Asian Journal of Surgery (2013) 36, 121–125

Available online at www.sciencedirect.com

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ORIGINAL ARTICLE

Emphysematous pyelonephritis: An 8-year retrospective review across four acute hospitals

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Received 3 January 2012; received in revised form 7 December 2012; accepted 9 January 2013
Available online 15 March 2013

KEYWORDS
emphysematous pyelonephritis;
diabetes;
kidney infection;
nephrectomy;
pyelonephritis;
urosepsis

Summary *Objective:* To retrospectively review our experience of managing patients with emphysematous pyelonephritis (EPN).
Methods: Case notes of patients with EPN were reviewed. The patients' demographic data, clinical presentation, investigation findings, treatment, and outcome were studied.
Results: Twelve patients were diagnosed with EPN. Majority (66.7%) of them had diabetes mellitus. All patients had been evaluated by computed tomography (CT). Using the classification proposed by Wan et al, five patients had type 1 EPN, whereas six, two, and four patients had Huang and Tseng CT class 2, 3a, and 3b EPN, respectively. Immediate nephrectomy was performed in six patients, whereas conservative treatment was adopted in the other six. In the nephrectomy group, one patient died of disseminated sepsis after a protracted course. Conservative treatment failed in three patients, who succumbed despite salvage nephrectomy in two of them. Analysis revealed that severe hyperglycemia and radiological CT class (both Wan and Huang systems) were significant predictors of mortality from EPN.
Conclusion: Severe hyperglycemia and CT class of EPN are significant risk factors for death. CT is the investigation of choice for correct diagnosis of EPN. Additional intervention should be offered to EPN patients with Wan type 1 and Huang and Tseng class 3 CT features.

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http://dx.doi.org/10.1016/j.asjsur.2013.01.003

1. Introduction

Emphysematous pyelonephritis (EPN) is defined as an acute, severe necrotizing infection of the renal parenchyma and its surrounding tissues, which results in gas formation in the renal parenchyma, collecting system, or perinephric tissue.[1] It was first reported in 1898 by Kelly and MacCallum,[2] and the term "emphysematous pyelonephritis" was coined by Schultz and Klorfein[3] in 1962 to describe this serious infection. It is an uncommon but serious condition with deaths primarily attributed to septic complications. Mortality rates up to 40–50% have been reported in published series.[4,5] Although it is most commonly seen in diabetic patients, EPN has been reported in patients with ureteral obstruction and immunocompromised conditions.[1,6–9]

The conventional treatment of EPN has historically been surgery via open drainage and/or nephrectomy along with antimicrobial therapy. The ideal management, however, remains controversial. Herein, we present our 8-year experience of management of EPN with analysis for risk factors for poor outcome.

2. Patients and methods

The details of patients with the diagnosis of "pyelonephritis" or "pyonephrosis" and had computed tomography (CT) scans performed within the same admission in four acute hospitals in Hong Kong (Princess Margaret Hospital, Caritas Medical Centre, Kwong Wah Hospital, and Yan Chai Hospital) were retrieved from a computer database. Their case records were reviewed to identify the presence of symptoms or signs of upper urinary tract infection and the presence of gas in the renal collecting system, parenchyma, or perinephric or paranephric space as demonstrated on CT, in order for these patients to be considered as suffering from EPN. Patients with known fistula between the gastrointestinal and urinary tracts and patients with a recent history of penetrating trauma, catheter, or needle insertion to their kidneys were excluded. The included patients' clinical presentation, investigation findings, treatment modalities, and outcomes were reviewed.

The patients were categorized into two groups depending on whether they survived or died from EPN: survivors and nonsurvivors. Demographic factors (age, gender, background, diabetes mellitus), clinical factors on presentation (symptom duration, septic shock, azotemia, thrombocytopenia, hypoalbuminemia, prolonged prothrombin time, severe hyperglycemia), radiological data (initial imaging modality, CT classification), and treatment methods (medical or surgical) were compared between the two groups. In total, 14 factors were analyzed in order to identify the risk factors for adverse clinical outcomes. Azotemia is defined as serum creatinine greater than 2.5 mg/dL. Thrombocytopenia is defined as platelet count less than 150×10^9/L. Hypoalbuminemia is defined as less than 25 g/dL. Severe hyperglycemia is defined as blood glucose >20 mmol/L. For radiologic staging, we used the classifications proposed by Wan et al[10] and Huang and Tseng[11] in 1996 and 2000, respectively. The former system classifies EPN with parenchymal destruction with an absence of fluid collection as Type 1, whereas those EPN with either renal or perinephric fluid collection were classified as Type 2, with Type 1 having a more fulminant clinical course. The latter system classifies EPN into four classes: Class 1—gas in the collecting system only; Class 2—gas in the parenchyma without extension into extrarenal space; Class 3a—extension of gas or abscess into the perinephric space; Class 3b—extension of gas or abscess into the pararenal space; and Class 4—bilateral EPN or EPN in a solitary kidney. Huang and Tseng[11] showed a tendency toward higher mortality and failure rate of percutaneous catheter drainage (PCD) from Class 1 to Class 4 EPN.

