

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

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**Abstract:** Emphysematous Pyelonephritis (EPN) is an infection of the renal parenchyma and perinephric tissue which resulted in the presence of gas in the collecting system, renal parenchyma or perinephric tissue. Researchers presented three cases of EPN and performed a comprehensive review of the literature on EPN to describe and summarize the causation, clinical manifestation, diagnosis, treatment and prevention. Early diagnosis is essential for a positive outcome. A high index of suspicion coupled with a good imaging study of the abdomen can lead to early diagnosis and optimizing management modality which are fundamental for a favorable outcome.

**Key words:** Emphysematous pyelonephritis, case report, review, perinephric tissue, abdomen

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### INTRODUCTION

The emphysematous pyelonephritis is a rare severe renal infection characterized by the presence of gas in renal parenchyma and (or) perirenal spaces. With regard to this disease, up to present, except that the standards of diagnosis and epidemiology are clear, the definition is not unified. The causations, clinical manifestation and prognostic factors of EPN are still needed to be tidied up and organized. There have been never-ending controversy and variance in the treatment mode since the first case report. Hereon, researchers presented a case report series of three patients and extensive literature review for the above questions.

### MATERIALS AND METHODS

#### Case report

**Case 1:** A previously healthy 72 years old nondiabetic woman presented acutely to the institution with unremitting pain over right upper abdomen white vomiting, fever and chill. She had received antibiotic therapy (intravenous levofloxacin) for 3 days in community hospital without markedly pain relief. On examination, the patient appeared ill-looking and poorly compliant and the abdomen was soft, distended and tender in the right flank with attenuated bowel sounds.

There was a markedly tender lump palpable in her right upper quadrant and suspicious Murphy's sign; she was also sensitive to percussion of the renal region. The initial diagnosis was nephrocolic or cholecystitis and urgent imaging examination was performed. Laboratory investigations show sensitive to percussion of the renal region that increased peripheral white cell count of  $16.6 \times 10^9/L$  with polymorphs 91.4%, serum creatinine  $130 \mu\text{mol L}^{-1}$  and blood urea nitrogen  $21 \text{ mg dL}^{-1}$ . The urinalysis showed that plenty of pus cells with glucosuria. Subsequent urine culture showed that there was *E. coli* in the urine with sensitivity to aztreonam. No bacteremia appeared in blood culture. The blood-glucose was  $8.9 \text{ mmol L}^{-1}$ . Computed tomography scan shown as an axial image (Fig. 1) and the definitive diagnosis was emphysematous pyelonephritis. Then, researchers performed nephrectomy in 15 h after the onset of symptoms. Aztreonam with appropriate agent targeting *E. coli* was intravenous administrated as well as appropriate nutrition. Dramatic regression of the renal mass was seen the 2nd day after operation. She was discharged from hospital and remained asymptomatic at 1 year follow up.

**Case 2:** A 53 years old diabetic woman presented with left flank pain for the previous 4 days with fever and chill but no nausea or vomiting. The 2 years earlier, she had

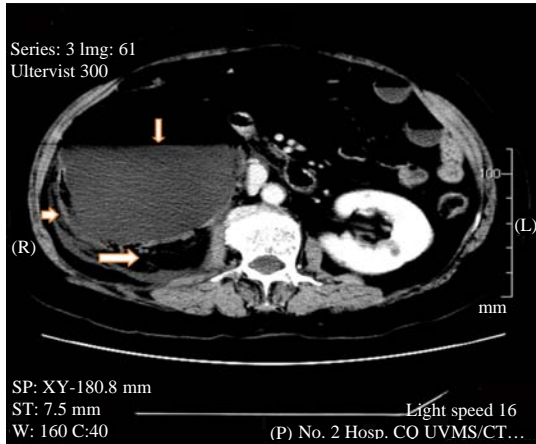


Fig. 1: (Case 1) Computed tomography of the abdomen revealed the original left kidney region replaced by a huge sac filled with a mass of gas and fluid. Severe hydronephrosis and the gas-fluid interface (long narrow arrow) can be seen, Gerota's fascia was inflamed (short broad arrow) and thickened

