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Management of emphysematous pyelonephritis in a tertiary Centre: A case series review

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Abstract
Introduction: Emphysematous pyelonephritis (EPN) is an uncommon acute severe necrotizing infection of the kidney. This study describes the management of patients with EPN who were admitted to a tertiary center in Doha, Qatar.
Methods: This retrospective case series included all admitted patients who were diagnosed clinically and radiologically with EPN over a 5-year period. Their clinical presentation, risk factors, and management plans were analyzed.
Results: Over the 5-year study period, 26 patients, including 11 men and 15 women, were diagnosed with EPN. Diabetes mellitus was the most frequent risk factor, and *Escherichia coli* was the most common pathogen. Conservative management was successful in nine patients. The other 17 patients required early drainage, either by percutaneous nephrostomy or ureteral stenting, with two patients undergoing elective nephrectomy after stabilization of their septic condition. None of these patients died.
Conclusion: EPN usually occurs in adults with poorly controlled type 2 diabetes mellitus and obstructive ureteral stones. Early diagnosis and management with a multidisciplinary approach and minimally invasive drainage procedures reduces patient morbidity and mortality.

Keywords: emphysematous; pyelonephritis; urinary tract infection; stones

Introduction

Emphysematous pyelonephritis (EPN) is an acute severe necrotizing infection of the renal parenchyma, with or without involvement of the surrounding peri-renal tissue, and characterized by gas formation [1]. The first such patient was described in 1898 [2]. Because EPN involves severe infection, it may be complicated by sepsis and septic shock, leading to death. The mortality rate in patients with EPN was as high as 78% in the late 1970s [3]. Advances in ICU care, antibiotics and surgical techniques reduced the mortality rate from this condition to 13% [4], with a recent study reporting a mortality rate of 0.5% [5]. EPN diagnosis is based on clinical findings of severe pyelonephritis in addition to radiologic findings of gas formation within the renal parenchyma, collecting system and peri-renal tissue [6]. There is no consensus on the optimal management plan. Medical management alone has been reported successful [7], as have aggressive surgical management [8] and intense medical treatment aided by drainage using percutaneous nephrostomy [4] or double J ureteric stents [5]. Our center is an easily accessible government hospital that provides secondary and tertiary care and thus admits and treats patients with EPN. This study evaluated the management of EPN in our hospital over a 5-year period.

Methods

This retrospective descriptive study evaluated all patients admitted to our center for EPN from January 2014 to December 2018. The hospital database was searched for all patients aged ≥18 years who were admitted to our hospital with a radiological diagnosis of EPN.

Twenty-six cases were included. The demographic data, clinical presentations, and laboratory and radiologic findings of all included patients were evaluated. In addition, their management strategies were recorded, including whether they were conservatively managed with antibiotics alone or required surgical intervention, such as percutaneous nephrostomy, retrograde ureteric stenting or nephrectomy. Other factors recorded included ICU and hospital stay. EPN was radiologic classified as described by Huang and Tseng [12].

The management protocol at our center starts with active emergency management of any patients who are sick or suspected of having sepsis. After history taking and examination, blood and urine samples are collected for laboratory investigations, including complete blood count, renal function tests, albumin, C-reactive protein (CRP), and blood and urine cultures. Patients subsequently undergo radiologic imaging, using ultrasound or computed tomography (CT) scanning, with or without contrast, based on the suspected diagnosis. Patients are started on treatment with a broad-spectrum antibiotic, along with intravenous hydration and correction of any disturbances in electrolytes. Decisions on further interventions are made by the urologist on call. Patient improvement on follow up is based on clinical and radiologic findings.

Descriptive statistics were used to summarize all demographic and clinical characteristics. The means of all quantitative measurements were compared in two specified groups by unpaired t-tests. The associations between qualitative factors and patient outcomes were assessed by chi-square tests. Data were analyzed using SPSS V20.0 software, with P-values <0.05 considered statistically significant.

Results

Of the 28 patients identified in the database of our center, two

were excluded, one with air loculi in the renal pelvis after undergoing ureteroscopy who did not fulfill the clinical criteria of pyelonephritis, and the other who went home against medical advice before any treatment was initiated. Thus, 26 patients were analyzed. Their ages ranged from 21 to 83 years, with a mean age of 51 years. Of the 26 patients, 15 were women and 11 were men (1.4:1). Patients presented to the emergency department after a mean symptom duration of 3.0 ± 1.7 days. The main symptom at presentation was groin pain and fever; other symptoms are shown in the Table.

Of the 26 patients, 18 (69.2%) had type 2 diabetes, including 11 who had diabetes for more than 10 years, with poorly controlled hyperglycemia associated with microvascular complications. Other associated co-morbidities included hypertension in nine patients, chronic kidney disease in three, and coronary artery disease in five. Eight patients (30.8%) did not have any relevant medical history.

Urine cultures were positive in 16 patients (61.5%), including 11 positives for *Escherichia coli*, one for ESBL and one positive for both *E. coli* and *Enterococcus faecalis*. Two patients were infected with *Klebsiella pneumonia*, with one also infected with *Proteus mirabilis*. Other infecting organisms are shown in the Table.

