ORIGINAL ARTICLE

Retrospective Study

Comparison of computed tomography findings between bacteremic and non-bacteremic acute pyelonephritis due to *Escherichia coli*

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Abstract

AIM: To identify computed tomography (CT) findings that are associated with the presence of bacteremia in patients with acute pyelonephritis (APN) due to *Escherichia coli* (*E. coli*).

METHODS: The clinical data and contrast-enhanced CT findings of 128 patients who were diagnosed with APN due to *E. coli* and showed renal abnormality on contrast-enhanced CT between January 2003 and November 2013 were retrospectively reviewed. The patients were divided into two groups according to the presence of bacteremia: The bacteremia group and the non-bacteremia group. The abnormality on contrast-enhanced CT were categorized into 5 renal and 4 extrarenal CT findings and compared between the two groups using the χ^2 test and multivariate logistic regression.

RESULTS: Among the 128 patients, 34 patients (26.6%) were classified into the bacteremia group and 94 patients (73.4%) into the non-bacteremia group. There was no statistically significant difference in gender between the two groups (P = 0.09), but the age of the

patients in the bacteremia group was higher than that of the patients in the non-bacteremia group ($P < 0.01$). Compared to the non-bacteremia group, 1 renal CT finding such as urothelial thickening and 3 extrarenal CT findings such as diffuse peritoneal thickening, cystitis and pulmonary congestion were more frequently observed in the bacteremia group with statistical significance. The logistic regression analysis revealed that CT findings, including urothelial thickening, diffuse peritoneal thickening, cystitis and pulmonary congestion were suggested as the predictive CT findings of bacteremic APN.

CONCLUSION: On CT, urothelial thickening, diffuse peritoneal thickening, cystitis, and pulmonary congestion are more frequently observed in patients with bacteremic APN due to *E. coli*.

Key words: *Escherichia coli*; Pyelonephritis; Urinary tract infections; Bacteremia; Multidetector computed tomography

Core tip: This is a retrospective study to evaluate the different computed tomography (CT) findings between the bacteremic and non-bacteremic acute pyelonephritis (APN) due to *Escherichia coli* (*E. coli*). Current study includes 128 subjects diagnosed with APN due to *E. coli* and performed contrast-enhanced CT. The usefulness of blood culture that was routinely performed in the patients with APN have been doubted; therefore, several studies which aimed to determine the predictive model of bacteremia by using some clinical features have been published. Here, we analyzed the CT findings of APN according to the presence of bacteremia and suggested the significant CT features predicting bacteremia which were urothelial thickening, diffuse peritoneal thickening, cystitis, and pulmonary congestion.

INTRODUCTION

Acute pyelonephritis (APN) is an inflammation of the upper urinary tract, including renal parenchyma, calyces, and pelvis, which is considered as an ascending infection from the lower urinary tract[1-3]. The clinical spectrum of APN is diverse ranging from dysuria to systemic illness complicated by sepsis or death. The urine and blood cultures are performed as routine workups to identify the true pathogen and to obtain the antibiotic susceptibility test[4-7]. Although several studies have suggested that blood cultures provide no useful information toward the clinical management of APN, it is still essential to differentiate the patients with bacteremia from those without bacteremia, considering that the mortality from urosepsis reaches 7.5%-30%, especially at the initial presentation[8-11]. There have been several studies that aimed to determine the predictive model of bacteremia in the patients with APN by using the clinical features[11-14]; however, there has been no study that evaluates the radiologic features that are associated with bacteremic APN. Therefore, the purpose of this study was to identify computed tomographic (CT) findings associated with the presence of bacteremia in patients with APN due to *Escherichia coli (E. coli)*.

MATERIALS AND METHODS

This retrospective study was approved by the institutional review board and was compliant with HIPAA. The requirement for informed consent was waived.

