

Emphysematous Pyelonephritis with Abscesses Masquerading as an Ordinary Urinary Tract Infection

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Abstract: Emphysematous Pyelonephritis (EPN) is a rare, gas-forming infection of the renal parenchyma associated with significant morbidity and mortality. We report the case of a 39 year-old woman with uncontrolled diabetes who presented with abdominal pain, fevers and chills for one month. Physical exam was notable for dry oral mucosa and left costovertebral angle tenderness. Labs showed acute kidney injury and a hyperglycemic hyperosmotic state. CT abdomen revealed emphysematous pyelonephritis with a large left renal abscess. EPN should be considered in diabetic patients, especially those with uncontrolled or new-onset diabetes and those presenting with symptoms of urinary tract obstruction. Prognostic factors include thrombocytopenia, shock, altered mental status and need for hemodialysis. Our patient was treated successfully with intravenous antibiotics, percutaneous drainage, strict glucose control and monitored with serial imaging. She underwent laparoscopic nephrectomy one month later. Early diagnosis of EPN is essential as it carries a high mortality and a strong clinical suspicion is required, as patients may have an atypical presentation.

Keywords: Emphysematous, Pyelonephritis, Diabetes Mellitus, Complicated Urinary Tract Infections

Introduction

Emphysematous Pyelonephritis (EPN) is a rare necrotizing infection of the renal parenchyma, perinephric tissue and surrounding areas caused by gas forming organisms. One of the first accounts of gas forming kidney infection was described by Kelly and MacCallum in 1898. EPN falls under a spectrum of gas forming infections of the urinary tract that include emphysematous pyelitis and cystitis. The mean patient age is approximately 60 years and there is female predominance, with a ratio of 6:1. Diabetes was noted in about 90% of patients and urinary tract obstruction in approximately 20% (Aswathaman *et al.*, 2008; Best *et al.*, 1999). Although these infections account for only a small percentage of all urinary tract infections, recognition and early diagnosis is essential as they are associated with a high morbidity and mortality (Yao *et al.*, 2007). Pyelitis must be differentiated from pyelonephritis, as the former is often treated successfully with antibiotics alone, while

the latter can be life threatening. We describe a case of a patient who had an atypical presentation of emphysematous pyelonephritis and was treated early with intravenous antibiotics, percutaneous drainage and strict glucose control.

Case Presentation

A 39-year-old woman with newly diagnosed diabetes presented with nausea and abdominal pain for three days. The pain was diffuse, dull, and not related to eating. Associated symptoms included malaise and fatigue with exertion. Upon further questioning, the patient also reported fever, chills and polyuria over the past month. She denied dysuria, diarrhea, chest pain, shortness of breath, or lower extremity edema. She worked as a nurse practitioner in a nearby nursing home. She was diagnosed with diabetes about a month ago, treated with Glimiperide and has a history of iron deficiency anemia secondary to menorrhagia.

On initial evaluation, the patient was noted to be febrile to 103 F, with tachycardia to 144 beats/min, with a blood pressure of 92/59 mmHg, respiratory rate of 22 breaths/min and an oxygen saturation of 96% on ambient air. Her physical exam was remarkable for dry oral mucous membranes and non-specific left lower back tenderness, with a soft abdomen, non-tender, non-distended. Initial laboratory values were significant for acute kidney injury, hyperglycemia, hyponatremia, leukocytosis with neutrophilic predominance, thrombocytopenia and a microcytic anemia. Urinalysis showed cloudy urine, specific gravity of 1.020, glycosuria and 20-30 WBCs. Table 1 lists pertinent laboratory tests and their results.

A renal ultrasound was obtained to rule out hydronephrosis, which showed a complex mass on the lower pole of the left kidney and pyelocaliectasis. A CT scan of the abdomen and pelvis revealed emphysematous pyelonephritis with gas extending through the medulla into the cortex in the upper pole of the left kidney and a 6 cm fluid collection in the lower pole (Fig. 1). The patient underwent emergent drainage of the abscess of the left kidney with a placement of a percutaneous drain. About 75 cc of purulent drainage was removed initially but the patient continued to have purulent drainage for several days after the procedure. Blood culture, urine culture and culture from the purulent drainage all grew *Klebsiella pneumoniae*. The patient was initially treated

with piperacillin-tazobactam as the bacteria was found to be sensitive with a minimum inhibitory concentration of less than or equal to 4. However, she continued to have fevers and leukocytosis with bandemia. A repeat CT scan of the abdomen and pelvis done ten days into the admission showed a new medially located left perinephric abscess in the midpole region (Fig. 1). This new abscess was drained and a second percutaneous drain was placed. Again purulent drainage was noted for a few days after placement of the second percutaneous drain. On day 11 of antibiotic treatment with piperacillin-tazobactam due to continued fevers and leukocytosis, the antibiotic regimen was changed to Meropenem. The second abscess cultures also grew *Klebsiella pneumoniae*. The patient underwent a renal scan which revealed 27% function of the left kidney.