left-sided acute nephric colic for a middle ureteral stones and the stones were removed by ureterolithotomy. Her vital signs were as followings: pulse 108 min<sup>-1</sup>, temperature 38.8°C and blood pressure 140/110 mm Hg. Physical examination revealed an obese and ill-looking woman with a tender lump palpable in her left upper quadrant of the abdomen. Pertinent laboratory investigations revealed white blood cell count 12.6×10<sup>9</sup>/L with neutrophils 83.4%, platelet count 365×10<sup>9</sup>/L, C-reactive protein 22.1 mg dL<sup>-1</sup>, random blood glucose 15.6 mmol L<sup>-1</sup>, blood urea nitrogen 13.5 mg L<sup>-1</sup>, creatinine 129 μmol L<sup>-1</sup>, serum Na<sup>+</sup> 126 mmol L<sup>-1</sup> and K<sup>+</sup> 3.9 mmol L<sup>-1</sup>. The urinalysis showed pyuria (numerous WBCs/high power field) with glucosuria and acetone body. Urine culture grew *Enterococcus faecium* with sensitivity to teicoplanin. According to the imaging features of computed tomography shown as an axial image (Fig. 2), emphysematous pyelonephritis was established.

Fluid replacement, electrolyte and glucose correction and antimicrobial therapy were administrated and the patient's general health status improved with resolution of left flank pain. But on the 2nd day of admission, the patient underwent a sudden deterioration with signs of sepsis and the temperature was of 39.6°C. An urgent further surgical intervention was performed. On the 20th day of admission, she was discharged in good health.

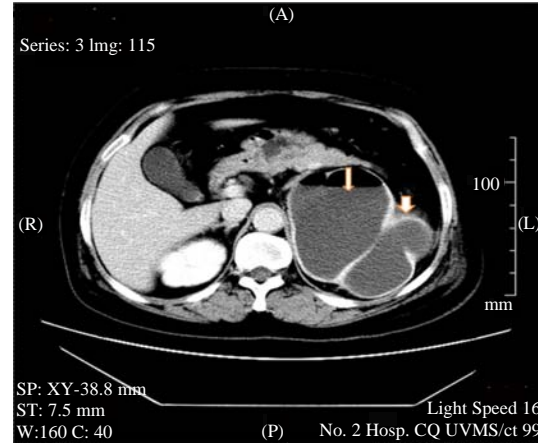


Fig. 2: (Case 2) Notable enlargement and lobulated profile of the left kidney with attenuation of the renal parenchyma. Dilate and dropsy of calyx, renal pelvis and upper ureter are showed. Gas-fluid interfaces (long narrow arrow) in dilated calyx and exudations in the perirenal space (long broad arrow). Gerota's fascia is inflamed and thickened

**Case 3:** A 61 years old, insulin-dependent and diabetic woman admitted for a 2 days history of abdominal pain and nausea without fever or pyuria. Previously, she had received many courses of antibiotics for recurrent urinary infections or pyelonephritis. The patient had been in poor glycemic control for 20 years. She also has a history of abdominal hysterectomy for hysteromyoma. On examination, she was afebrile with body temperature 37.2°C and blood pressure was 130/70 mm Hg; heart rate was 105 beats min<sup>-1</sup>; respiratory rate was 20/min. Laboratory data revealed that leukocyte count was 6.93×10<sup>9</sup>/L with neutrophils 67.5%; platelet count was 296×10<sup>9</sup>/L; hemoglobin A1C was 7.5%; serum creatinine was 220.4 μmol L<sup>-1</sup> and blood urea nitrogen 30 mg L<sup>-1</sup>. The urinalysis showed 6 white blood cells per high-power field. The initial electrolytes, liver function, amylase and lipase tests were within normal limits. The fasting blood-glucose was 9.8 mmol L<sup>-1</sup>. Urine cultures could see *Escherichia coli* producing no ESBLs. Pyelonephritis is suspected initially according to the physical examination and laboratory data but the image findings (Fig. 3) are characteristic of emphysematous pyelitis within the right kidney.