Patient selection

This study included all consecutive subjects who underwent contrast-enhanced CT scan of the kidneys with a clinical diagnosis of APN between January 2003 and November 2013. A total of 491 patients met these two criteria. Then, we selected the following patients: (1) the patients with renal abnormality on contrast-enhanced CT that was performed at their first visit; and (2) the patients in whom both blood and urine cultures were performed at their first visit. One hundred and eighty-three patients were selected, and we excluded the following patients in the next step: (1) the patients in whom a microorganism other than *E. coli* was isolated from urine culture; and (2) the patients with the history of comorbidity other than APN which may affect the result of blood or urine culture. Finally, 128 patients (109 females, 19 males, median age 43 ± 25 years) comprised our study population. From this cohort, the patients were divided into the two groups according to the results of blood culture: The bacteremia group in which *E. coli* was isolated from blood culture and the non-bacteremia group with no bacterial growth in blood.

CT technique

Contrast-enhanced CT studies were performed by using two multidetector CT scanners (Brilliance 64, Philips Medical System, Cleveland, OH, United States; Aquilion 64, Toshiba Medical Systems, Tochigi, Japan) with intravenous contrast media (Ultravist 300 or 370, Bayer-Schering, Berlin, Germany; Omnipaque 300, GE Healthcare) administered at a rate of 3-4 mL/s, using power injectors (Medrad, Pittsburgh, PA, United States). The volume of contrast media administered varied depending on the body weight of each patient (2 mL/kg of body weight).
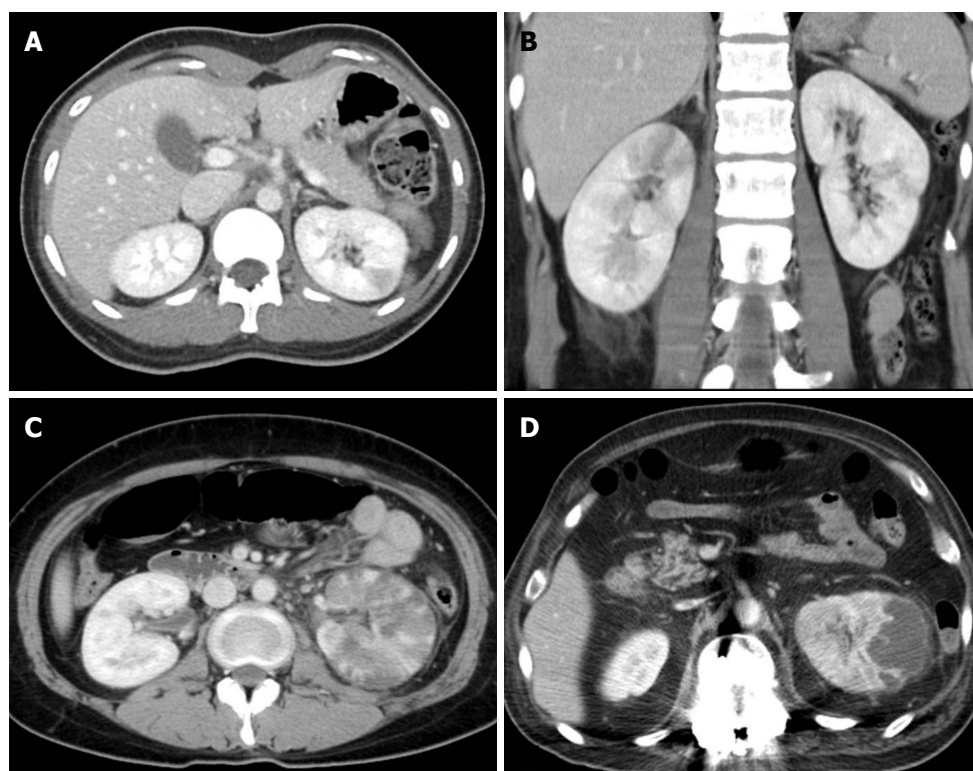
Figure 1 Grades of acute pyelonephritis. A: Grade 1 APN in the left kidney that is defined as a focal, wedge-shape, hypodense lesion; B: Grade 2 APN in the right kidney that is defined as multifocal or diffuse hypodense lesions; C: Grade 3 acute pyelonephritis in the left kidney that is defined as abscesses less than 2 cm within the APN lesion; D: Grade 4 APN in the left kidney that is defined as large abscess pockets more than 2 cm in the longest diameter. APN: Acute pyelonephritis.

