

## Emphysematous Pyelonephritis: A Case Report Series of Seven Patients with Review of Literature

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**ABSTRACT** Emphysematous pyelonephritis is a life-threatening, necrotizing infection in which the kidney parenchyma and surrounding tissues evolve with gas evolution. The clinical presentation of the cases is generally fever, flank pain, nausea and vomiting. Ultrasonography (USG) and plain abdominal radiography are diagnostic in 69% and 65% of cases, respectively. Therefore, computed tomography (CT) of the abdomen is required for early diagnosis and further treatment of emphysematous pyelonephritis (EPN). While EPN treatment included an open drainage or nephrectomy with systemic antibiotics formerly, urinary tract obstruction with systemic antibiotics has been left and percutaneous catheter drainage is performed to drain purulent material and gas today. The aim of the present study is to present our experience in diagnosis and treatment of 7 cases of EPN admitted to training and research hospital during 2 years under novel guidelines.

**Keywords:** Pyelonephritis; percutaneous nephrostomy; urologic diseases

**E**mphysematous pyelonephritis (EPN) is a rare urinary tract infection that occurs most commonly in the renal parenchyma and perirenal region by gas formation. It is caused by gas-forming organisms, most commonly *Escherichia coli* (*E. coli*), in addition to *Klebsiella*, *Clostridium*, *Candida*, *Aspergillus*, *Cryptococcus*, and *Amoeba*.<sup>1</sup>

Diabetes, neurogenic bladder, urinary tract obstruction and recurrent urinary tract infection increase the risk of EPN.<sup>2</sup> The clinical presentation of EPN is similar to uncomplicated pyelonephritis, it results in 90% mortality with high morbidity due to its rapid progression.<sup>3</sup>

Treatment of EPN includes glycemic control, fluid and electrolyte support and antibiotic treatment, the correction of urinary tract obstruction in appropriate cases. Further treatment includes conservative medical treatment with antibiotic, emergency nephrectomy together with medical treatment or elective nephrectomy together with medical treatment with or without percutaneous nephrostomy (PCN).<sup>4</sup>

### CASE REPORTS

#### CASE 1

A 93-year-old female patient who was admitted to the emergency room with flank pain and fever has no any disorders in her medical history. Right flank

pain and acute renal failure were detected in her physical examination. Computed tomography has revealed that right pelvicaliceal system was significantly wider and there were significant hydronephrosis, air densities in renal parenchyma and pelvicaliceal system and proximal ureter and stones 3 cm in diameter, with the largest located in the proximal ureter. Percutaneous nephrostomy was inserted to the patient and purulent material was drained. *E. coli* grew in drainage and urine cultures. There was no growth in blood culture. The patient was started empirically intravenous (IV) ceftriaxone and then switched to IV meropenem according to the antibiotic susceptibility test results. The percutaneous nephrolithotomy operation was planned for stone in the right kidney but the anesthetist considered she was a high risk patient due to the her age and low body weight. So the operation was not performed and right D/J catheter insertion was planned. Right PCN catheter was removed following right D/J catheter insertion. The patient was controlled for the DJ stent changing every year. She never had no complications during follow-up.

## CASE 2

A 57-year-old female patient with insulin-dependent diabetes mellitus was admitted to the emergency room with complaints of fever, lower abdominal pain and dysuria for 2 days. She was obese, dehydrated and had a temperature of 38.5°C in her physical examination, she had bilateral costovertebral angle tenderness in the her abdomen examination. Emphysematous pyelonephritis findings were found in the left kidney on ultrasonography. The air density was observed in the upper part of the left kidney and pelvis on CT examination. Air densities were common in urinary bladder and bladder wall thickness was significantly increased. Left emphysematous pyelonephritis and emphysematous cystitis in bladder were found (Figure 1). The patient was initially started IV Ciprofloxacin and subcutaneous (SC) insulin and fluid treatment. This was switched to tazobactam-piperacillin treatment upon ciprofloxacin-resistant *E. coli* growing in urine culture. The clinical condition of the patient has improved significantly by