Frank nepheloid *flavescens* pus was obtained when US-guided percutaneous catheter drainage of the fluid collection was performed. Intravenous Mezlocillin sodium and Sulbactam sodium were given based on the antibiotic-susceptibility testing results for the first 5 days and antibiotic therapy was continued for another 2 weeks

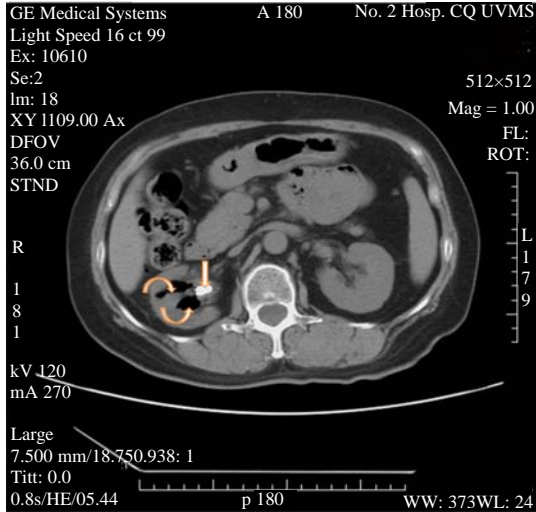


Fig. 3: (Case 3) Computed tomography of the abdomen revealed distortion and attenuation of the right renal parenchyma by the gas formbacteria with gas filled pockets in calyx (curved arrow). A large obstructing pelvic stones (long narrow arrow) (1.2×0.6 cm) and hydrocalycosis are present

by taking cefixime orally outside hospital. On follow-up at 2 weeks, the renal function was improved (BUN 19 mg L<sup>-1</sup> and creatinine 86 μmol L<sup>-1</sup>) and the urinalysis was normal. Two-stage percutaneous nephrolithotomy was successfully performed to remove the stone and the catheter was removed after complete drainage of turbid fluid. The patient was managed with antibiotics accompanied by percutaneous drainage and the renal function was normal without hydronephrosis at half a year follow-up.

## RESULTS AND DISCUSSION

Kelly reported the first case of gas-forming renal infection in 1898. Schultz and Klorfein denominated this disease as Emphysematous Pyelonephritis (EPN), emphasizing on the relation between gas formation and acute infectious process (Schultz and Klorfein, 1962). Some investigators suggested that the term emphysematous pyelonephritis should be applied only to gas restricted to the renal parenchyma and (or) perinephric space (Michaeli *et al.*, 1984; Ahlering *et al.*, 1985; Shokeir *et al.*, 1997; Huang and Tseng, 2000) while others considered that emphysematous pyelitis referred to infection formed within the collecting system (Evanoff *et al.*, 1987). Even it has been suggested that emphysematous pyelonephritis, emphysematous pyelitis, perinephric emphysema should be distinguished

with each other. However, many researchers advocated that EPN was an infection of the renal parenchyma and perinephric tissue which resulted in the presence of gas in the collecting system, renal parenchyma or perinephric tissue (Hudson *et al.*, 1986; Wan *et al.*, 1996). This definition is widely observable for that it includes all the possible extent of involvement by gas-forming acute renal infections.

