



## Clinical characteristics of emphysematous pyelonephritis

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A total of 21 patients (20 women and one man) with emphysematous pyelonephritis (EPN), treated in the Kaohsiung Veterans General Hospital during the period from 1991 through 1999 were included in this study. All of the patients were diabetic. The most common symptoms or signs were fever/chills (80%) and costovertebral angle knocking pain (71%). Diagnosis was confirmed by the presence of gas in the parenchyma or paranephric space on plain X-ray of the abdomen or computed tomography. The left kidney (11 cases, 52%) was more frequently affected than the right one (nine cases, 43%), and both kidneys were involved in one case. Obstruction of the corresponding renoureteral unit was found in 19% of the patients, and renal or ureteral stone was found in 23% of the patients. One third of the patients had type I EPN, and two-thirds had type II EPN. *Escherichia coli* was the most commonly isolated organism, accounting for 61%, 76%, and 47% of isolates from blood, urine, and aspirated pus culture respectively. Prompt control of blood sugar was begun and intravenous antibiotics were given. Drainage was performed in 71% of the patients, and two persons required nephrectomy because of poor control of the infection or complications. Overall survival was 72%. Emphysematous pyelonephritis is a rare, life-threatening, suppurative infection of the renal parenchyma and perirenal tissues. For successful management of EPN, appropriate medical treatment should be initiated, and immediate nephrectomy or drainage should not be delayed.

**Key words:** Diabetes mellitus, emphysematous pyelonephritis

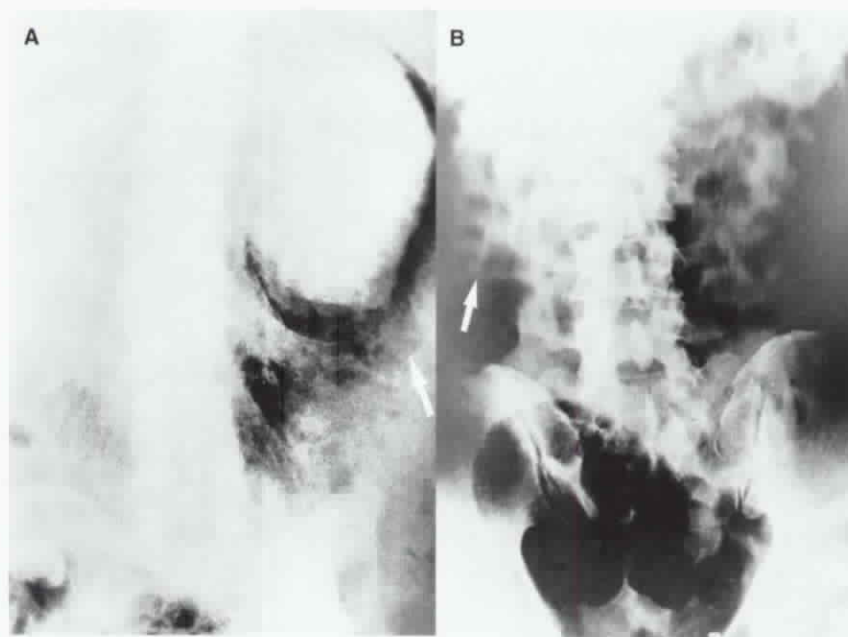
Emphysematous pyelonephritis (EPN) is a rare but life-threatening acute suppurative infection of the kidney characterized by production of gas within the renal parenchyma, collecting system, or perinephric tissue. Since the first case reported by Kelly and MacCullum [1] in 1898, more than 180 cases of EPN have been reported in the literature. Of the cases, 60% to 70% are associated with uncontrolled diabetes mellitus (DM), with or without obstructive uropathy and superimposed with infection caused by gas-forming organisms [2]. The lack of a strict definition of this severe infection has resulted in the use of a multiplicity of terms, which include renal emphysema, pneumonephritis, pyelonephritis emphysematosa, and pneumonephrogram. The term emphysematous pyelonephritis was recommended by Schultz and Klorferro [2] due to its stress on the relationship between the gas formation and acute infectious process. In this study, we analyzed the characteristics of 21 patients with EPN, with respect to

their underlying diseases, clinical presentation, microbiological findings, treatment modality, outcome, and prognostic factors.

