic accuracy of procalcitonin calculated from its sensitivity and specificity was 75.4%.<sup>11</sup> In this study, the sensitivity and

**Table 2** Relationship between procalcitonin levels and positive blood culture rate

PCT levels	Total number	Number of blood culture-positive	Rate
PCT $< 0.5$ ng/mL	5	2	40%
PCT $\geq 0.5$ ng/mL	–	–	–
PCT $\geq 2$ ng/mL	6	6	100%
PCT $\geq 10$ ng/mL	9	8	88.9%

**Table 3** Patients with procalcitonin levels  $\geq 10$  ng/mL

	Age	Sex	Disease	Stone	Drainage	DM <sup>h</sup>	Steroid	DIC
Case 1	72	F <sup>a</sup>	APN <sup>c</sup>	(+)	(-)	(-)	(+)	(-)
Case 2	63	F	APN	(+)	D-J <sup>e</sup>	(-)	(-)	(+)
Case 3	75	F	APN	(+)	D-J	(+)	(-)	(+)
Case 4	80	F	APN	(+)	PNS <sup>f</sup>	(+)	(-)	(+)
Case 5	73	F	APN	(+)	D-J	(-)	(+)	(-)
Case 6	37	F	APN	(+)	D-J	(-)	(+)	(+)
Case 7	58	F	EPN <sup>d</sup>	(-)	NpX <sup>g</sup>	(-)	(-)	(-)
Case 8	66	F	APN	(-)	(-)	(+)	(+)	(-)
Case 9	66	F	APN	(+)	D-J	(+)	(-)	(+)
Case 10	38	F	APN	(+)	D-J	(+)	(-)	(-)
Case 11	92	M <sup>b</sup>	APN	(+)	(-)	(-)	(-)	(-)

**Notes:** <sup>a</sup>Female; <sup>b</sup>male; <sup>c</sup>acute pyelonephritis; <sup>d</sup>emphysematous pyelonephritis; <sup>e</sup>Double J catheter; <sup>f</sup>percutaneous nephrostomy; <sup>g</sup>nephrectomy; <sup>h</sup>diabetes mellitus.

specificity calculated for procalcitonin was 78%, indicating very high diagnostic efficiency.

The recommended treatment for urosepsis is drainage of the obstructed urinary tract to secure its patency and removal of an infected lesion if present. Any delay in appropriate treatment can be fatal. The results of this study show that all 11 patients with a procalcitonin level  $\geq 10$  ng/mL had severe bacterial urosepsis. Of these patients, five also had disseminated intravascular coagulation and eight needed relief of an obstructed urinary tract.

With regard to pathogenic micro-organisms, others have found no significant difference in procalcitonin levels between Gram-positive cocci and Gram-negative rods.<sup>11,13</sup> Similar results were noted in our patients.

The superior usefulness of procalcitonin levels in the diagnosis of sepsis in comparison with C-reactive protein has been previously reported.<sup>14,15</sup> Our findings further confirm that the procalcitonin level is a useful parameter on which to base a treatment strategy because it allows prompt diagnosis of urosepsis without the need to wait for the results of blood culture. Consequently, procalcitonin should be used as an adjunctive marker to aid in the diagnosis.

## Disclosure

The authors report no conflicts of interest in this work.

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