A month later the patient was readmitted with worsening renal function and the decision was made to proceed with nephrectomy. The patient underwent laparoscopic left radical nephrectomy and was continued on intravenous Meropenem for three days after the procedure and then switched to Cefazolin for three days. She was discharged on oral Cephalexin for one week. Our patient was successfully treated with antibiotics, percutaneous drainage, tight glucose control, monitoring with serial imaging and ultimately required nephrectomy.

Table 1. Laboratory values

Serum/blood lab test	Results	Reference range
Sodium	125 mmol/L	136-142 mmol/l
Potassium	4.2 mmol/l	3.5-5.0 mmol/l
Chloride	86 mmol/l	98-108 mmol/l
Bicarbonate	21 mmol/l	23-32 mmol/l
Urea nitrogen	46 mg dL ⁻¹	9-25 mg dL ⁻¹
Creatinine	2.0 mg dL ⁻¹	0.5-1.1 mg dL ⁻¹
Glucose	536 mg dL ⁻¹	54-118 mg dL ⁻¹
Protein	6.3 g dL ⁻¹	6.4-8.3 g dL ⁻¹
Albumin	3.1 g dL ⁻¹	3.7-5.4 g dL ⁻¹
Total bilirubin	0.8 mg/	0.0-1.0 mg dL ⁻¹
AST	75 U/l	7-30 U/l
ALT	51 U/l	9-32 U/l
Alkaline Phosphatase	146 U/l	30-100 U/l
Lactic Acid	3.4 mmol/l	0.5-2.2 mmol/l
Acetone	Negative	Negative
Hemoglobin A1C	13.1	3.8-6.4
CBC		
White blood count	19.8 k/mcl	4.5-11.0 k/mcl
Neutrophils	92%	40-70%
Lymphocytes	4%	22-44%
Monocytes	2%	0-10%
Eosinophils	1%	0-3%
Basophils	1%	0-1%
Hemoglobin	9.0 g dL ⁻¹	11.7-16.0 g/dl (women)
Hematocrit	27.90%	35-45% (women)
Platelets	103 k/mcl	150-350 k/mcl
MCV	79.0 fl	80-100 fl
Urine		
Urinalysis	Cloudy, pH 5.5, specific gravity 1.020, glucose 500mg/dL, moderate blood, 4+ protein, 20-30 WBCs, many bacteria, 8-12 squamous epithelial cells	
Beta HCG	Negative	Negative

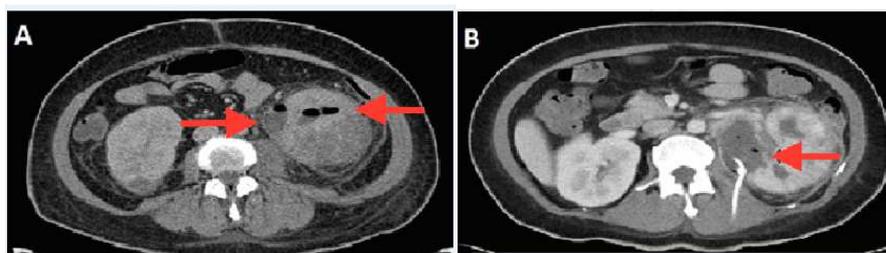


Fig. 1. (A) Computed tomography scan of the abdomen revealed left emphysematous pyelonephritis-air radiating through the medulla into the cortex (arrow, right), a complex fluid collection in the inferior pole measuring 6.2×6.4 cm (arrow, left) and air tracking into the retroperitoneum (B) Repeat CT abdomen 10 days after treatment with intravenous antibiotics and percutaneous drainage demonstrated an enlarged left kidney with areas of necrosis and a decrease in abscess size and amount of air (arrow)

Discussion

Major risk factors for emphysematous pyelonephritis include uncontrolled diabetes mellitus and urinary tract obstruction. These infections occur with a higher frequency in females and may be due to the higher occurrence of urinary tract infections in females. A few cases have been reported in non-diabetic patients with a history of immunosuppression or urinary tract obstruction secondary to nephrolithiasis or a tumor (Ali and Barlas, 2010; Mokabberi and Ravakhah, 2007). Patients with uncontrolled diabetes, such as our patient, are particularly susceptible to these infections due to high levels of glycosylated hemoglobin and impaired host defense mechanisms.

Factors that may be involved in the pathogenesis of EPN include elevated glucose levels, presence of gas-forming organisms, weakened host immunity and impaired tissue perfusion. *Escherichia coli* (69%) and *Klebsiella pneumoniae* (29%) are noted to be the most common pathogens. Other microbes cultured include *Proteus mirabilis*, *Pseudomonas aeruginosa* and *Enterococcus* species. Anaerobes such as *Bacteroides fragilis* and *Clostridium septicum* have also been implicated in emphysematous pyelonephritis (Lu *et al.*, 2014). Organisms found in blood cultures were also simultaneously noted in the abscess and urine cultures. High glucose levels may provide a more favorable environment for these organisms, leading to increased rate of growth and catabolism. Enterobacteriaceae lead to mixed acid fermentation of glucose, thus producing gas in the renal parenchyma (Huang and Tseng, 2000). Pathological analysis of gas has shown that they contained hydrogen, carbon dioxide and nitrogen (Huang and Tseng, 2000).