### Materials and Methods

The Kaohsiung Veterans General Hospital is a 1000-bed medical center in Southern Taiwan. All patients with a discharge diagnosis of pyelonephritis (ICD-9-CM: 590.10; 590.80) during the period from 1991 through 1999 were included in this study. A total of 1304 patients were included based on the findings from a computer-generated list. Patients with a clinical diagnosis of pyelonephritis or any gas in the parenchyma, or paranephric space by either plain X-ray of the abdomen or computed tomography (CT) were included in the study. Patients who had a non-gas forming intrarenal abscess or pararenal abscess were excluded. All specimens from blood and aspirated pus were sent for aerobic and anaerobic culture, and urine was sent for aerobic culture. The charts were reviewed; data on complete medical history, physical examination, and results of laboratory investigations were recorded. Blood sugar controlled at less than 180 mg/dL, or a glycated hemoglobin (HbA<sub>1c</sub>) level of less than 9%,

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**Fig. 1(A)** A 42-year-old woman with left side emphysematous pyelonephritis (EPN). Gas shadow (arrow) around left kidney and blunting of psoas muscle shadow was noted from Kidney Ureter Bladder (KUB). **(B)** Another patient with right EPN. KUB only disclosed a mottling pattern over the right renal fossa (arrow).

was defined as fair control. Patients whose condition was complicated with diabetic ketoacidosis (DKA) or nonketotic hyperosmolar syndrome (NKHS) were defined as having poor control of blood sugar. All patients were followed up for about 6 to 12 months. Data on the types of medical and surgical management, imaging, clinical course, and outcome were also recorded. All patients were categorized into two groups, type I or type II. Type I EPN was defined as renal necrosis with either total absence of fluid content on CT or the presence of a streaky/mottled gas pattern demonstrated on radiograph or CT with lung window display (Fig. 1). Type II EPN was defined as either the presence of renal/perirenal fluid in association with a bubbly/loculated gas pattern, or by the presence of gas in the collecting system (Fig. 2) [3]. All CT images were jointly reviewed by a radiologist and a urologist. Statistical comparisons were performed with Mann-Whitney U test and Fisher's exact test, and a *p* value less than 0.05 was considered to be statistically significant.

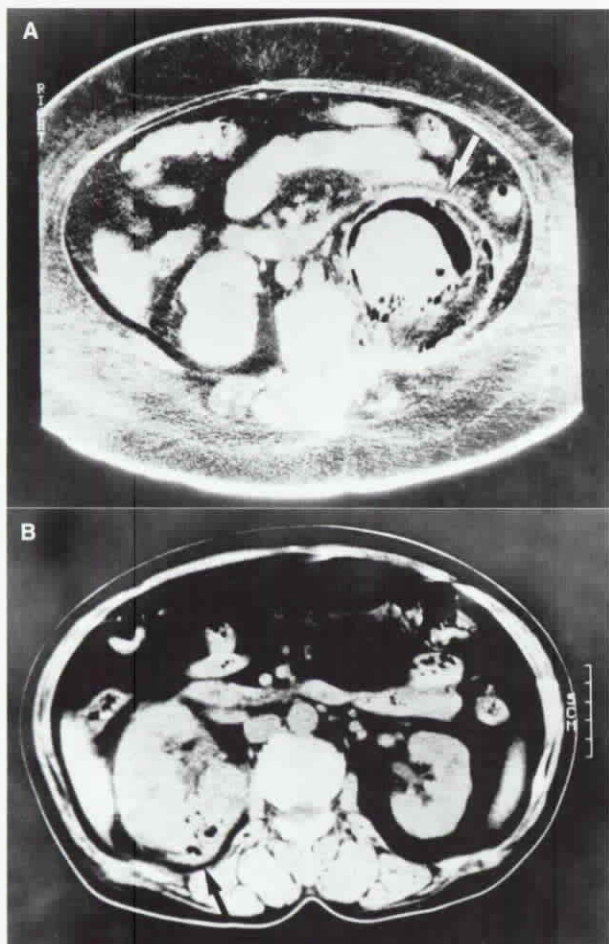
## Results

### Clinical data

Because the charts of 10 patients were not available, we reviewed the discharge diagnosis of these 10

patients. A diagnosis of EPN was not identified in any of these 10 patients. Overall, 21(1.6%) patients were included in this study. The underlying diseases, and demographic and clinical characteristics of the patients with EPN are summarized in Table 1. There were 20 women and one man with a median age of 66 years (range, 39-75 years). All patients were diabetic. Fair control of diabetes was maintained in 15 (71%) patients. The disease involved the left kidney in 11 patients (52%), right kidney in nine patients (43%), and both kidneys in one patient. Of the patients, 33% were classified as having type I EPN and 67% as type II. The most common underlying diseases included hydronephrosis or corresponding obstructive uropathy in four patients (19%), stone in five (24%), cervical cancer in two (10%), and transitional cell carcinoma of the urinary bladder in one (5%). The symptom duration before admission ranged from 1 to 30 days (median, 5 days). The median duration of hospitalization was 24 days (range, 5-46 days).

