The Usefulness of the Interpretation of Initial Plain CT Scan in Hospitalized Patients with Acute Pyelonephritis without Obstructive Uropathy

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Abstract: To investigate the association between plain computed tomography (CT) findings and clinical characteristics and to characterize the potential factors affecting the disease outcome in hospitalized patients with acute pyelonephritis (APN) without obstructive uropathy, we reviewed our clinical database retrospectively. Five plain CT scan abnormal kidney findings of perirenal fat stranding, thickening of perirenal fasciae, kidney enlargement, dilation of renal pelvis, and abnormal density of renal parenchyma were elucidated in 70 patients with APN without obstructive uropathy who were hospitalized. The association between CT scan findings and clinical characteristics were analyzed. Logistic regression analysis was performed to characterize the potential factors that affect the period until the patient was afebrile using various clinical factors and five defined CT scan findings. Perirenal fat stranding and dilation of renal pelvis were significantly frequent in females and patients with diabetes mellitus. Serum inflammation markers were significantly deteriorated in patients with perirenal fat stranding, thickening of perirenal fasciae and kidney enlargement compared to patients with normal findings. An age-adjusted Charlson comorbidity index ≥ 5 and low serum albumin values were significantly associated with a prolonged febrile period. In conclusion, although abnormal plain CT scan findings at diagnosis are associated with some clinical characteristics, the patient's intrinsic factors are more useful for predicting the disease outcome in hospitalized patients with APN without obstructive uropathy.

Keywords: Computed Tomography, Hospitalized Patient, Kidney, Pyelonephritis

1. Introduction

Acute pyelonephritis (APN) is traditionally characterized by bacterial or fungal invasion of the kidney, causing acute interstitial inflammation and tubular cell necrosis. The diagnosis is mainly based on a combination of typical clinical symptoms and laboratory findings. The classical presentation is an abrupt onset of chills, fever and unilateral or bilateral flank or costovertebral angle pain and/or tenderness. These symptoms are often accompanied by dysuria, increased urinary frequency and urgency. In the laboratory tests, the patient may have leukocytosis with a predominance of neutrophils. Urinalysis usually reveals numerous leukocytes, which are often in clumps, and bacterial rods or chains of cocci.

Computed tomography (CT) is particularly recommended in severely ill patients who have a high risk of complications with atypical symptoms or no response to antibiotic therapy within 72 hours [1]. However, initial CT scanning provides important information on the range of inflammation and other accompanying complications to help to establish a precise diagnosis. The use of a multiphase CT protocol (pre- and post-contrast) has been widespread in current practice in APN [2-5]. Recently, Taniguchi et al. suggested that unenhanced

and excretory CT phases are not really necessary because CT assessment of APN and urolithiasis can be accurately performed using only the late nephrographic phase [6]. However, physicians often hesitate to utilize enhanced CT scanning for prompt diagnosis of APN because they are afraid of renal functional deterioration and side effects of contrast material, especially in elderly patients with comorbidities or a poor general condition in the real clinical world. Plain CT scanning is a secure diagnostic method that is easy to use in clinical emergencies. Despite the clinical efficacy of several studies utilizing enhanced CT scanning, there is no study focusing on evaluation of the usefulness of plain CT scan. Moreover, the association between plain CT findings and clinical factors, including disease severity, has been poorly elucidated in APN.

In this study, we investigated the association between plain CT findings and clinical characteristics, and we characterized the potential factors affecting the disease outcome in APN without obstructive uropathy patients who underwent therapy in the hospital.

