

A rare but potentially fatal bacterial infection in a patient with poorly controlled diabetes mellitus: emphysematous pyelonephritis

一個糖尿病控制差劣的病人，罕有但可致命的細菌感染：氣腫性腎盂炎

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Emphysematous pyelonephritis, a necrotizing infection of the renal parenchyma caused by gas-producing organism, is a rare but life-threatening condition. The initial presentation could be non-specific. We report a case of emphysematous pyelonephritis in a patient presenting with poorly controlled diabetes mellitus and severe sepsis. Its pathogenesis and management are briefly discussed. (*Hong Kong j.emerg.med.* 2010;17: 61-65)

氣腫性腎盂炎是罕有但威脅生命的疾病，是由產生氣體的有機體引致腎主質壞死的感染。初期的徵狀可以是非特異性的。本文報告一個氣腫性腎盂炎的個案，病人呈現控制差劣的糖尿病及嚴重的敗血症；並簡要地討論其發病機理及處理。

Keywords: Diabetes complications, pyelonephritis, urinary tract infections

關鍵詞：糖尿病併發症、腎盂炎、泌尿道感染

Introduction

Gas-producing infections account for a very small percentage of bacterial infections in the urinary tract. Emphysematous pyelonephritis is an uncommon but life-threatening suppurative infection of the renal parenchyma and surrounding areas leading to gas formation in the collecting tubules, renal parenchyma, or perinephric tissues. Emphysematous pyelonephritis, together with emphysematous pyelitis (in the collecting

system) and emphysematous cystitis (in the bladder), represent a spectrum of gas-producing infections in the urinary tract. Yet, the three diseases have fairly different clinical course, management and prognosis.^{1,2} Among them, emphysematous pyelonephritis carries the highest mortality. This infection happens mostly in patients with diabetes mellitus.³ The management strategy is early recognition by a high index of suspicion with proper treatment including antimicrobial therapy, surgical drainage and nephrectomy.

Case

A 43-year-old man was brought to the emergency department in late May 2009 because of generalised weakness and on-and-off fever for a few days. The patient had history of diabetes mellitus with prescription of anti-diabetic drug in mainland China for more than ten years. He did not have respiratory, gastrointestinal or urinary symptoms.

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On arrival, he had a Glasgow Coma Scale score 15/15 but appeared dull. The blood pressure was 89/46 mmHg, pulse rate 86/min, temperature 37°C, and respiratory rate 30 shallow breaths per minute. He was managed in the resuscitation room. The physical examination revealed a very obese man with poor hydration status. His chest was clear and the abdomen was soft. There was no palpable intra-abdominal mass. The neurological examination was normal.

The bedside spot blood glucose test showed hyperglycaemia with blood glucose level 23.6 mmol/L. The arterial blood gas results revealed high anion gap metabolic acidosis with pH 7.28, bicarbonate 10.3 mmol/L, base excess -14.6 and anion gap 24 mmol/L. Urine for ketone was negative. The electrocardiogram showed normal sinus rhythm. The chest radiograph showed clear lungs. The patient was treated with fluid resuscitation and insulin infusion. He was subsequently transferred to the intensive care unit for further management.

He developed fever after admission with highest body temperature 38.5°C. The white cell count elevated to $27 \times 10^9/L$ (reference range: 3.9 to $10.7 \times 10^9/L$) and

the platelet count was normal. He was found to have impaired renal function with urea 29.8 mmol/L (reference range: 3.5 to 8.1 mmol/L) and creatinine 261 $\mu\text{mol/L}$ (reference range: 62 to 106 $\mu\text{mol/L}$). His liver function was also deranged with elevated alkaline phosphatase 514 U/L (reference range: 46 to 127 U/L), marginally elevated alanine transaminase 60 U/L (reference range: 10 to 57 U/L) and bilirubin 28 $\mu\text{mol/L}$ (reference range: 5 to 20 $\mu\text{mol/L}$). The plasma lactate was marginally elevated at 2.4 mmol/L (reference range: 0.5 to 2.2 mmol/L). The urine multistix showed pyruvia.