The median age of patients with type II EPN was 12.5 years older than that of patients with type I EPN, and the median delay in diagnosis was 3.5 days longer in patients with type II EPN. The left side kidney (65%) was more commonly involved in type II EPN, and the right side more commonly involved in type I EPN. The median duration of hospitalization was longer in



**Fig. 2(A)** For the same patient of Fig. 1A, an abdominal CT revealed gas and pus around the renal parenchyma and perirenal space (arrow). This patient was classified as having type II EPN. **(B)** In the same patient as in Fig. 1B, an intrarenal gas pattern was revealed which distributed over the posterior pole of the right kidney (arrow). No perirenal or pararenal space involvement was seen. This case was classified as type I EPN.

patients with type I EPN. The incidence of other factors such as poor control of blood sugar complicated with DKA or NKHS, genitourinary tract stone, malignancy, corresponding obstructive uropathy, and liver cirrhosis were not significantly different between the two groups.

Clinical presentations included fever/chills (80%), flank knocking tenderness (71%), lethargy or confusion (47%), nausea/vomiting (10%), and abdominal mass (5%). The most commonly encountered symptoms of urinary tract infection such as dysuria or frequency (10%) were only infrequently found in both types of EPN.

Fever/chills and costovertebral knocking tenderness were the most common symptoms in both types of EPN, whereas patients with type II EPN developed drowsiness and nonspecific symptoms, such as general

weakness, poor appetite, diarrhea, decreased urine output, and unstable blood pressure significantly more frequently than patients with type I EPN. Abdominal or flank pain occurred more frequently in patients with type I EPN.

#### Laboratory and radiological data

A plain X-ray of the abdomen was obtained in all patients but was diagnostic in only 47% of patients. Ultrasonography was performed in 17 patients and confirmed the presence of EPN in 14 patients (82%). Computed tomography was performed in all patients and all scans were diagnostic for EPN.

Pyuria was diagnosed in 18 (86%) patients (uncentrifuged urine WBC  $\geq 10$  cells per high-power field and bacteriuria in 17 (81%) patients). The white blood cell (WBC) counts, platelet counts, urinary red blood cell (RBC) counts, serum creatinine level, and blood sugar on admission were comparable between patients with type I and II EPN. We also compared clinical and laboratory data between surviving and nonsurviving patients and found that the nonsurviving patients had higher urinary RBC counts ( $p = 0.045$ ,  $p$  value is calculated by Mann-Whitney  $U$  test). The serum creatinine level, platelet counts, blood sugar, and WBC counts were not significantly different between these two groups.

#### Microbiologic data

Blood and urine cultures were obtained from all patients, and aspirated pus from 15 patients. *Escherichia coli* was the most commonly isolated organism and was isolated in 90% of the patients, accounting for 62%, 76%, and 67% of the isolates from blood, urine, and aspirated pus culture, respectively. Polymicrobial infection occurred in one patient who had *Pseudomonas aeruginosa* isolated from the blood culture, *Klebsiella pneumoniae* from the urine culture, and mixed organisms (*K. pneumoniae*, *Proteus mirabilis*, Group D *Streptococcus*, and coagulase-negative *Staphylococcus*) in the culture of the aspirated pus. Another patient had *Candida* spp. isolated from a pus specimen 2 weeks after admission, which was thought to be a superinfection, because *E. coli* grew in blood and urine cultures simultaneously at admission. Among the 21 patients, the same pathogen (*E. coli*) was isolated in blood, urine, and aspirated pus in only six patients. In the remaining patients, *E. coli* was isolated from one or two of the three culture sites. Only one patient was culture-negative in all specimens. The 19 strains of *E. coli* isolated had similar antibiotic susceptibility, which included susceptibility to ampicillin (5%), carbenicillin