2. Materials and Methods

2.1. Patients and the Definition of Abnormal CT Findings

We retrospectively collected clinical data from 106 patients with APN without obstructive uropathy between January 2015 and December 2016. Of these patients, 70 who were admitted and underwent medical therapy were included in the study. The reason we focused on hospitalized patients is that all patients underwent plain CT scans and that the rate of abnormal findings in plain CT scans was relatively high because of the severity of APN without obstructive uropathy. The study was approved by an appropriately constituted ethics committee at our institution (Approval No. H30B-0012). The diagnostic definition of APN without obstructive uropathy was APN without any radiographic findings of obstructive uropathy. In terms of CT findings, five abnormal plain CT findings were defined (Figure 1). These findings are as follows: 1) perirenal fat stranding, 2) thickening of perirenal fasciae, 3) kidney enlargement, 4) dilation of renal pelvis, and 5) abnormal density of renal parenchyma.
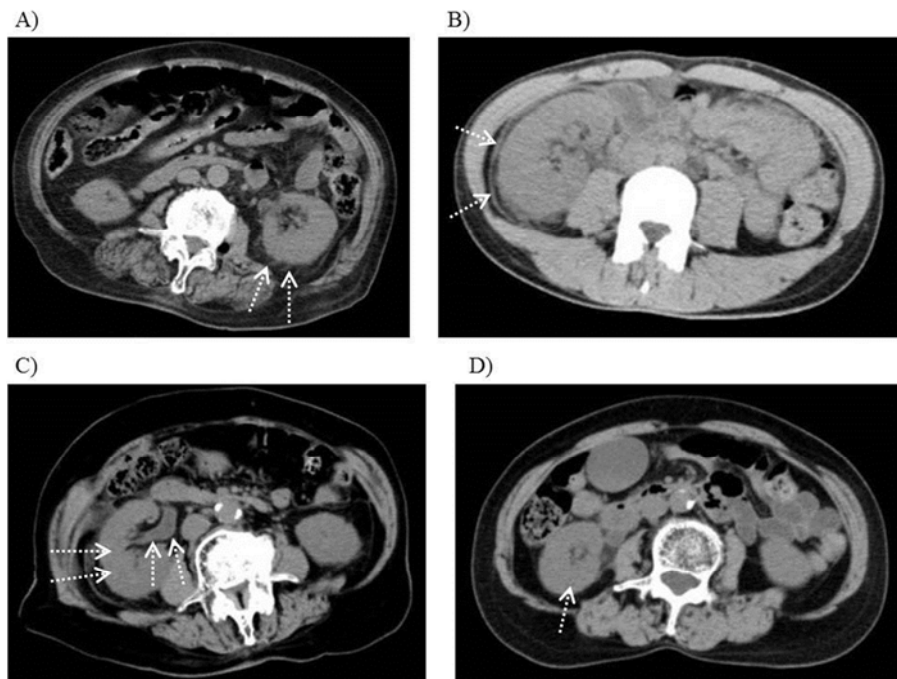

Figure 1. *An example of abnormal plain computed tomography (CT) scan findings. Arrows indicate the findings. A) perirenal fat stranding, B) thickening of perirenal fasciae, C) kidney enlargement (facing right arrows) and dilation of renal pelvis (upward arrows), and D) abnormal density of renal parenchyma.*

2.2. The Analyses of the Association Between CT Findings and Clinical Factors

All CT scan findings were retrospectively reviewed by a single radiologist (I. H.). The associations between five abnormal CT findings and clinical factors were analyzed. The analyzed clinical factors were categorized as nominal or continuous variables. The analyzed nominal factors are as follows: 1) gender (male vs. female), 2) diabetes mellitus (DM) (absence vs. presence), 3) past history of cardiovascular disease (CVD) (absence vs. presence), 4) age-adjusted Charlson comorbidity index (CCI) (5 > vs. 5 ≤),

5) The Eastern Cooperative Oncology Group performance status (ECOG PS) (0, 1 vs. 2 − 4), 6) disturbance of consciousness (absence vs. presence), 7) CVA pain (absence vs. presence), 8) systemic inflammatory response syndrome (SIRS) (absence vs. presence), 9) death due to APN (absence vs. presence), 10) white blood cell (WBC) reaction in urinalysis (negative vs. positive), 11) the number of WBCs in urinary sediment (50 > vs. 50 ≤), 12) blood bacterial culture (negative vs. positive), and 13) urine bacterial culture (negative vs. positive). Additionally, the analyzed continuous factors are as follows: 1) patient's age, 2) WBC count in peripheral blood, 3) platelet (PLT) count in

peripheral blood, 4) serum C-reacted protein (CRP), 5) serum total protein (TP), and 6) serum albumin.

2.3. The Analyses of the Potential Factors That Affect the Period Until the Patient Was Afebrile

Because the most important evaluation of the effectiveness of medical therapy is whether the patient becomes afebrile, the duration from the date of therapy initiation to the date of afebrile status is critical. If the duration was over a week, the outcome of such cases should be considered deteriorated. Therefore, the potential factors that prolong the duration over seven days were searched using all analyzed clinical and radiological factors.

2.4. Statistical Analyses

The associations between abnormal CT finings and clinical nominal factors were analyzed using the chi-squared test. The associations between abnormal CT findings and clinical continuous factors were analyzed using Student's t test or Mann-Whitney test according to the fitness of the data to a Gaussian distribution. In searching the potential factors affecting the disease outcome of APN, logistic regression analysis was used.