Chi-square and Fisher's exact tests were used to compare the categorical variables, and Mann–Whitney *U*-test was used to compare the continuous variables. Statistical significance was accepted when $p < 0.05$, and analysis was performed using SPSS version 19 (SPSS Inc., Chicago, IL, USA).

3. Results

From January 2003 to October 2011, 12 patients were diagnosed with EPN using CT. Their mean age was 64.3 ± 13.7 (range 39–87) years, with male/female ratio being 5:7. Eight patients (66.7%) were known to be diabetic. Among the nondiabetics, one patient was debilitated and bedridden owing to spastic paraplegia, two patients had nonfunctional renal units due to urolithiasis, and one patient suffered from active ureteral obstruction by a small calculus. The mean duration of symptoms before admission was 4.7 ± 3.1 days, and the most common symptom was fever. Other symptoms included loin pain (33.3%), hematuria (8.3%), and palpable mass (16.7%). On presentation, three patients (25%) had septic shock, one of whom also required immediate hemodialysis for acute renal failure.

The patients' abnormal laboratory results are shown in Table 1. Seven patients received ultrasonography as their first dedicated renal imaging, whereas the rest had CT scans. However, the presence of gas was missed in three of these seven patients (42.9%), and their diagnoses of EPN were only established with subsequent CT scans. All cases of EPN were correctly diagnosed on CT. Radiologically, the left and right kidneys were affected roughly equally (L/R = 7:5), and no patient had bilateral EPN. Using the CT systems proposed by Wan et al and Huang and Tseng, our

Table 1 Abnormal laboratory results of 12 patients with EPN.

Laboratory test result	Patients, *n* (%)
Hemoglobin <11 g/dL	6 (50)
White cell count >10 × 10^9/L	9 (75)
Thrombocytopenia	7 (58.3)
Azotemia	7 (58.3)
Alkaline phosphatase >120 IU/L	12 (100)
Hypoalbuminemia	10 (83.3)
Prolonged PT	8 (66.7)
Severe hyperglycemia	3 (25)

EPN = emphysematous pyelonephritis; PT = prothrombin time.

cohort of EPN patients can be classified into different types as shown in Table 2.

After the diagnosis of EPN was made, six patients underwent immediate nephrectomy, whereas conservative treatment in the form of close observation and parenteral antimicrobials only were adopted in the other six (one patient refused surgery). All patients in the former group had their source of sepsis removed successfully by nephrectomy. Intraoperatively, there was gross involvement of contiguous organs by the suppurative process in two patients (iliopsoas muscle and liver, respectively). Two patients required temporary hemodialysis, whereas one patient became permanently dialysis-dependent after nephrectomy. He was subsequently put on long-term peritoneal dialysis. Of these six patients, one died after a protracted postoperative course from disseminated sepsis with multiple medical complications in the postoperative period including cerebrovascular accident and deep vein thrombosis. The other five patients survived to be discharged.

Of the six patients placed on initial conservative treatment, three deteriorated clinically with one succumbing shortly before any surgical intervention could be offered. The other two patients underwent emergency nephrectomy as salvage successfully, but both patients' condition continued a rapid downhill course postoperatively and they expired shortly after surgery. The other three patients who were managed conservatively improved with complete resolution of clinical and laboratory parameters. Two survived to be discharged, whereas one died of sudden myocardial infarction during convalescence 54 days after her admission.

Microbiologically, positive growth was obtained from either urine or blood culture in 10 patients with culture not performed in two patients. The most common organism isolated was *Escherichia coli* (60%), followed by *Klebsiella* (20%), *Citrobacter* (10%), *Enterococcus* (10%), and *Proteus* species (10%). Of the eight patients with nephrectomy performed, pathology of the specimen revealed severe pyelonephritic changes in all of them.