The pathogeny of EPN can be summarized as followings: High tissue glucose level which may provide gas-forming microbes with a more favorable microenvironment for their growth and rapid catabolism (Yang and Shen, 1990; Huang *et al.*, 1991; Chen *et al.*, 1994; Huang and Tseng, 2000). EPN occurs mainly (around 90-96%) in diabetic patients (Ahlering *et al.*, 1985; Shokeir *et al.*, 1997; Huang and Tseng, 2000; Aswathaman *et al.*, 2008; Somani *et al.*, 2008). The 3 patients are all diabetics. The renal circulation can be impaired for the high tissue glucose level and the delivery of immunologic substance and antibiotics to the site of infection is not effective which leads to out of control of local inflammation. Pathology examinations have provided the evidence of impaired tissue perfusion (Hall *et al.*, 1988; Huang *et al.*, 1991; Huang and Tseng, 2000; Ortiz *et al.*, 2007) thus gas is not effectively transported away and remains localized at the site of inflammation (Hall *et al.*, 1988; Yang and Shen, 1990; Huang *et al.*, 1991). The accepted theory for the mechanism of gas formation in EPN is mixed acid fermentation of glucose (Schultz *et al.*, 1962; Yang and Shen, 1990; Huang *et al.*, 1991); another pathway is butyric fermentation of glucose by anaerobes (Huang and Tseng, 2000) and upper tract obstruction. All the three patients had upper tract obstruction. In such situations, the renal parenchyma will be oppressed by uronephrosis, leading to impaired renal circulation. The facultative anaerobes infection. *Escherichia coli* is the commonest causative bacterial agent and *Klebsiella pneumoniae* is the second (Wan *et al.*, 1996; Shokeir *et al.*, 1997; Huang and Tseng, 2000; Somani *et al.*, 2008); mixed infections (20%) is relatively uncommon (Michaeli *et al.*, 1984; Evanoff *et al.*, 1987). In the report, all the pathogen are *Escherichia coli* and immune suppression or impaired immunity. There are cases with EPN reported who had no diabetes mellitus and urinary tract obstruction but rheumatism or systemic lupus erythematosus who took immunosuppressor to keep them in remission from discomfort (Kumar *et al.*, 2001; Tokuyama *et al.*, 2009; Watanabe *et al.*, 2010). Occasionally, there are patients with EPN related to polycystic kidney, blunt abdominal trauma, caesarean section or urinary bladder catheterization for long time who have no evidences of immunodeficiency, diabetes or

urinary tract obstruction (Boltan *et al.*, 2008; Azzini *et al.*, 2009; Kumar *et al.*, 2009; McNeill *et al.*, 2009). Occasional renal transplant recipients were reported to have developed EPN (Schmidt *et al.*, 2009), the probable mechanism is the absence of blood supply (Huang and Tseng, 2000; Ortiz *et al.*, 2007). Moreover, many cases were reported to develop EPN without evidence of immunodeficiency, diabetes or urinary tract obstruction and the specific reason was not clear (Hart *et al.*, 2007; Cheng *et al.*, 2009). Patients with pre-existing renal impairment, especially chronic diabetic nephropathy are at special risk of developing this infection (Michaeli *et al.*, 1984; Evanoff *et al.*, 1987).

All the documented cases of EPN have been in adults and juvenile diabetic patients did not appear to be at risk (Wang *et al.*, 2007). Women patients outnumbered men patients; the ratio is from 1:2 to 1:8 (Wan *et al.*, 1996; Shokeir *et al.*, 1997; Huang and Tseng, 2000; Karasavidou *et al.*, 2006; Wang *et al.*, 2007). Researchers suppose the reason of high rate of occurrence in women is that the female are prone to urinary tract infection. The 3 patients, researchers reported are all elderly diabetic women. The left kidney was more frequently affected than the right one (Chen *et al.*, 1997; Shokeir *et al.*, 1997). The possible reason is that urinary tract obstruction occurs more frequently in the left kidney than in the right one (Michaeli *et al.*, 1984; Evanoff *et al.*, 1987; Huang and Tseng, 2000).

Plain abdominal radiography and ultrasonography can be initial device for diagnosing EPN as low cost and readily accessible technique (Wan *et al.*, 1996; Huang and Tseng, 2000). Plain radiographs are good technique to depict air which appears as mottled gas shadows over the involved kidney and the finding of a crescentic collection of gas within the Gerota's fascia frequently indicates extension into perirenal fat (Somani *et al.*, 2008). Ultrasonography usually demonstrates strong focal echoes which suggest the presence of gas (Derouiche *et al.*, 2008). But the accuracy of plain film and ultrasonography is low, the gas could be demonstrated only 36% by plain abdominal radiographs (Michaeli *et al.*, 1984; Wang *et al.*, 2007) while 50% by ultrasonography (Wang *et al.*, 2007). Therefore, the imaging of plain radiographs and ultrasonography gas in the kidney can be often confused with bowel gas (Michaeli *et al.*, 1984; Somani *et al.*, 2008). Sometimes, the involved kidney could not be visualized sonographically because of multiple irregular air-fluid interfaces (Brenbridge *et al.*, 1979) and the depth of parenchymal involvement may be underestimated in US. Besides, multiple renal stones may also manifest as echogenic foci without clean posterior shadowing on US so, differentiation between gas and