In an attempt to explain the deranged liver function, hepatitis serology was performed, which showed positive hepatitis B surface antigen and negative anti-hepatitis C virus antibody. Ultrasound scan of the abdomen was arranged to delineate suspected biliary sepsis. It was performed by the radiologist showing no dilatation of intrahepatic and common ducts, and no gallstone. However, echogenic foci with acoustic shadowing were noticed over the anterior aspect of the upper pole of the right kidney which was suggestive of the presence of gas (Figure 1). Computed tomography (CT) of the abdomen with contrast was performed,

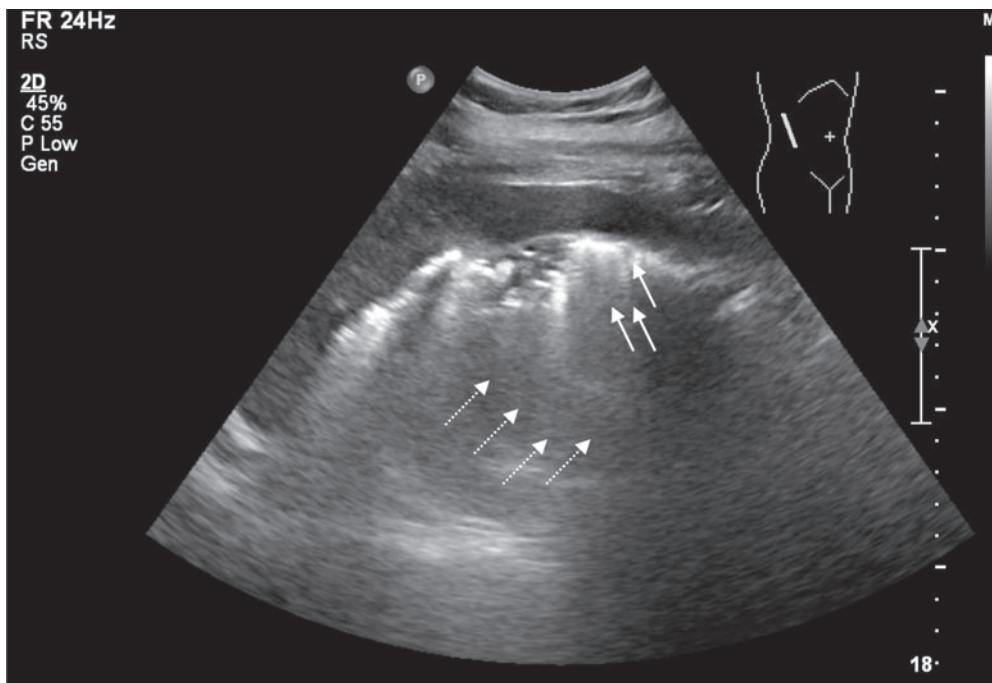


Figure 1. Ultrasound scan of right renal region showing multiple "ring-down" artefacts (arrows) with acoustic "dirty" shadowing (broken arrows) at upper part of kidney, suspicious of the presence of gas.

which showed impaired contrast-enhancement of the right kidney with air at the lower pole, perinephric and subcapsular spaces. There was heterogeneous soft tissue density around the right kidney, which represented a mixture of debris and fluid (Figure 2). The diagnosis of emphysematous pyelonephritis was made.

Blood culture grew *Escherichia coli* which was resistant to ceftriazone, while urine culture showed *Escherichia coli* as well which was an extended spectrum beta-lactamase producer. The patient was treated with fluid resuscitation, insulin, intravenous levofloxacin and meropenem. Though blood pressure could be maintained without inotropes, the patient had persistent tachycardia, fever and rising white cell count trend. In view of uncontrolled sepsis, right total nephrectomy was performed four days after admission. Intra-operatively, ascites and oedematous perinephric tissue were noted. The right kidney parenchyma was replaced by necrotic tissue. Histology of the infected kidney showed marked suppurative inflammation associated with necrotic debris. The patient clinically improved after operation. Liver and renal function normalised. He was discharged with oral anti-diabetic drug after a total hospital stay of 19 days.

Discussion

Emphysematous pyelonephritis is a rare disease which is rapidly progressive and fatal if untreated. Many names have been used to describe the disease including renal emphysema and pneumonephritis. The disease has a female preponderance (41:7), due to greater susceptibility of the urinary tract infection in females.³ The left kidney is involved more frequently than the right (67% vs. 25%).³ The overall mortality rate of emphysematous pyelonephritis ranges from 11% to 42%, averaging 25%.⁴ Therefore, prompt recognition and aggressive treatment are needed to improve clinical outcome.