CT scanning parameters were 100-120 kVp, 130-700 mAs, and 3-5 mm slice thickness with no gap. CT protocols applied to the patients were diverse due to retrospective enrollment of the patients. Forty-three patients underwent 3-phase CT scan which was obtained during pre-contrast, portal venous, and excretory phases; 27 patients underwent 2-phase CT scan which was obtained during pre-contrast and portal venous phases; 21 patients underwent 4-phase CT scan which was obtained during pre-contrast, arterial, portal venous, and excretory phases; 13 patients underwent single phase CT scan which was obtained during portal venous phase; 9 patients underwent 2-phase CT scan which was obtained during arterial and excretory phases; 5 patients underwent 2-phase CT scan which was obtained during portal venous and excretory phases; 5 patients underwent 3-phase CT scan which was obtained during arterial, portal venous, and excretory phases; 3 patients underwent 3-phase CT scan which was obtained during pre-contrast, arterial and excretory phases; and 2 patients underwent 2-phase CT scan which was obtained during pre-contrast and excretory phases. After acquisition of the pre-contrast images, arterial phase scanning was performed 10-15 s after the trigger attenuation threshold (100 HU) was reached at the level of the supra-celiac abdominal aorta. The time delays were 70-80 s for portal venous phase and 180 s for excretory phase.

Image interpretation

Contrast-enhanced CT images of 128 patients were reviewed on the Picture Archiving and Communication System workstation (G3; Infinitt Co., Seoul, South Korea) by two radiologists in consensus (the first author with 15 years of experience in radiology and the second author with 4 years of experience in radiology). The readers were aware that *E. coli* was isolated from urine culture, but were blinded to the results of blood culture.

Contrast-enhanced CT findings were categorized into the renal and extrarenal findings.

The renal findings were recorded as follows: (1) APN grade on a scale of 4; (2) the presence of urothelial thickening; (3) bilateral involvement; and (4) perirenal infiltration; (5) rupture of renal abscess. APN grades were defined as follows (Figure 1): Grade 1 was simple APN presenting with a focal, wedge-shaped hypodensity radiating from the papilla in the medulla to the cortical space of the kidney; grade 2 was severe APN presenting as multifocal or diffusely scattered hypodensities in the kidney; grade 3 was a microabscess which was less than 2 cm in size; grade 4 was a macroabscess which was more than 2 cm in longest diameter. The urothelial thickening is defined as thickening of renal pelvis, calyces, and ureter (Figure 2). In cases with bilateral APN of different grades in each kidney, the higher grade was recorded. Perirenal infiltration was defined as the obliteration of perirenal fat or thickening of Gerota's fascia.

Figure 2 Urothelial thickening of bilateral renal pelvis (arrows) in a 64-year-old female with bacteremic acute pyelonephritis due to *Escherichia coli*.
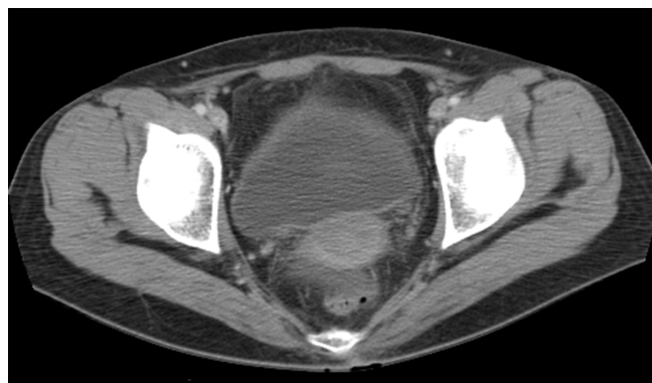

Figure 4 Infiltration into perivesical fat in a 31-year-old female with bacteremic acute pyelonephritis due to *Escherichia coli*.