Urinary stones were present in 16 patients, including 11 with obstructive and five with non-obstructive renal stones. One patient had a pelvi-ureteric junction obstruction.

Ten patients were placed in the ICU upon admission because of sepsis, reflecting the severity of their condition upon presentation. Six patients had septic shock, but none of these had a reduced level of consciousness or multi-organ failure.

Most patients were managed safely by antibiotics alone, with some also requiring ureteric stenting or percutaneous nephrostomy. Nine patients were managed conservatively with antibiotics. Nineteen required intervention in addition to antibiotics, including 12 who underwent percutaneous nephrostomy and seven who underwent retrograde ureteric stenting. Stenting, however, failed in one of the latter patients, resulting in percutaneous nephrostomy. Following stabilization of their septic conditions with antibiotics and percutaneous nephrostomy, two patients required elective nephrectomy for their poorly functioning kidneys. Only one patient required hemodialysis, with none requiring emergency nephrectomy to control sepsis. No patient died of EPN during the 5-year study period.

The mean hospital stay was 12 ± 5 days, with 14 patients remaining in hospital for more than 10 days. Analysis of factors possibly associated with prolonged hospital stay, including patient age, co-morbidities, history of previous UTI, fever upon presentation, leukocytosis, hypoalbuminemia, high CRP, radiologic classification of EPN, presence of stones and obstruction, found that none was prognostic of length of hospital stay.

Other descriptive data are presented in the Table.

Table 1: Baseline demographic and clinical characteristics of patients with emphysematous pyelonephritis (EPN)

Parameter			Number	Percentage
Gender	Female		15	58%
	Male		11	42%
Laterality	Right		11	42%
	Left		14	53%
	Bilateral		1	4%
Symptoms				
	Pain		26	100%
	Fever		25	96%
	LUTS		10	38%
	Oliguria		4	15%
	Vomiting		3	11.5%
	Pneumaturia		1	4%
History of UTI			6	23%
Medical history	None		8	31%
	Diabetes mellitus		18	62%
		Controlled	7	
		Poor control	11	
	Hypertension		9	35%
	CKD		3	11.5%
	CAD		5	19%
Leukocytosis				65%
Thrombocytopenia				26%
Hypoalbuminemia				96%
High CRP				94%
Positive MSU culture			16	61.5%
	Escherichia coli		11	
	Enterococcus fecalis		1	
	Klebsiella pneumonia		3	
	Proteus mirabilis		1	
	Streptococcus constella		1	
Urolithiasis			16	61.5%

Diagnostic imaging modality			
	Non-contrast CT	23	
	Contrast CT	3	
	Obstructive	11+1(PUJO)	
	Non-obstructive	5	
Management			
	Conservative (no drainage)	9	35%
	Retrograde stenting	6 (4 subjects +1 bilateral)	23%
	PCN	12	46%
	Hemodialysis	1	4%
	Elective Nephrectomy	2	8%
Antibiotics			
	Ceftriaxone	6	
	Tazocin “Piperacillin+Tazobactam”	5	
	Meropenem	15	
Hospital stay, days		12 +/- 5	

Discussion

EPN is an uncommon, severe fulminant disease resulting from acute necrotizing infection of the kidneys by gas forming organisms leading to sepsis. EPN was associated with high morbidity and mortality rates, the latter as high as 78%, [3]. Improvements in health care, diagnostic modalities, medications, minimally invasive techniques and knowledge have lowered these rates considerably. To our knowledge, all previous studies of EPN were case series, as it is difficult to perform well formulated randomized prospective trials on patients with a rare severe acute disease with high mortality rates [9].

This retrospective case series was performed to evaluate the management of EPN in a public hospital that provides secondary and tertiary services. The study included 26 patients who were managed over 5 years. Mean patient age was 51 years, consistent with previous findings [9]. Moreover, we observed a female-to-male ratio of 1.4:1, lower than previously reported ratios of 17:1 [10] and 3:1 [9]. The reduced female predominance in our series may be due to the predominance of males in the population of Qatar, which has been estimated to be about 3:1 [11].

Most common presenting symptoms of EPN were fever and abdominal pain, in agreement with a previous study showing pain in 71% and fever in 79% of patients [12]. Similarly, another study reported that pain and fever were each present in more than 90% of patients [13].