By comparing the risk factors between the patients in our cohort who survived and died from their EPN, we found severe hyperglycemia on presentation and radiological CT class of the EPN (both the Wan and Huang and Tseng systems) to be the only predictors of mortality ($p = 0.018$, 0.01, and 0.041, respectively). The analyses are shown in Table 3.

Table 2 Radiological profile of 12 patients with EPN and their respective treatment.

CT classification	Conservative	Nephrectomy	Total, *n* (%)
Wan et al			
Type 1	3	2	5 (41.7)
Type 2	3	4	7 (58.3)
Huang and Tseng			
Class 2	2	4	6 (50)
Class 3a	2	0	2 (16.7)
Class 3b	2	2	4 (33.3)

EPN = emphysematous pyelonephritis.

Table 3 Comparison of variables between survivors and nonsurvivors from EPN.

Variable	Survived EPN	Died from EPN	*p*
Age	61.5 ± 12.1	70 ± 16.7	0.409
M/F	4:4	3:1	0.576
Diabetes mellitus	5	3	1.000
Symptoms duration	5.3 ± 3.7	3.5 ± 0.6	0.233
Septic shock	2	1	1.000
Azotemia	4	3	0.576
Thrombocytopenia	4	3	0.576
Hypoalbuminemia	7	3	1.000
Prolonged PT	5	3	1.000
Severe hypoglycemia	0	3	0.018
Initial ultrasonography	5	2	1.000
Radiological staging (Wan et al)			
Type 1	1	4	0.010
Type 2	7	0	
Radiological staging (Huang and Tseng)			
Type 2	6	0	0.041
Type 3a	1	1	
Type 3b	1	3	
Treatment			
Medical treatment	3	3	0.545
Immediate nephrectomy	5	1	

EPN = emphysematous pyelonephritis; PT = prothrombin time.

4. Discussion

EPN is an uncommon but potentially life-threatening urologic emergency. Factors involved in its pathogenesis include high levels of glucose within the tissues, presence of gas-forming organisms, impaired vascular supply, reduced host immunity, and the presence of obstruction in the urinary tract.[12] High levels of tissue glucose coupled with impaired tissue blood supply are commonly seen in diabetics, and this explains the condition's strong association with diabetes mellitus. Similar to other published series, the majority of the patients (66.7%) in our cohort suffered from diabetes mellitus.[10,11,13] However, it is noteworthy that although the random glucose of all diabetic patients were raised, only three presented with severe hyperglycemia of >20 mmol/L. From the literature, there is a preponderance of EPN in females, owing presumably to their increased susceptibility to urinary tract infection.[8,10,13] The female/male ratio of our cohort is similar to that reported by Dhabalia et al, but much higher ratios have been reported previously.[7,14] In line with other series, the majority of our patients presented with fever with or without loin pain. On average, our patients had symptoms for 4 days or more before admission. This may explain why in three patients, the infective process had lapsed into septic shock.

Laboratory data in our cohort conformed to those reported in the literature, with leukocytosis, thrombocytopenia, and renal impairment being the most common findings.[7,12,15] Similar to published series, the most common

causative pathogen in our cohort was *E. coli*, followed by other Gram-negative organisms.[5,16] Interestingly, all of our patients were found to have raised alkaline phosphatase. The reason for this is unknown, but may be due to transient liver function derangement as a result of the systemic inflammatory process. Elevated alkaline phosphatase is not uncommonly seen in previous reports of EPN.[17,18]

To reach a diagnosis of EPN, seven patients received ultrasonography as their first dedicated imaging of the kidney (but gas was missed in three patients), whereas the accuracy of CT in diagnosis was 100%. From published series, the accuracy of ultrasonography in diagnosing EPN ranged from 50% to 86% only, and CT has been recommended as the imaging of choice for early diagnosis of EPN.[7,10,15,19] The mean time from ultrasonography to subsequent correct diagnosis of EPN by CT among these three patients was 20.3 hours.