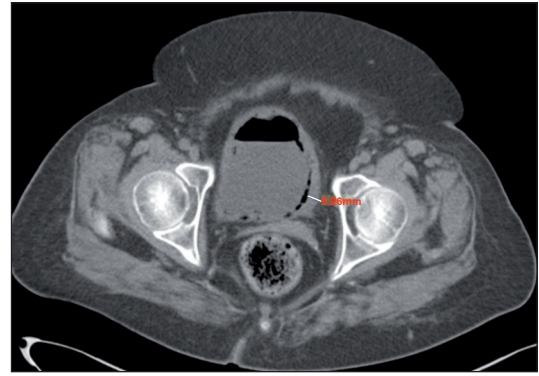


FIGURE 1: Transvers section tomography (arrow shows the air in bladder).

treatment. There was no bacterial growing in control urine culture. There was no air density in sections of the same level in the the upper part of the left kidney on control CT. Air densities in the bladder disappeared and bladder wall thickness was substantially decreased in axial sections at the level of bladder. The patient whose clinical condition significantly improved was discharged on oral quinolone treatment with creatinine: 2.3 mg/dL.

The patient was re-admitted with fever, flank pain, nausea, vomiting 10 days after her discharge. Her body temperature was 39 °C, pulse rate was 90 bpm and she had lower quadrant tenderness. Bladder wall thickness had increased and air was observed within it on abdominal CT. Recurrent emphysematous cystitis was considered. BUN was 117 mg/dL, creatinine was 3.9 mg/dL, sodium was 129 mg/dL, potassium was 4 mg/dL, CRP was 16. Urine analysis revealed hematuria, proteinuria and leucocyturia. Meropenem-susceptible ESBL grew in urine culture. The clinical condition of patient improved on day 5 and antibiotherapy was completed on day 21. Control CT taken that bladder wall thickness and the air densities in the bladder lumen disappeared. The patient who was clinically improved was discharged on oral antibiotic treatment with creatinine: 2.3 mg/dL and BUN: 45 mg/dL.

## CASE 3

A 46-year-old female patient with diabetes mellitus was admitted to the emergency room with the complaints of sudden onset of nausea, vomiting, di-

arrea and abdominal pain. She had extensive abdominal tenderness in her physical examination. Intravenous ciprofloxacin and metronidazole, insulin infusion and fluid treatment were started. There was no growth in blood and urine cultures. Amoeba cysts were seen in the stool. Left emphysematous pyelonephritis was found on abdominal CT (Figure 2). Left nephrectomy was planned as the general condition of the patient has deteriorated on day 4 of treatment and she had higher body temperature. The patient was neurologically evaluated due to speech and walking difficulties, loss of power in the right hand and foot, which developed one day after nephrectomy, there were 70% stenosis in left internal carotid artery and also infarction in the left temporal region on cerebral CT. Enoxaparin 0.4 SC bid and mannitol 75 mg quid were administered. Chest pain started in the course of treatment. Coronary angiography (CAG) was planned due to ST-segment elevation in the posterior inferior leads on electrocardiogram and CAG revealed 80-90% occlusion in right coronary artery (RCA), 80% occlusion in circumflex artery (CX), 70-80% occlusion in left anterior descending (LAD) artery. No interventions were performed as her chest pain has improved and cardiac enzymes were normal. The patient's neurological deficits decreased, she has started to talk and walk without support. She was consulted again to neurology, mannitol treatment was tapered. Her sutures were removed on postoperative day 7. The patient who

was clinically improved was discharged on day 14 on oral quinolone treatment with creatinine: 0.8 mg/dL and urea: 32 mg/dL.

#### CASE 4

A 70-year-old female patient was admitted to the emergency room with left flank pain which has persisted for a long time and suddenly exacerbated. She had diabetes and hypertension in her medical history. Left costovertebral tenderness was positive and she had abdominal rebound and tenderness in her physical examination. Computed tomography of the abdomen revealed left emphysematous pyelonephritis, and stone in the proximal ureter (Figure 3). The fluid and antibiotic treatments were initially started. *E. coli* grew in urine culture and IV ertapenem treatment was started. Insertion of D/J stent was planned due to stone-related hydronephrosis however it could not be achieved as ureteral orifice could not be seen. Left nephrectomy was performed as the general condition of the patient deteriorated. Wound culture was obtained due to wound infection at nephrectomy site. Imipenem 500 mg quid and teicoplanin 400 mg once daily were administered in accordance to the antibiogram upon ESBL (Extended-spectrum beta-lactamases) growing. There was no bacterial growing in control wound culture. Wound site was closed again on postoperative day 14 and the patient was discharged with creatinine: 1.3 mg/dL after urology control had been scheduled.