3. Results

3.1. The Baseline Patients' Clinical Characteristics and Outcome

The data are summarized in table 1. Gender distribution was predominance of female, and most patients were elderly. General condition of patients was relatively poor. Namely, ECOG PS rated 2 and over and SIRS presentation at first visit were recognized in approximately half of patients. The median period until afebrile was five (range 0 – 30). Three patients died due to the progression of pyelonephritis.

Table 1. Patient's clinical characteristics at first visit and outcome.

Characteristics	Values or Number of cases	
Gender	Male	9
	Female	61
Age (y) (mean, range)	77.2 (25 – 95)	
ECOG PS	0 – 1	36
	2 – 4	34
Age-adjusted CCI (median, range)	4 (0 – 7)	
Comorbidity	No	24
	DM	15
	Past history of CVD	10
	others	21
Disturbance of consciousness	No	63
	Yes	7
CVA pain	No	41
	Yes	29
Body temperature (°C) (mean, range)	38.7 (35.9 – 40.8)	
Systolic blood pressure (mmHg)	90 >	6
	90 – 160	53
	160 <	11
Heart rate (/min.)	60 >	5
	60 – 90	11
	90 <	54

Characteristics	Values or Number of cases	
SpO2 (%)	92 >	17
	92 – 95	30
	95 <	23
SIRS	No	33
	Yes	37
Period until afebrile (day) (median, range)	5 (0 – 30)	
Death due to APN	No	67
	Yes	3

APN: acute pyelonephritis; CCI: Charlson comorbidity index; CVA: costovertebral angle; CVD: cardiovascular disease;
DM: diabetes mellitus; ECOG PS: The Eastern Cooperative Oncology Group performance status;
SIRS: systemic inflammatory response syndrome; SpO2: arterial oxygen saturation of pulse oxymetry

3.2. The Case Distributions According to Five Abnormal CT Findings

The case distributions according to five abnormal CT findings are summarized in table 2. The common findings were perirenal fat stranding and thickening of perirenal fasciae, which were observed in 72.9 and 71.4% of cases, respectively. In contrast, an abnormal density of renal parenchyma was observed in only 10% of cases. Additionally, 74.3% of cases had more than two abnormal findings.

Table 2. Case distributions according to five abnormal CT findings.

CT finding	Number of cases (%)
Perirenal fat stranding	
No	19 (27.1%)
Yes	51 (72.9%)
Thickening of perirenal fasciae	
No	20 (28.6%)
Yes	50 (71.4%)
Kidney enlargement	
No	36 (51.4%)
Yes	34 (48.6%)
Dilation of renal pelvis	
No	44 (62.9%)
Yes	26 (37.1%)
Abnormal density of renal parenchyma	
No	63 (90.0%)
Yes	7 (10.0%)
The number of abnormal CT findings	
0	6 (8.6%)
1	12 (17.1%)
2 ≤	52 (74.3%)

CT: computed tomograph

3.3. The Association Between Abnormal CT Finings and Clinical Factors

In the analysis of nominal clinical factors, perirenal fat stranding and dilation of renal pelvis were significantly recognized in females and patients with DM, respectively. In the analysis of continuous clinical factors, some hematological parameters were significantly different between abnormal CT findings in negative and positive cases (Table 3). Regarding perirenal fat stranding, the values of CRP and PLT were significantly higher in positive cases than in negative cases. In contrast, the TP value was significantly

lower in positive cases than in negative cases. With regard to thickening of perirenal fasciae, the TP value was significantly lower in positive cases than in negative cases. With regard to kidney enlargement, the CRP value was significantly higher in positive cases than in negative cases. With regard to the abnormal density of renal parenchyma, the PLT value was significantly higher in positive cases than in negative cases.