Emphysematous pyelonephritis is highly associated with diabetes mellitus (up to 96%). It is also implicated in urinary tract obstruction, debilitating alcoholism, immunocompromised state and renal allografts.^{3,5}

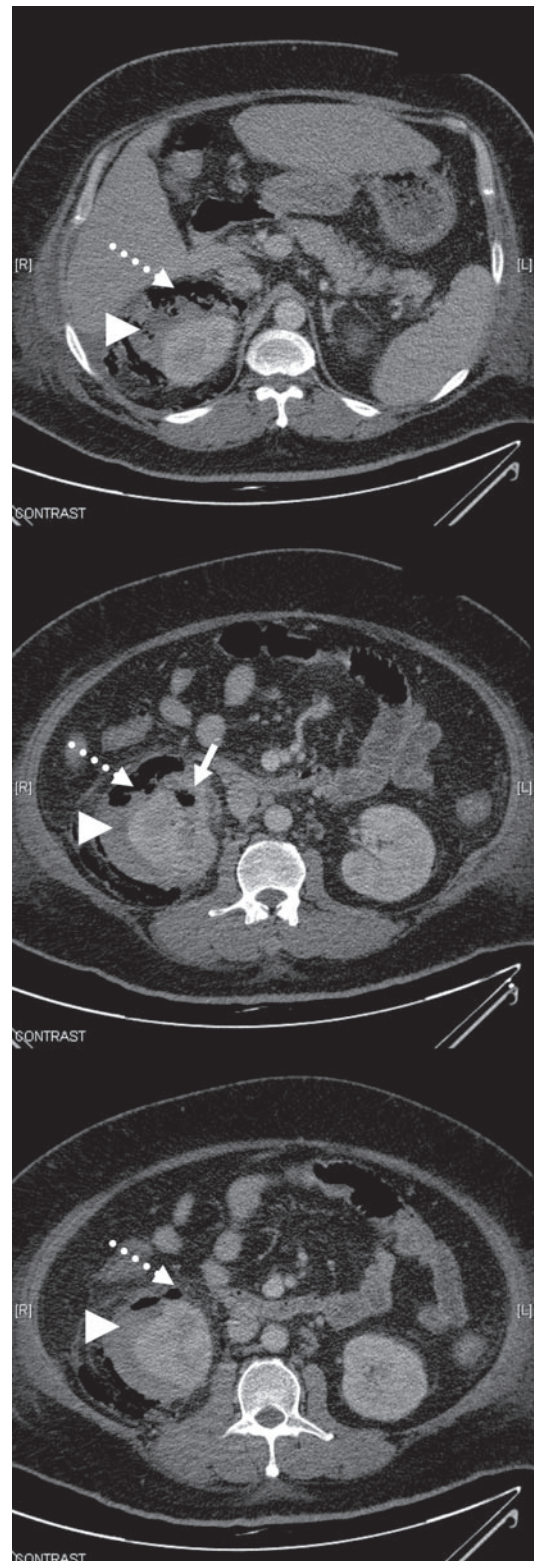


Figure 2. CT abdomen with contrast (axial images from cephalic downwards) showing the presence of gas in renal parenchyma (arrow) and peri-renal space (broken arrow). There was heterogeneous soft tissue density (arrowhead) around the right kidney.

The pathogenesis of gas production in emphysematous pyelonephritis was thought to be due to glucose fermentation. According to the results from analysis of the compositions of gas in the emphysematous infected kidneys, the pathogenesis was postulated to involve four essential factors including gas forming bacteria, high tissue glucose level, impaired tissue perfusion and underlying defective immunity. High tissue glucose levels in patients with diabetes mellitus provides gas forming microbes with a microenvironment favourable for their growth and rapid catabolism, which cause massive gas production in the ischemic environment.⁶ Mixed acid fermentation of glucose was implicated to be one of the pathway for the development of emphysematous urinary tract infection.⁷ Most infections are due to *Escherichia coli* (approximately 70%), *Klebsiella pneumoniae* (29%), *Proteus*, streptococci or mixed organisms (10%).^{3,8}

The clinical presentation is often quite acute. Most present with fever and chills (56%), followed by flank pain (48%). Some present with vomiting, shortness of breath, crepitus overlying the affected kidney, disturbance of consciousness and shock.^{3,9} Pontin et al reviewed 22 diabetic patients with emphysematous pyelonephritis, and found most of them had poor control of their diabetes in which 16 of them presented with ketoacidosis.¹⁰ In our patient, the clinical manifestation of urosepsis was not straightforward. He did not have loin pain or urinary symptoms, but exhibited severe sepsis and poorly controlled diabetes.