Figure 3 Diffuse peritoneal thickening (arrows) in a 42-year-old female with bacteremic acute pyelonephritis due to *Escherichia coli*.

The extrarenal findings were recorded as follows: (1) diffuse peritoneal thickening; (2) cystitis; (3) pulmonary congestion; and (4) pleural effusion (Figure 3). Cystitis was defined as the presence of a thickened and enhanced wall of the urinary bladder accompanied by infiltration into the perivesical fat (Figure 4).

Statistical analysis
The frequency of each CT finding was compared statistically between the two groups by χ^2 test using SPSS® software (Version 20.0 for Windows, SPSS Institute, Chicago, IL, United States). All variables were entered into a logistic regression model to assess the predictive CT findings of bacteremia. The multivariate logistic regression was performed to calculate the odds ratios with 95%CI and *P* values. In both methods of analyses, a *P* value of < 0.05 was considered to be statistically significant.

RESULTS
A total of 128 CT scans of 128 patients were included: 34 patients (32 females, 2 males, median age 63 ± 18 years) in the bacteremia group and 94 patients (77 females, 17 males, median age 39 ± 25 years) in the non-bacteremia group. There was no statistically signi-

ficant difference in gender between the two groups (*P* = 0.09), but the age of the patients in the bacteremia group was higher than that of the patients in the non-bacteremia group in the result of *t* test (*P* < 0.01).

The frequencies of renal and extrarenal CT findings in the two groups and the results of χ^2 test are shown in Table 1. Compared to the non-bacteremia group, 4 CT findings, including 1 renal finding such as urothelial thickening and 3 extrarenal findings such as diffuse peritoneal thickening, cystitis and pulmonary congestion, were more frequently observed in the bacteremia group with statistical significance (Figure 2).

To identify a predictive CT finding of bacteremia, we performed multivariate logistic regression analysis (Table 2). The logistic regression analysis revealed that urothelial thickening, diffuse peritoneal thickening, cystitis, and pulmonary congestion were significantly associated with bacteremia.

DISCUSSION
Urinary tract infection (UTI) usually starts from the bladder and can spread up to the kidneys, which is called APN[6]. When the infection spreads into the bloodstream, it results in a systemic illness called bacteremia. The identification of bacteremia is important, because it may lead to severe urosepsis and mortality reaching 7.5%-30%[4-7,13,15-18]. Blood culture is a simple test which can isolate the microorganism with high specificity, although the general yields are less than 10%[12,13]. Among the patients with APN, blood cultures have been reported to be positive in 18%-32% of APN cases[11,13,15-17,19,20]. Some studies have doubted the usefulness of routine blood cultures in the patients with uncomplicated APN, based on the limited information from blood culture and little effect of antibiotic therapy[8-10,15,18]. However, blood cultures are still performed frequently, due to particular concern about higher mortality and complication rate related with bacteremia and increasing prevalence of resistant strains[21,22]. Considering the prediction of bacteremia before or without obtaining the result of blood culture,

Table 1 Frequencies of computed tomography findings in patients with or without bacteremia *n* (%)

CT findings	Patients with bacteremia (*n* = 34)	Patients without bacteremia (*n* = 94)	*P* value
Renal findings			
APN grade			0.88
1	2 (5.8)	7 (7.0)	
2	21 (61.8)	50 (53.2)	
3	8 (23.5)	24 (25.5)	
4	3 (8.8)	13 (13.8)	
Urothelial thickening	29 (85.3)	61 (64.9)	0.03
Bilateral involvement	10 (29.4)	31 (33.0)	0.70
Perirenal infiltration	27 (79.4)	69 (73.4)	0.49
Rupture of abscess	0	4 (4.3)	0.22
Extrarenal findings			
Diffuse peritoneal thickening	9 (26.5)	4 (4.3)	< 0.01
Cystitis	15 (44.1)	19 (20.2)	< 0.01
Pulmonary congestion	16 (47.1)	20 (21.3)	< 0.01
Pleural effusion	8 (23.5)	14 (14.9)	0.25

APN: Acute pyelonephritis; CT: Computed tomography.