FIGURE 2: Transvers section tomography (arrow shows the air in left kidney zone).

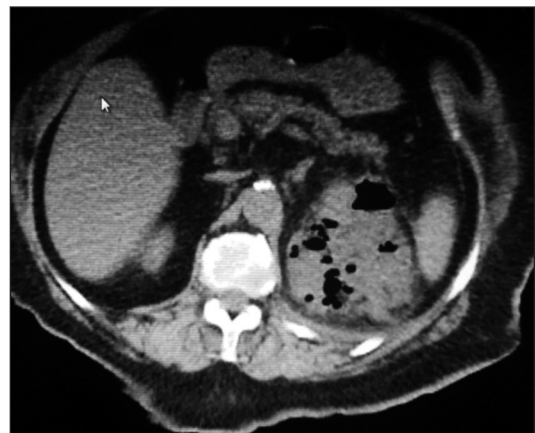


FIGURE 3: Transvers section tomography (air in the left kidney zone).

### CASE 5

A 50-year-old female patient was admitted to the emergency room with complaints of fever and fatigue, she had diabetes mellitus but was not receiving regular insulin treatment. She was living as a refugee in poor conditions in a tent city established in Turkey due to Syria war. Her general condition was poor, she was conscious anemic, her body temperature was 39°C and she had extensive abdominal tenderness and acute renal failure. Intravenous fluid, SC insulin and erythrocyte suspension and piperacillin tazobactam 2.25 g tid were initially started. Hemodialysis was started due to congestion findings and high creatinine level. A D/J stent was inserted under local anesthesia and purulent material was drained and *E. coli* that showed low susceptibility to piperacillin-tazobactam grew in drainage culture and therefore Ertapenem 500 mg once daily was administered. The patient was lost due to atrial fibrillation with rapid ventricular response which developed during dialysis on day 5 of treatment.

### CASE 6

A 61-year-old, morbid obese female patient was admitted with complaints of burning with urination and fever for one week. She was receiving insulin and diltiazem treatment for diabetes mellitus and hypertension for 13 years. When she was admitted to primary care with this complaint, oral ciprofloxacin treatment was started with the diagnosis of urinary tract infection and she was referred to endocrinology due to high plasma glucose. When she was admitted to hospital, she had a temperature of 39.5 °C and lower quadrant tenderness in her physical examination. Gas densities were detected in the right renal pelvis and ureter on CT (Figure 4). *E. coli* and *Enterococcus faecalis* grew in urine culture. Intravenous hydration, quadruple insulin and imipenem were initially started. Teicoplanin 400 mg IV was started because of the resistance in the control urine culture. There was infected poached kidney in the right kidney on abdominal USG, air-liquid level at the upper pole of in the right kidney and abscess formation measuring 8x7 cm and right proximal ureteral dilatation



FIGURE 4: Coronal section tomography (arrow shows the air in the right kidney).

on CT but no stone was detected (Figure 4). A D/J stent was inserted to the patient on third day. PCN catheter insertion was planned but it could not be achieved due to morbid obesity. Control CT revealed regression of the abscess but the dilation continued. The patient whose general condition and laboratory values on improved day 14 was discharged on oral quinolone treatment and after urology control had been scheduled.