calcification was difficult in US (Goyzueta *et al.*, 1994). CT can evaluate the case that is uncertain by plain abdominal radiography and ultrasonography. CT is more sensitive than ultrasound and plain X-radiology to evaluate renal and perirenal infections (Best *et al.*, 1999) and more accurate and elegant to depict the renal and perirenal anatomy and the spread of infection to the perinephric tissues, permitting visualization of the gas and a radiologic classification with a prognostic value (Wan *et al.*, 1996; Huang and Tseng, 2000; Thornton *et al.*, 2001; Sheth and Fishman, 2004). Most researchers, currently, consider non-contrast abdominal computed tomographic to be the main imaging tool for its highly specific findings and accurate assessment of the extent of EPN (Huang and Tseng, 2000; Thornton *et al.*, 2001; Schreyer *et al.*, 2002). Some researchers suggested that the gold standard imaging technique for diagnosis of EPN should be contrast enhanced computed tomography for indicating the degree of renal function (Michaeli *et al.*, 1984; Kamaliah *et al.*, 2005) however, others advocated that contrast CT is not required for the compromised renal reserve and the presence of active infection (Schreyer *et al.*, 2002). For the cases, contrast enhanced CT was performed for two of them for the consideration of the risk of tumor in abdominal organs kidneys.

Additionally, CT is also an efficient imaging method for helping to make a specific therapeutic regimen guiding the drainage procedures, monitoring response to treatment and rechecking patient's condition at follow-up (Karasavidou *et al.*, 2006; Wang *et al.*, 2007; Tokuyama *et al.*, 2009). CT can also rule out the other differential diagnosis for gas shadowing the kidney (Joseph *et al.*, 1996; Wang *et al.*, 2007; Derouiche *et al.*, 2008).

Previously, the total mortality of EPN and mortality with antibiotic therapy alone from EPN were reported to be 40-50 and 60-75% (Ahlering *et al.*, 1985; Chen *et al.*, 1997; Shokeir *et al.*, 1997; Karasavidou *et al.*, 2006), respectively. With the advanced index of suspicion, extensive use of CT and timely and optimizing management, currently, the mortality have fallen to 17-25 and 50% (Langston and Pfister, 1970; Falagas *et al.*, 2007; Aswathaman *et al.*, 2008; Somani *et al.*, 2008). There is no significant difference in the mortality associated to antibiotic treatment combined nephrectomy between past and present which is both approximately 25% (Huang and Tseng, 2000; Falagas *et al.*, 2007; Liu *et al.*, 2007). Researchers considered the reason may be that the conditions in patients treated with nephrectomy are commonly serious and the surgeon tends to choose nephrectomy for the emergency cases. The mortality in patients receiving nephrectomy is attributed to the severity of emergency cases.

The initial management of EPN generally includes resuscitation, electrolyte correction, antibiotic treatment targeting Gram-negative bacterias and control of diabetes if present. Many cases were managed medically but only one case reported (Schreyer *et al.*, 2002), most researchers considered that medicine alone was often inadequate to cure and preserve renal function for EPN (Ahlering *et al.*, 1985), leading to a high mortality (Langston and Pfister, 1970) and easily making patients develop recurrent (Soo Park *et al.*, 2006).