Because EPN is an infectious disease that requires bacteria to predominate over a patient’s immune system, EPN is more frequent in older patients, especially those with diabetes, accompanied by high levels of glucose in tissue and impaired tissue perfusion. These conditions promote colonization by bacteria such as *E. coli*, which produce gas by glucose fermentation [14]. Diabetes mellitus (DM) has been reported to be a prominent risk factor for EPN [15, 16]. Of the 26 patients in our study, 18 (69.2%) had DM, including 11 with poorly controlled hyperglycemia. DM predominance confirms the hypothesis that glucose fermentation is associated with EPN. The risk factors for EPN in the eight other non-diabetic, younger patients remain unclear. The most frequent cause of EPN in non-diabetic individuals is obstructive uropathy due to ureteric stones [17], with one study finding that EPN in 32% of patients was secondary to urolithiasis [13]. A comparison of the diabetic and non-diabetic patients in our study found that, of the eight non-diabetics, seven had obstructing ureteral stones, whereas one had infected renal stones. Nevertheless, eight of our diabetic patients also had urolithiasis, which contributed to the pathogenesis of EPN. Of these eight diabetic patients with renal stones, six had obstructive and two had non-obstructive renal stones, whereas the other 10 diabetic patients did not have stones or obstruction. These findings can explain the infectious processes in older diabetics in comparison to younger non-diabetics, along with the need for drainage in all patients with obstruction rather than conservative management with antibiotics alone.

Based on the EPN classification system [12], all non-diabetic patients in our series had class I or II EPN. In contrast, diabetics tended to have more severe disease, including six with EPN class III and one patient with class IV.

Consistent with previous observations, we found that *E. coli* was the most common pathogen (42%) in mid-stream urine culture, either alone or together with other organisms, followed by *Klebsiella pneumonia*. Previous reports were showing similar results [5, 9].

The pathogenesis of EPN is multi-factorial, with immediate management consisting of starting intravenous fluids, controlling diabetes and initiating treatment with broad spectrum antibiotics, all of which improve patient survival. Selected patients may require drainage, either percutaneously or through a ureteral stent [20]. The selection of antibiotics is dependent on the infectious organism and its predominance in that geographic region. Third-generation cephalosporins have been recommended as initial treatment of EPN, whereas carbapenems were the empiric antibiotics of choice for patients with a history of prior hospitalization and antibiotic use and those needing emergency hemodialysis or developing DIC. Fluoroquinolones and gentamicin, however, should be avoided [18]. Because of the predominance of multi-drug resistant *E. coli*, carbapenems have been first antibiotic of choice at our center, followed by the third generation cephalosporins ceftriaxone and Tazocin (piperacillin plus tazobactam). Based on culture sensitivity, seven patients were switched from carbapenems and Tazocin to cephalosporins.

The main and initial steps in the management of patients without obstruction consists of conservative management with antibiotics and fluids, without drainage. Predictors of failure of conservative treatment were found to include thrombocytopenia, shock, altered sensorium, and need for hemodialysis [21]. Another study [22] reported that severe hypoalbuminemia (<3.0 g/dl) was associated with a higher risk of conservative treatment failure, suggesting

that additional management may be required.

In contrast, we found that conservative management was successful in nine patients, none of whom had obstructive uropathy. Four of these patients had severe hypoalbuminemia, two had thrombocytopenia (43 & $114*10^3$/ul) and one required hemodialysis. Five patients were class I, three were class II and two were class IIIa. Conservative management was even successful in treating four patients who presented with septic shock, including two class I and two class IIIa patients.

EPN is considered a severe disease with an average mortality rate of 18% [9]. Factors found to be prognostic of mortality in 32 patients with EPN included hypoalbuminemia, shock at initial presentation, bacteremia, indications for hemodialysis and polymicrobial infection [18]. A second study reported that depressed level of consciousness, shock, hypoalbuminemia and thrombocytopenia were prognostic of higher morbidity and mortality rates [5]. In our case series, all 26 patients presented at an early stage of disease, with none having a reduced level of consciousness. Although five patients (19%) had thrombocytopenia, 17 **(**65%) had leukocytosis, 25 (96%) had hypoalbuminemia, and 24 (94%) had elevated CRP, none of these factors was significantly associated with poorer outcomes.

A meta-analysis found that higher survival rates were associated with conservative management of EPN, with the possibility of drainage rather than emergency nephrectomy [9]. Higher survival rates have also been observed if diabetic management is initiated at the same time as the aggressive treatment of sepsis.

Of our 26 patients, none died, and none required emergency nephrectomy to control sepsis. This was likely due to their early presentation (mean 3.0 ±1.7 days), less than previously reported [9], in addition to early diagnosis and aggressive management by a multidisciplinary team approach, consisting of emergency physicians, urologists, intensivists, interventional radiologists and nephrologists. This approach resulted in a rapid start of antibiotics, intravenous fluids, and correction of electrolyte imbalance, plus, in selected patients, early minimally invasive drainage, either percutaneously or via transurethral retrograde ureteral stenting.

The study had several limitations, including its retrospective design and the inconsistencies in patient management. Management plans were tailored to each individual patient, based on guidelines and previous reports recommendations.

Conclusion

EPN is a severe infection renal disease most frequently caused by *E. coli*. It occurs commonly in patients with infectious stones and/or DM, especially if poorly controlled. Pain and fever are the predominant presenting symptoms. Leukocytosis, hypoalbuminemia and elevated CRP are common laboratory findings. Early aggressive management by a multidisciplinary team and minimally invasive techniques can reduce morbidity and mortality rates.

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