### CASE 7

A 41-year-old female patient was admitted to the emergency room with fever, nausea, vomiting for one week and blurring of consciousness during the last two days. She had type II diabetes mellitus and has been using insulin for 5 years, and aortic-mitral valves replacement operation 10 years ago. In her physical examination, her body temperature was 38.9 °C and her pulse rate was 120 bpm and her blood pressure was 180/100 mmHg, she had hypervolemia findings and acute renal failure and early inspiratory crackles on the base of the left lung. She had pneumonic infiltration in the left lower lobe on chest radiography. There was no evidence in favor of endocarditis on echocardiography. The dimensions and echogenicity of the kidney were found to increase on ultrasonography. After the blood and

urine cultures had been obtained, IV Teicoplanin 400 mg daily together with hemodialysis was started for pneumonia of the patient. Her general condition improved and fever decreased during follow-up. Renal functions improved so as to interrupt dialysis but abscess foci measuring 7 cm and contained air densities were detected at the upper pole of the right kidney on CT upon she had a temperature of up to 40.5 °C on day 10 of treatment. After EPN was diagnosed, PCN was inserted by CT guided and purulent material was drained. *E. coli* grew in abscess drainage culture and it was susceptible to ciprofloxacin. The abscess and gas foci were shown to disappear on control CT. Thus, drainage catheter was removed on day 18 and the patient was discharged on oral quinolone treatment with creatinine:1.4 g/dL and BUN: 64 mg/dl.

## DISCUSSION

EPN is a life-threatening necrotising infection which occurs by gas formation in renal parenchyma and/or perirenal tissue.<sup>5</sup> Although these infections which are caused by gas-producing microorganisms are being rare among all bacterial infections involving the urinary system, they are very important due to high mortality.<sup>6</sup> It results in 90% mortality with high morbidity due to its rapid progression.<sup>3</sup> Risk factors in the pathogenesis include the pathogenic bacteria capable of mixed acid fermentation, high tissue glucose level, impaired tissue perfusion. Local tissue ischemia will exacerbate tissue destruction in the presence of gas-producing bacteria, will prepare the environment for purulent infection, will prevent the removal of the gas produced. Because EPN is seen in the ratio of 90% in uncontrolled diabetics, EPN should be considered in the differential diagnosis of unexplained sepsis in diabetic patients.<sup>6</sup> Moreover, immune-compromised patients particularly the patients with ischemic and diabetic nephropathy who have renal failure constitute the other risk groups for EPN.<sup>7</sup> Six of our seven cases were obese and uncontrolled diabetic patients and all seven were female consistently with literature.

There was kidney stone in four cases in our series. The risk of EPN is 25-40% in urinary tract ob-

struction and ureteral stenosis is the second most common risk factor for EPN.<sup>8</sup> Ureteral obstruction exacerbates the tissue destruction in the presence of gas-producing bacteria, prepares environment for purulent infection and causes local tissue ischemia which triggers bacterial infection by preventing the removal of gas produced.<sup>5</sup> In the presence of obstruction, attempts should be planned in order to eliminate and drain abscess.

EPN often occurs in the fourth or fifth decade of life.<sup>9</sup> Its clinical signs and symptoms occur as pyelonephritis symptoms such as flank pain, nausea, vomiting, fever/rigours, dysuria. Loin tenderness is most common clinical finding, it is detected around the renal area and as crepitus can be felt in the scrotum in some patients.<sup>10</sup> The pneumaturia is not seen unless the infection involves collecting system. About 93% of EPNs involve kidneys unilaterally and the left kidney is affected much more than the right kidney.<sup>11</sup> When it occurs on the double-sided, long-term need for dialysis will be inevitable.<sup>12</sup> The clinical presentation of our case series was as fever, flank pain, nausea and vomiting and there was no crepitation. Of our 7 cases, there were left kidney involvement in four cases and right kidney involvement in three cases. While there was a need for hemodialysis in case 5 and case 7. The others did not need hemodialysis.

*Escherichia coli* which is the most common causative pathogen in EPN, was reported to grow at 70% in urine and pus cultures.<sup>10</sup> In our case series, *E. coli* grew in urine culture of 4 cases, in drainage culture of one case, *Klebsiella* grew in urine culture of one case, there was no growth in urine culture of one case. This may result from timely commencement of antibiotic treatment due to diarrhea.