Some researchers have advocated that most of the patients' required nephrectomy. Nephrectomy often contributed to a complete resolution of this life-threatening infection. They considered the nephrectomy should be regarded as the standard of care for the management of EPN in patients capable of undergoing surgery (Hudson *et al.*, 1986; Shokeir *et al.*, 1997; Ramanathan *et al.*, 2006; Kapoor *et al.*, 2010) accordingly, 2 of the 3 patients received nephrectomy and the infection were controlled timely but nephrectomy is an unattractive option for solitary kidney, bilateral renal involvement and inoperable cases (Somani *et al.*, 2008; Kapoor *et al.*, 2010). Moreover, early (<1 week) nephrectomy can lead to a higher mortality rate than initial conservative management (Ahlering *et al.*, 1985; Ramanathan *et al.*, 2006).

Recently, more and more case reports of series of patients with EPN have been published who were treated with antibiotics accompanied by percutaneous drainage (Ramanathan *et al.*, 2006; Aswathaman *et al.*, 2008) with a high successful treatment (approximately 65-80%) (Huang and Tseng, 2000; Falagas *et al.*, 2007; Aswathaman *et al.*, 2008). Percutaneous drainage offers an effective therapy for emphysematous pyelonephritis especially for certain cases with focal abnormalities and those in initial stage. Although, there were some failed treatment who developed recurrent according to the theory of gas transportation (Chen *et al.*, 1994), percutaneous drainage is justified. Some researchers considered that functioning renal tissue could be salvaged and EPN could be eradicated with a combination of antibiotics and radiologically guided percutaneous drainage or open drainage (Shokeir *et al.*, 1997; Huang and Tseng, 2000; Karasavidou *et al.*, 2006; Falagas *et al.*, 2007; Somani *et al.*, 2008). The mortality matched each other for nephrectomy and percutaneous drainage (Ahlering *et al.*, 1985; Shokeir *et al.*, 1997) but percutaneous drainage offers several advantages over nephrectomy, the procedure is cost effective and easy to perform and takes very little time it is performed under local anesthesia and does not require a sterile operating

theatre in addition there is no absolute contraindication to this procedure. Generally speaking, treatment is now increasingly conservative (Chen *et al.*, 1997) and nephrectomy should not be the first line of therapy for EPN, especially for the patients who have a response to conservative management (Kapoor *et al.*, 2010). However, it is recommended that patients should be closely monitored both clinically and radiologically if the conservative treatment effectiveness below the mark, selective nephrectomy should be considered, especially in high-risk patients combining with shock, thrombocytopenia, acute renal failure or disturbed consciousness (Shokeir *et al.*, 1997; Eloubeidi and Fowler, 1999; Huang and Tseng, 2000; Somani *et al.*, 2008).

The salient factors associated with poor outcome, including increased serum creatinine level, thrombocytopenia, altered mental status, renal function impairment and shock. Serum creatinine level is the most reliable predictor of outcome that patients with creatinine level >1.4 mg dL<sup>-1</sup> were at high risk (Eloubeidi and Fowler, 1999). It has been showed that patients with different numbers of risk factors had different outcome (Aswathaman *et al.*, 2008) and that prognosis is not related to age, sex, diabetes mellitus history, blood glucose level, leukocyte count and presence or absence of urinary tract obstruction or urolithiasis (Michaeli *et al.*, 1984; Eloubeidi and Fowler, 1999). Fortunately, the 3 patients have no or serious risk factors above and the outcome are good. High tissue glucose level has been supposed a risk for bad outcome which provided gas-forming microbes with a microenvironment more favorable for growth and rapid catabolism and cause a fulminant course in patients with EPN (Yang and Shen, 1990; Chen *et al.*, 1994) whereas, some researcher considered that poor control of blood glucose level had no clear association with poor prognosis for EPN (Langston and Pfister, 1970; Michaeli *et al.*, 1984; Eloubeidi and Fowler, 1999).

## CONCLUSION

Several researchers considered obesity, smoking and urinary red blood counts to be factors predicting the mortality (Eloubeidi and Fowler, 1999; Wang *et al.*, 2007). Wang found that type I EPN had frequently a fulminant course and a bad outcome while the outcome of type II EPN was relatively good (Wan *et al.*, 1996). Emphysematous pyelitis was commonly considered to have an excellent outcome under prompt diagnosis and treatment (Wan *et al.*, 1998).

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