Table 3. *The relationships between abnormal CT findings and continuous factors (age and hematological data).*

	Perirenal fat stranding	Thickening of perirenal fasciae	Kidney enlargement	Dilation of renal pelvis	Abnormal density of renal parenchyma
	No / Yes	No / Yes	No / Yes	No / Yes	No / Yes
Age	75.3 / 78.9	77.8 / 76.9	76.8 / 78.4	74.8 / 79.2	76.9 / 77.6
(mean; ys.)	(P = 0.256)	(P = 0.897)	(P = 0.452)	(P = 0.187)	(P = 0.745)
WBC	13450 / 14520	12710 / 14520	14320 / 13690	11910 / 15220	13410 / 14780
(mean; /μL)	(P = 0.452)	(P = 0.256)	(P = 0.892)	(P = 0.092)	(P = 0.244)
PLT	13.4 / 18.1	19.2 / 21.5	18.2 / 23.3	19.2 / 20.9	17.0 / 24.1
(mean; $\times 10^4$/μL)	(P = 0.031)	(P = 0.398)	(P = 0.084)	(P = 0.432)	(P = 0.037)
CRP	6.5 / 11.9	8.2 / 9.8	7.0 / 13.5	6.9 / 10.8	8.0 / 9.7
(mean; mg/dL)	(P = 0.039)	(P = 0.128)	(P = 0.006)	(P = 0.083)	(P = 0.118)
TP	6.8 / 6.3	7.0 / 6.3	6.7 / 6.4	6.6 / 6.4	6.7 / 6.3
(mean; g/dL)	(P = 0.043)	(P = 0.008)	(P = 0.167)	(P = 0.672)	(P = 0.210)
Albumin	3.9 / 3.3	3.6 / 3.8	3.9 / 3.2	3.8 / 3.5	4.0 / 3.2
(mean; g/dL)	(P = 0.145)	(P = 0.870)	(P = 0.076)	(P = 0.124)	(P = 0.110)

CRP: C-reacted protein; CT: computed tomography; PLT: platelet; TP: total protein

3.4. The Potential Factors Affecting the APN Disease Outcome

In the first step, the potential factors that prolong the duration from the initiation of therapy until the patient is afebrile over seven days were analyzed with univariate analysis of all clinical and radiological factors. The age-adjusted CCI (5 ≤), ECOG PS (2 – 4), and lower value of TP and serum albumin significantly prolonged the duration until afebrile. In the second step, multivariate analysis was performed with the factors that had a P value below 0.1 in the univariate analysis. Age-adjusted CCI (5 ≤) and a lower value of serum albumin were independent factors prolonging the duration until afebrile (Table 4).

Table 4. *Potential factors that prolong the duration from the initiation of therapy until the patient was afebrile over seven days.*

Factors	Univariate Odds ratio		Multivariate Odds ratio	
	(95% CI)	P value	(95% CI)	P value
DM (Yes)	4.571 (0.821 – 25.469)	0.0828	0.118 (0.003 – 5.225)	0.2642
Age-adjusted CCI (5 ≤)	10.678 (1.874 – 60.941)	0.0056	7.126 (1.288 – 50.44)	0.0345
ECOG PS (2 – 4)	6.545 (1.179 – 36.331)	0.0317	5.561 (0.302 – 102.41)	0.2483
Serum CRP	1.098 (0.993 – 1.215)	0.0689	1.165 (0.943 – 1.483)	0.1571
Serum TP	0.183 (0.043 – 0.768)	0.0103	0.344 (0.152 – 2.26)	0.2025
Serum albumin	0.046 (0.005 – 0.434)	0.0071	0.131 (0.006 – 2.979)	0.0412
Kidney enlargement (Yes)	3.879 (0.837 – 17.969)	0.0831	1.698 (0.129 – 22.32)	0.687

CCI: Charlson comorbidity index; CI: confidence interval; CRP: C-reacted protein; DM: diabetes mellitus;
ECOG PS: The Eastern Cooperative Oncology Group performance status; TP: total protein

4. Discussion

The population of Japan is aging rapidly likewise other civilized nations. Therefore, increasing number of elderly patients with APN without obstructive uropathy is a critical problem. These patients are often advancing severity. Similarly, our patient characteristics showed aging and severe general condition. In fact, approximately half of patients were managed as sepsis because they all presented SIRS at the first visit. On the other hand, most patients with APN without obstructive uropathy are managed by non-urologists and residents in regional medical treatment. Therefore, it is difficult to diagnose such severe pyelonephritis using ultrasound which is known as appropriate imaging diagnostic method for uncomplicated APN. In such situation, the importance of diagnostic method using CT scan is emphasized. Our study was focused on the management of elderly patients with severe APN without obstructive uropathy.