Table 2 Variables selected for logistic regression analysis for predicting bacteremia

CT findings	OR (98%CI)	*P* value
Renal findings		
Urothelial thickening	3.16 (1.20-8.28)	0.02
Bilateral involvement	1.05 (0.49-2.29)	0.90
Perirenal infiltration	1.50 (0.61-3.67)	0.38
Rupture of abscess	0.56 (0.06-5.19)	0.61
Renal findings		
Diffuse peritoneal thickening	7.50 (2.18-25.81)	< 0.01
Cystitis	4.15 (1.82-9.45)	< 0.01
Pulmonary congestion	4.73 (2.15-10.42)	< 0.01
Pleural effusion	1.61 (0.63-4.08)	0.32

CT: Computed tomography.

several studies aimed to determine the predictive model of bacteremia in the patients with APN by using the clinical features[11-14]; age, systolic blood pressure of < 90 mmHg, body temperature of > 39 ℃, and procalcitonin level of > 0.5 ng/dL in the study by Lee *et al*[11], and indwelling urinary catheters before UTI and high C-reactive protein in the study by Shigemura *et al*[14]. However, there has been no study which evaluates the radiologic features that are associated with bacteremic APN.

CT has a role in defining the extent of APN and in identifying the presence of complications[23]. Review of the literatures identified two studies which introduced the grading system of APN, using CT images[24,25]. Lim *et al*[24] graded APN into 3 groups according to the progression of disease, such as simple, severe and abscess formation. In addition, Paick *et al*[25] graded APN into 4 groups according to the extent of renal involvement; no renal parenchymal involvement as grade 1; less than 25% involvement as grade 2; 25% to 50% involvement as grade 3; and greater than 50% as grade 4. Since we enrolled the patients whose CT findings showed renal abnormality on contrast-enhanced CT, we modified the Lim's APN grading system on a scale of 4. In this study, the grades of APN showed no statistical difference between the patients with and without bacteremia, as the proportion of the patients in each APN grade were similar in both groups.

Among the CT findings, urothelial thickening, diffuse peritoneal thickening, cystitis and pulmonary congestion were more frequently observed in the patients with bacteremia with statistical significance; moreover, these findings were also significantly associated with bacteremia on multivariate analysis. All renal CT findings other than urothelial thickening were not associated with the presence of bacteremia, while

3 of the 4 extrarenal CT findings were statistically significantly associated with the presence of bacteremia. Based on these results, we presumed that there were 3 concerns with respect to bacteremia associated with APN. First, we could assume that the 4 significant CT findings indicated the entrance of the pathogen from the urinary tract into the blood-stream, which might occur through the peritoneal cavity, and not through the kidney. The microorganism in the urinary bladder, ureter, and renal pelvis might have directly spread through the peritoneal cavity, which could explain the 4 significant CT findings in our results. In contrast, perirenal infiltration in APN or the rupture of a renal abscess showed no statistically significant difference between the two groups, which might suggest that the inflammation in the perirenal space did not lead to bacteremia. Second, we could assume that the 4 significant CT findings were secondary to sepsis in the patients with bacteremia. Earlier, Zissin *et al*[26] described the extrarenal CT findings of APN in 21 cases, such as gallbladder wall thickening, periportal tracking, peritoneal fluid, congested inferior vena cava, pleural fluid, and interlobular septal thickening in the basal lungs, and suggested that the cause of the extrarenal CT findings was probably APN-related sepsis. Third, we could assume that pulmonary congestion was due to the increased permeability of capillaries caused by sepsis or direct pleural irritation caused by spreading peritonitis.