USG was used initially in all of our patients in EPN but CT was also performed in order to ensure the distribution of gas and diagnosis. Computed tomography is the most valuable diagnostic method in the early diagnosis and follow-up of EPN. Ultrasonography and plain abdominal radiography are the definitive diagnostic in 69% and 65% of the cases, respectively. Therefore, abdominal CT is required for early diagnosis and further treatment of EPN.<sup>13</sup>

The treatment of EPN often contained an open drainage or nephrectomy together with systemic antibiotics in the past. In recent years, many new studies have been published reporting that urinary tract obstruction has been eliminated with systemic antibiotics and percutaneous catheter drainage was successfully made in order to drain purulent material and gas in the treatment of EPN.<sup>11</sup> The treatment of EPN yields better results due to medical imaging, interventional radiology, new effective antibiotics and dialysis-assisted intensive care. Treatment was mostly developed as conservative. Early and aggressive treatment plan must be made to contain diabetes control, correction of dehydration and treatment of the underlying infection, open PCN and/or nephrectomy if appropriate.<sup>12</sup> Our patient was managed according to current evidence-based protocols. Broad-spectrum antibiotic treatment with intravenous fluid and glycemic control was given to all patients as initial treatment. Antibiotic treatment was evaluated again according to the results of culture. Two of our patients underwent hemodialysis for renal support due to acute renal failure and it was found that dialysis for renal support has reduced mortality.<sup>10</sup>

An emergency nephrectomy that often can not respond despite appropriate antibiotic and fluid treatment together with hemodynamic deterioration has been defined as conditions not be delayed in management of EPN.<sup>8</sup> In our case series, PCN tube was inserted to two patients, ureteral stent (D/J) was inserted to three patients. Two cases un-

derwent nephrectomy. After ureteral stent had been placed, nephrectomy was planned for one case because of unresponsiveness to treatment and hemodynamic instability but the patient died from atrial fibrillation. Although our case series was small, our mortality rate (one out of seven) supports the literature. In a retrospective review including 10 studies, 210 patients were evaluated and mortality was found to be 50% with only medical treatment, mortality was 25% in the emergency nephrectomy together with medical treatment, mortality was 13.5% in the percutaneous drainage together with medical treatment. Mortality was significantly lower in the percutaneous drainage group. Mortality was 6.6% in a small number of patients who underwent elective nephrectomy received medical treatment together with percutaneous drainage.<sup>13</sup> Percutaneous drainage should be a part of the initial treatment of EPN. This strategy has a lower mortality compared to only medical treatment or emergency nephrectomy.<sup>14</sup> All patients and their approaches were presented on a single table (Table 1).

## CONCLUSION

Emphysematous pyelonephritis is a disease with very high mortality rates. The CT of the abdomen is the gold standard for diagnosis. First, a broad-spectrum antibiotic should be started. Later, endoscopic or percutaneous drainage is life-saving and preferred methods compared to open surgery.

TABLE 1: Patient characteristics.

Case no	Age/sex	Comorbity	Urine nitrate	HD	Urinary stone	Intervention	Bacteria in urine culture
1	41/F	DM MVR	+	+	+	PCN	E. coli
2	57/F	DM	+	-	-	-	E. coli
3	46/F	DM	+	-	-	NX	-
4	70/F	DM/HT	-	-	+	NX	E. coli
5	50/F	DM	-	+	+	DJ STENT	E. coli
6	61/F	DM/HT	-	-	-	DJ STENT	E. coli and eneterococcus feacalis
7	93/F	-	+	-	+	PCN DJ STENT	E. coli

DM: Diabetes Mellitus; HT: Hypertension; MVR: Mitral valve replacement; HD: Hemodialysis; CT: Computer Tomography; RK: Right Kidney; LK: Left Kidney; PCN: Percutaneous nephrostomy; NX: Nephrectomy.

### Informed Consent

It was obtained from all patients that their information would be published.

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### Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

### Authorship Contributions

**Idea/Concept:** Sibel Ada, Mehmet Eflatun Deniz; **Design:** Sibel Ada, Mehmet Eflatun Deniz; **Control/Supervision:** Sibel Ada; **Data Collection and/or Processing:** Mehmet Eflatun Deniz; **Analysis and/or Interpretation:** Sibel Ada; **Literature Review:** Sibel Ada, Mehmet Eflatun Deniz; **Writing the Article:** Sibel Ada, Mehmet Eflatun Deniz; **Critical Review:** Sibel Ada; **References and Fundings:** Sibel Ada; **Materials:** Sibel Ada.

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