In 1996, based on CT findings in 38 patients, Wan et al[10] categorized EPN into two types, with Type 1 carrying a worse prognosis. In 2000, Huang and Tseng,[11] based on the extent of gas on CT in 48 EPN patients, also classified EPN into four radiological classes and proposed patient management based on the CT classifications. In our cohort, all patients received immediate medical management consisting of fluid resuscitation, parenteral antimicrobials, and glycemic control. This type of conservative management was used exclusively in six patients. Three patients (Wan system: three Type 1; Huang and Tseng system: one Class 3a and two Class 3b) deteriorated while on conservative treatment and two died despite salvage nephrectomy, translating to a 50% EPN-specific mortality. By contrast, early nephrectomy was adopted in the other six patients. Only one patient (Wan system Type 1 and Huang and Tseng system Class 3b) died of disseminated sepsis after surgery, resulting in a mortality of 16.7%. It is worth noting that none of our conservatively treated patients received additional minimally invasive treatment modalities such as PCD. In their original report, Tseng and Huang[11] advocated that antimicrobial therapy with PCD of the obstructed system should be adopted in all Type 1 to Type 2 EPN and selected Type 3 to Type 4 EPN with good prognosticators. In our cohort, one of the patients who did not respond to medical treatment had dilated pelvicaliceal system, and hence PCD might have been beneficial. Among the conservatively treated, all patients who were classified by the Wan system to have Type 1 EPN and three-quarters of the patients classified Type 3 EPN by the Huang and Tseng system did not respond to medical treatment alone and died. Based on the experience from our cohort, we thus advocate against exclusive medical treatment in EPN patients with CT features falling into these two groups.

The choice of treatment for EPN has long been a matter of debate. Early investigators noted that early aggressive surgical treatment resulted in a successful outcome, as compared with medical treatment alone.[8,20] In 1986, Hudson et al[21] first described the imaging-guided PCD treatment of EPN with good clinical results. Since then, many EPN series have reported favorable outcomes with PCD treatment, which has been accepted as the initial intervention of choice in the majority of EPN patient.[16,22,23] It has been stated that the focus of EPN management nowadays should not be mere survival improvement but also to maximize the change of renal salvage. In contrast to early reports, recent series of EPN have found a higher mortality resulting from early nephrectomy compared with an initial conservative approach consisting of antimicrobials and appropriate use of PCD.[15,17] However, investigators have cautioned against the universal use of PCD on all patients with EPN, with subsequent nephrectomy only if required. Akpek et al[24] reported that of the 19 patients who had percutaneous drainage attempted, the procedure failed in 11 of them, five of whom subsequently died. In Huang and Tseng's[11] series, 92% of the patients with poor risk CT Class 3 and Class 4 failed PCD treatment, with a mortality rate of 15%.

In our cohort, we found—similar to the earlier series—a higher mortality among conservatively treated patients as compared with those who received early nephrectomy. When we compared the outcome of patients who were conservatively treated to those who received early nephrectomy, although a larger proportion of patients died from conservative treatment, the difference did not reach statistical significance ($p = 0.545$). This is most likely attributable to our sample size in each arm. Analysis of patients who did or did not survive from EPN revealed that severe hyperglycemia (defined by blood glucose $>$20 mmol/L) and CT class of the EPN were significant predictors for EPN-related mortality, regardless whether the Wan or the Huang and Tseng system was used. Falagas et al,[25] in the largest meta-analysis of EPN series to date, concluded that conservative treatment (without PCD), Type 1 EPN using the Wan system, thrombocytopenia, and bilateral EPN were predictors for mortality. In a recent series, Kapoor et al[16] found altered mental status, thrombocytopenia, renal failure, and severe hyponatremia to be associated with higher mortality in EPN. Owing to the small size of our cohort, we did not find the said factors to be significant adverse prognosticators. By contrast, severe hyperglycemia has been identified as a predictor for EPN-related mortality in other series.[26] It has been proposed that high tissue level of glucose may be a risk factor for EPN to develop a more fulminant course in DM patients, because it can provide gas-forming microbes a favorable microenvironment for growth and rapid catabolism.[27,28] Clinically, in EPN patients, a finding of severe hyperglycemia likely reflects a mixture of the severe underlying sepsis and poor glycemic control. In line with previous reports, we found the different CT classes of EPN to be associated with outcome. Type 1 EPN according to the Wan system has been identified as an independent predictor for mortality in various reports.[10,11,25] A more advanced EPN stage according to the Huang and Tseng system has also been shown to have increased tendency toward mortality.[5,29] Clinicians encountering patients with EPN with these poor prognosticators should consider additional therapy besides medical treatment, for example, PCD (if indicated) or nephrectomy to remove the source of sepsis.

5. Conclusions

EPN remains a serious condition with significant mortality. CT is the best modality of dedicated renal imaging for its accurate diagnosis. Severe hyperglycemia, Type 1 CT class (Wan

system), and advanced CT class (Huang and Tseng system) are significant predictors for EPN-specific mortality. Additional therapy should be considered, besides medical treatment alone, in patients with Type 1 and Type 3 EPN according to the Wan and Huang and Tseng systems, respectively.

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