Besides the CT findings, we compared age and gender between the two groups. The age of the patients in the bacteremia group was higher than that of the patients in the non-bacteremia group, which was in agreement with the result of a recent study by Lee *et al*[11]. They concluded that old age was one of the predictive factors associated with bacteremia, in conjunction with low systolic blood pressure, high body temperature, and increased level of serum procalcitonin[11]. Even though there was a female predo-minance in the enrolled patients of our study, patients' gender was not statistically different between the two groups (*P* = 0.09).

This study has several limitations. First, we categorized the patients into the bacteremia or non-bacteremia group based on the clinical data from our institute. Data on previous treatment with antibiotics or previous hospitalization before visiting our institute were limited, which was inevitable due to the retrospective study design. The administration of antibiotics prior to the CT scan or blood and urine culture could impact on the number of the patients in both groups. Second, considering the number of patients, we limited the patients to those in whom *E. coli* was isolated, as *E. coli* was the most predominant bacteria isolated from urine cultures. Among the 183 patients, there were other bacterial strains isolated in urine cultures, such as *Klebsiella pneumoniae* (6%), *Enterococcus* species (5%), *Staphylococcus* species (3%), *Streptococcus* species (2%), *Proteus mirabilis* (1%), and *Pseudomonas* species (1%). Since we aimed to perform the statistical analysis between the bacteremia group and the non-bacteremia group, we enrolled the most frequently affected microorganism. In the future, other species but *E. coli* could be enrolled with more data. Third, there was a possibility that a patient whose renal function was severely impaired did not undergo contrast-enhanced CT scan, and hence he/she was excluded from this study.

In conclusion, renal CT findings, such as urothelial thickening, and extrarenal CT findings, such as diffuse peritoneal thickening, cystitis, and pulmonary congestion, were more commonly observed in the patients with bacteremia with statistical significance, as compared with the patients without bacteremia. Therefore, these CT findings may help physicians to identify bacteremia when managing the patients and initiating the proper treatment to decrease the mortality from bacteremia in APN.

COMMENTS

Background
Urinary tract infection (UTI) usually starts from the bladder and can spread up to the kidneys, which is called Acute pyelonephritis (APN). APN is an inflammation of the upper urinary tract, including renal parenchyma, calyces, and pelvis, which is considered as an ascending infection from the lower urinary tract. The clinical spectrum of APN is diverse. When the infection spreads into the bloodstream, it results in a systemic illness called bacteremia that may lead to severe urosepsis and mortality reaching 7.5%-30%. Therefore, the urine and blood cultures are usually performed as routine workups to identify the true pathogen and to obtain the antibiotic susceptibility test. Although several studies have suggested that blood cultures provide the limited information and little effect of antibiotic therapy toward the clinical management of APN, it is still essential to differentiate the patients with bacteremia from those without bacteremia, considering that the mortality from urosepsis reaches 7.5%-30%, especially at the initial presentation. There have been several studies that aimed to determine the predictive model of bacteremia in the patients with APN by using the clinical features; age, systolic blood pressure of < 90 mmHg, body temperature of > 39 ℃, and procalcitonin level of > 0.5 ng/dL, indwelling urinary catheters before UTI, and high C-reactive protein.

Research frontiers
Computed tomography (CT) has a role in defining the extent of APN and in identifying the presence of complications. However, there has been no study that evaluates the radiologic features that are associated with bacteremic APN. The result of this study contributes to identifying CT findings associated with the presence of bacteremia in patients with APN due to *Escherichia coli* (*E. coli*).

Innovations and breakthroughs
In this study, 1 renal CT finding such as urothelial thickening and 3 extrarenal CT findings such as diffuse peritoneal thickening, cystitis and pulmonary congestion were more frequently observed in the bacteremia group with statistical significance, compared to the non-bacteremia group.

Applications
This study suggests that the CT findings, including urothelial thickening, diffuse peritoneal thickening, cystitis and pulmonary congestion can be the predictive CT findings of bacteremic APN due to *E. coli*.

Peer-review
The study describes a retrospective CT finding analysis of *E. coli* pyelonephritis cases to predict bacteremic patients. The authors have presented the data well, and it is well written.

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