**Table 1.** Clinical characteristics of 21 patients with emphysematous pyelonephritis

Characteristic	No. (%) of patients			<i>p</i>
	Type I (n = 7)	Type II (n = 14)	Total (n = 21)	
Gender				
Male/Female	0/7	1/13	1/20	0.667
Median age (mean ± SD)	56 (56.7 ± 7.1)	68.5 (64.5 ± 12.0)	66 (61.9 ± 11.1)	0.056
Median delayed days <sup>4</sup> before diagnosis (mean ± SD)	7.5 (4.1 ± 2.4)	5 (15.3 ± 25.6)	(11.6 ± 21.4)	0.094
Side				
Right	5 (71)	4 (29)	9 (43)	0.080
Left	2 (29)	9 (65)	11 (52)	0.142
Bilateral	0 (0)	1 (6)	1 (5)	0.667
Median days of hospitalization (mean ± SD)	32 (33 ± 9.8)	20.5 (22.3 ± 13.0)	24 (25.9 ± 12.9)	0.067
Underlying diseases				
Diabetes mellitus	7 (100)	14 (100)	21 (100)	-
DKA or NKHS	3 (42)	3 (21)	6 (29)	0.299
GU tract stone	1 (14)	4 (28)	5 (24)	0.443
Malignancy	0 (0)	3 (21)	3 (14)	0.274
Obstructive uropathy	0 (0)	4 (28)	4 (19)	0.443
Liver cirrhosis	0 (0)	1 (7)	1 (5)	0.667

Abbreviations: DKA = diabetic ketoacidosis; NKHS = nonketotic hyperosmolar syndrome; GU = genitourinary

(5%), piperacillin (5%), chloramphenicol (5%), minocycline (5%), trimethoprim/sulfamethoxazole (26%), cefazolin (90%), cefuroxime (100%), ceftazidime (100%), ceftriaxone (100%), ceftazidime (100%), imipenem (100%), ciprofloxacin (100%), and gentamicin (100%), and amikacin (100%). Only one strain isolated from pus was susceptible to all antibiotics.

### Treatment and outcome

A prompt attempt to control diabetes was made in all patients. All patients received adequate fluid resuscitation plus a combination of antibiotics, usually a cephalosporin and an aminoglycoside. Six (29%) of the patients received medical therapy and 13 (62%) received medical therapy with percutaneous drainage. Only two (9%) patients required surgical intervention

in addition to medical therapy and drainage. Surgery was performed as a result of pseudoaneurysm formation in one patient and in another because of poor response to medical therapy and percutaneous drainage. Relapse of EPN occurred months later in three (14%) patients, and five (23%) patients developed complications related to EPN, which include nosocomial pneumonia, empyema of lung, pseudoaneurysm of abdominal aorta, and osteomyelitis of the thoracic spine. The overall mortality rate was 28% (Table 2).

Medical therapy alone was given in three (43%) of seven patients with type I EPN and three (21%) of 14 patients with type II EPN. One third of patients died in both groups. In contrast, no mortality occurred among patients with type I EPN who received percutaneous drainage in addition to medical therapy. A mortality rate of 40% was observed, however, among patients with

**Table 2.** Clinical outcome in 21 patients with emphysematous pyelonephritis

Treatment	Outcome		<i>p</i>
	Type I, n = 7 Survival/Total (%)	Type II, n = 14 Survival/Total (%)	
Medical treatment alone	2/3 (66)	2/3 (66)	
Medical treatment + drainage	3/3 (100)	6/10 (60)	
Medical treatment + drainage + surgery	1/1 (100)	1/1 (100)	
Total	6/7 (86)	9/14 (64)	0.31

type II EPN receiving the same therapy. One patient in each group required surgical intervention, and no mortality occurred in these patients. Overall, the mortality rate for type II was 36% and 14% for type I. The difference between the type I and II mortality rate was not statistically significant ( $p = 0.31$ ).

## Discussion

Emphysematous pyelonephritis is a relatively uncommon, severe, necrotizing infection of the kidneys characterized by the presence of gas within the renal parenchyma. This potentially life-threatening condition is associated with DM [3], although it has also been reported in nondiabetics [4]. The presence of gas in the genitourinary tract is most often resulted from an etiology involving tumor embolization, trauma, endoscopy (transurethral resection of prostate), and fistula communicating with the gastrointestinal tract, or is produced by bacteria [5,6]. This disease affects women more commonly than men, as in results of the present study, presumably because of their increased susceptibility to urinary tract infection [7], although in Japan it appears to be more common in men [8].