Diagnosis rests on high clinical suspicion, combined with appropriate imaging and culture. Abdominal X-ray may show the presence of renal gas. However, it is insensitive with a yield of less than 50%.¹¹ The gas may also be misinterpreted as bowel gas. Bedside ultrasonography, as readily available equipment in most emergency departments, is a useful tool to detect significant renal pathologies in patients presenting with acute renal failure or urosepsis. Renal ultrasound can confirm the presence of emphysematous pyelonephritis in 80% of cases.¹² The sonographic features of emphysematous pyelonephritis are characterised by "dirty" shadows and "ring-down" artefacts. "Dirty" shadows are caused by reverberations of air within the kidney (contrast to clean shadow produced by

calcifications and most gallstones). "Dirty" shadows have indistinct margins and contain echoes within the shadow. "Ring down" artefacts are originated in air bubbles trapped in fluid collections within the renal parenchyma. The artefacts are a collection of closely spaced perpendicular echoes along one or two vectors in the ultrasound image.¹³ The presence of these characteristic sonographic findings can hint the emergency physicians for the diagnosis of emphysematous pyelonephritis, thus leading to early appropriate management.⁸

The definitive diagnostic modality is CT, which can show gas bubbles, extent of involvement, abscess formation and obstructive uropathy.¹⁴

There are several classification systems for emphysematous pyelonephritis according to CT findings. One commonly used classification was described by Wan et al. It classifies emphysematous pyelonephritis into two types, which have differences in prognosis and treatment choice. Type I emphysematous pyelonephritis is characterised by renal parenchymal necrosis with absence of fluid content, or presence of streaky, spotted gas pattern. It is more fulminant and has a higher mortality rate (69%). Type II emphysematous pyelonephritis is characterised by the presence of renal or perirenal fluid accompanied by a bubbly gas pattern, or presence of gas in the collecting system. It has a lower mortality rate (18%). Absence of fluid was thought to reflect compromised immune response, and streaky gas was attributed to rapid destruction of renal parenchyma. These are features of more severe infection. In general, type I emphysematous pyelonephritis requires more aggressive surgical treatment.¹⁵ Our patient exhibited type II disease.

Besides emphysematous pyelonephritis, the differential diagnoses of renal gas collection in imaging include ileal loop diversion, reflux of gas from the bladder, urethral instrumentation, and spontaneous fistula formation with bowel, skin or lungs.¹⁶

Management requires a combination of medical and surgical treatments. Medical treatments include aggressive antibiotic treatment for the sepsis and

tight glycaemic control. Surgical management involves percutaneous catheter drainage, or nephrectomy for life-threatening infection.^{14,17} Percutaneous drainage is the preferred choice of treatment for patients with a solitary kidneys, bilateral renal involvement,¹³ or emphysematous pyelonephritis in a renal allograft.⁵

The prognosis of emphysematous pyelonephritis depends on the underlying disease, clinical status and treatment modalities. For clinical status, thrombocytopenia, acute renal function impairment, disturbance of consciousness and shock are associated with higher mortality, as they represent organ dysfunction of the haematological, renal, central nervous or cardiovascular system. On the other hand, age, sex, site of infection, and blood glucose level are not prognostic factors.^{3,4} For treatment modalities, medical treatment alone is associated with increased mortality.³ Our patient presented with extensive renal infection which manifested as acute renal function impairment and shock. Radical treatment in the form of nephrectomy was subsequently performed and he had a favourable outcome.

Conclusion

The urinary tract is one of the most frequent foci of infection in diabetic patients with sepsis. Emphysematous pyelonephritis is an uncommon disease but exhibiting high mortality. Successful outcome relies on a high index of suspicion and aggressive treatment. In case of septic shock and acute renal insufficiency, early parenteral antibiotic administration and nephrectomy are critical.

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