In this study, we defined five abnormal plain CT findings that can easily be evaluated in the radiographic diagnosis. Our study demonstrated that the most common CT findings were perirenal fat stranding and thickening of perirenal fasciae in 72.9% and 71.4% of the cases, respectively. Renal parenchymal inflammation causes perirenal tissue changes that are recognized as perirenal fat stranding and thickening of perirenal fasciae. Kim et al. investigated the relationship between "uncommon CT findings" and clinical aspects in APN; however, the most common CT finding was perirenal fat infiltration (55% of cases) [7]. Our results and previous

studies suggest that the perirenal tissue change detected by CT scanning is a common pathogenesis of APN. Although the patient cohort had APN without obstructive uropathy, which was defined as APN without retention of urine passage from the anatomical and the physiological aspects, dilation of renal pelvis was seen in 37.1% of cases. Deteriorated ureter peristalsis caused by inflammation, a well-known pathophysiology of APN might cause dilation of the pelvis.

In the analysis of the association between abnormal CT findings and clinical nominal factors, our results demonstrated a positive relationship between perirenal fat stranding and dilation of renal pelvis with female gender and DM, respectively. The disease rate of APN was four-to five-fold higher in female patients from a large US database [8]. Similarly, our patient cohort showed female predominance (87.1% of cases). Therefore, the significant association between CT abnormal findings and female gender is not conclusive because of the small sample size with a low rate of male gender. With regard to DM, it has been demonstrated that APN is five times more frequent in patients with DM than in non-DM patients and could lead to complications in approximately 30% of cases [9, 10]. The significant high incidence of perirenal fat stranding in DM patients with APN without obstructive uropathy in our study suggests severe extension of inflammation and indicates there are therapeutic difficulties.

In the analysis of the association between abnormal CT finings and clinical continuous factors, one to three hematological inflammation markers (CRP, PLT, and TP) were significantly deteriorated in cases with perirenal fat stranding, thickening of perirenal fasciae, kidney enlargement or abnormal density of renal parenchyma. Kim et al reported on predictive severity of APN using nine criteria of abnormal CT scan findings and clinical factors that were indicated by the retrospective analysis of 193 APN patients [11]. In their study, global renal enlargement and abscess were part of the inclusion criteria. Although these two findings were obtained by enhanced CT scanning, it was possible that our findings of kidney enlargement and an abnormal renal parenchyma density correspond to global renal enlargement and abscess, respectively, in the previous study. In our four abnormal CT findings that were significantly associated with hematological inflammation markers, only perirenal fat stranding was associated with deterioration of all three markers (CRP, PLT, and TP). Therefore, perirenal fat stranding, which was a relatively frequent finding in our study, suggests the serious condition of APN.

All patients in our cohort were treated in the hospital. Pertel et al. reported on several risk factors, including hospitalization at baseline, for a poor outcome after therapy in outpatients and inpatients with uncomplicated APN [12]. Therefore, our patient cohort could be considered intractable to treatment. We emphasized the period until afebrile in such a characteristic patient cohort because afebrile status enables us to discharge patients from the hospital. Our study demonstrated that the age-adjusted CCI (5 ≤) and a lower

value of the serum albumin were independent factors affecting the prolonged duration until patients were afebrile. Although the serum albumin level is influenced by multifactorial factors, including inflammation progression of APN, these two independent factors are related to the host intrinsic features. Host intrinsic features, rather than direct inflammation, in APN were indicated as intractable factors for treatment in a previous study on an inpatient cohort in which prolonged hospitalization was noted among men and women with DM, long-term urinary catheterization, and a change in the initial antimicrobial therapy [13]. Careful observation and evaluation of patient characteristics in addition to hematological and radiographic inflammation findings at admission should be performed in APN.

The study has some limitations. First, the choice and method (intravenous or oral administration) of antibiotic agents depended on the policy decision of the physician in charge. A strict protocol for antibiotic therapy was not chosen. Therefore, it is possible that the period until the patients is afebrile might be affected by the skill of the physician in charge. However, this influence might be limited because the basic policy is that antibiotic agents should be selected based on the blood and urine bacterial culture results throughout the study period. Other limitations include the retrospective nature of the study and small sample size.

5. Conclusion

The assessment of APN without obstructive uropathy using initial plain CT scanning is a useful diagnostic method in patients who are treated in the hospital setting because of poor general condition, comorbidities and/or elderly age. Although abnormal plain CT scan findings at diagnosis are associated with clinical characteristics, the patient's intrinsic factors are more useful in predicting the disease outcome in APN without obstructive uropathy.

Conflict of Interest Statement

The authors declare that they have no competing interests.

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