The factors that may be involved the pathogenesis of EPN are as follows: 1. High level of tissue glucose; 2. The presence of glucose-fermenting bacteria (gas-forming coliform bacteria); 3. Impaired vascular supply with decreased tissue perfusion; 4. Impaired host immunity with a defective host defense mechanism; and 5. Obstruction of the urinary tract in non-DM patients [9,10]. Pyelonephritis in a diabetic kidney associated with renal ischemia results in a low oxygen tension, which induces anaerobic metabolism. Organisms such as *E. coli*, *P. mirabilis*, and *K. pneumoniae* are facultative anaerobes that are able to ferment glucose to lactate and carbon dioxide. On the other hand, despite their known propensity for gas production, anaerobic pathogens had little or no role in the pathogenesis of EPN. Only rarely has there been a case report of EPN induced by anaerobic species such as *Clostridium septicum* [12]. *Candida albicans*, *Cryptococcus neoformans*, and *Pneumocystis carinii* [13,14] have also been occasionally identified as the pathogens. In this study, *E. coli* was the most commonly isolated pathogen. *E. coli* was cultured from the blood, aspirated pus, and urine in most patients (90%), with the same susceptibility when isolated at different sites in the same patient.

The most common underlying disease in patients with EPN is diabetes. EPN usually occurs in patients with established DM, but it could also be the presenting feature of diabetes. The severity of the condition is not

related to whether the patient is insulin-dependent or not. Insulin dependence has no prognostic significance for EPN [11]. In this study, DKA or NKHS (29%) was also common, but these complications were not significantly related to mortality.

In 1997, Wan *et al* [15] reported that type I EPN is associated with more extensive parenchymal necrosis, a more fulminant clinical course, and a higher mortality than type II EPN. The pathological findings of type I EPN include necrosis, hemorrhagic infarction, and a fragile and spongy kidney with honeycomb-like gas containing spaces. Microscopic pathology reveals vasculitis, microscopic abscess, and infarction. These findings may be reflective of disseminated intravascular coagulation leading to renal thrombosis. Pathologically, type II EPN is characterized by diffuse infiltration of acute and chronic inflammatory cells, exudate, abscess formation, and necrosis. The streaky/mottled gas pattern and absence of exudative response in patients with type I EPN may reflect a defective immune reaction in the host, whereas the presence of exudate in patients with type II EPN suggests a better host immunity and hence a more favorable prognosis [11]. In this study, however, a higher mortality rate was observed in type II EPN compared to type I EPN. This result could be attributed to the fact that our patients with type II EPN were older, more complicated, presented with more underlying malignancy, corresponding obstructive uropathy, greater delay in diagnosis before admission, and initial sepsis and septic shock.

In the same study, Wan *et al* [15] also found three laboratory results that are predictors of the clinical course. They found that patients with elevated platelet counts, lower serum creatinine level, or low urinary RBC counts had good prognosis. Findings in this study were different from their results—only urinary RBC counts could predict the prognosis ( $p < 0.05$ ). These differences might have been resulted from an insufficient sample size in this study. The severity of hematuria in patients with EPN might partly reflect the degree of necrosis or destruction of the kidney as a result of infectious process and the presence of renal vein thrombosis.

Generally, the most useful diagnostic tool for EPN is abdominal CT scan. In this study, an abnormal gas pattern on abdominal X-ray was noted only in 47% of patients; CT scan was always diagnostic and could serve as the diagnostic tool for classifying type I and II EPN. Although ultrasonography usually confirmed the presence of intraparenchymal gas (82% in our study), its main role was to exclude ureteral obstruction. Because many of the patients were obese, it was often

difficult to distinguish a necrotic gas-filled kidney from gas in the bowel on ultrasound.

Most of the patients in this study had unilateral EPN, and only one of them had bilateral EPN. Seventeen cases of bilateral EPN have been previously reported. The clinical presentation of bilateral EPN is similar to unilateral EPN [16]. The mortality of bilateral EPN was higher than that in unilateral EPN, and more aggressive surgical or percutaneous drainage was indicated. However, the only patient with bilateral EPN in this study survived after medical therapy and percutaneous drainage.

Before the advance of invasive radiology, surgery was the gold standard for treating EPN. In 1996, Chen *et al* [17] reported that antibiotic therapy combined with CT guided percutaneous drainage of EPN was an acceptable alternative to antibiotic therapy with surgical intervention. In this study, most patients received medical and percutaneous therapy. Only two patients required further nephrectomy because of pseudoaneurysm formation; both survived.

In conclusion, patients with EPN in this study were mostly diabetic women, and *E. coli* was the most commonly isolated pathogen. The most common presenting symptoms were fever, chills, and flank pain. Urinary RBC count can be used as a prognostic indicator in EPN. A poor response to antibiotic therapy in diabetic patients thought to have uncomplicated pyelonephritis should raise the suspicion of EPN and prompt further investigation using a variety of imaging studies. Because of its high mortality rate, intensive blood sugar control, antibiotic therapy, percutaneous drainage and even surgery should be aggressively pursued in the management of EPN.

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