Patients often present with fevers, chills, vague abdominal pain, nausea, flank pain and dysuria-symptoms typical of acute severe pyelonephritis. However, some patients may initially present with severe sepsis, acute kidney injury, thrombocytopenia, altered consciousness and even shock. The left kidney was found to be more frequently involved than the right (67% Vs 25%) (Huang and Tseng, 2000; Falagas *et al.*,

2007). Our patient did not have the typical symptoms of pyelonephritis such as dysuria or flank pain, but was noted to have non-specific lower back tenderness which prompted consideration of pyelonephritis and further imaging. Our clinical suspicion for severe pyelonephritis was high given her history of uncontrolled diabetes. The diagnosis of EPN should be considered in diabetic patients, especially those with uncontrolled or new-onset diabetes and those presenting with symptoms of urinary tract obstruction.

Computed tomography scan is the most reliable diagnostic imaging modality and can be used to characterize the extent of disease (Huang and Tseng, 2000). Ultrasound is operator dependent and not sensitive when imaging gas (Rauf *et al.*, 2007). Gas may appear as nonspecific echogenic foci and may be mistaken for nephrolithiasis. Abdominal x-ray can be utilized as an initial imaging modality, however gas may be seen in only 33% of cases and may not be distinguishable from air in the bowel (Huang and Tseng, 2000). Likewise, our patient initially had a renal ultrasound. No hydronephrosis was noted, however a large complex mass suspected to be an abscess was seen, along with pyelocaliectasis and questionable left renal calculi; no gas was reported. Given the high clinical suspicion for complicated pyelonephritis, a CT abdomen was ordered, which confirmed the diagnosis of EPN. Of note, the echogenic foci thought to be calculi on ultrasound were confirmed to be areas of gas on CT. Thus, our case further supports the superiority of CT scan in the diagnosis of EPN.

Poor prognostic factors in EPN include thrombocytopenia, azotemia, high urinary red blood cell counts, altered mentation, low blood pressure, worsening proteinuria, shock, altered mental status, extension of infection to the perinephric space and the need for hemodialysis (Aswathaman *et al.*, 2008; Falagas *et al.*, 2007; Misgar *et al.*, 2015). In some cases, the degree of hematuria may be used to identify the extent of necrosis from the infection and the presence of renal vein thrombosis (Misgar *et al.*, 2015). Thrombocytopenia was likely due to severe sepsis and disseminated intravascular coagulation. Mortality increased significantly with the presence of more risk factors, from 27% with one risk factor to 100% with several.

Michaeli *et al.* (1984) originally characterized emphysematous pyelonephritis into three classes (Sharma *et al.*, 2013). This categorization was later re-classified with the use of CT imaging. Class I is defined as gas in the collecting system; Class II as parenchymal gas only; Class III is further sub-divided into either extension into the perinephric space (Class IIIA) or into the pararenal space (Class IIIB) and Class IV involves bilateral disease (Huang and Tseng, 2000).

There is no consensus on what constitutes ideal management of patients with emphysematous pyelonephritis. However, all patients should be treated with parenteral antibiotics. In patients with Class I disease, antibiotics alone are often sufficient. Patients with Class I and II disease are treated with antibiotics and percutaneous drainage. In patients with Class IV disease (bilateral EPN), nephrectomy is to be avoided and used as a last resort. Antibiotics are chosen by the same guidelines as those for patients with pyelonephritis: A third generation cephalosporin or fluoroquinolone for mild to moderate pyelonephritis (aztreonam for those with a beta lactam allergy) and broader antibiotic coverage (ampicillin-sulbactam, ticercillin-clavulanate, piperacillin-tazobactam, meropenem, or imipenem) for those patients with severe pyelonephritis, immunosuppression and/or incomplete urinary drainage (Stamm and Hooton, 1993). Vancomycin in combination with imipenem or ceftazidime is the empiric treatment of choice in patients presenting with sepsis and septic shock Lu *et al.* (2014). Older patients with uncontrolled diabetes presenting with symptoms of septic shock with a prior history of recently treated pyelonephritis should undergo emergent nonenhanced computed tomography scan (Chen and Chen, 2014).

For patients with IIIA or IIIB classification and two or more prognostic factors (thrombocytopenia, shock, altered sensorium and need for hemodialysis), nephrectomy may be considered. Nephrectomy may be necessary in all patients who fail therapy with antibiotics and percutaneous drainage (Aswathaman *et al.*, 2008; Falagas *et al.*, 2007). Patients with severe hypoalbuminemia were found to have a higher risk of conservative treatment failure (Falagas *et al.*, 2007). However, more recent studies show that the treatment success rate was over 80% with a combination of antibiotics and percutaneous drainage. Treatment has evolved over the years from a surgical approach such as emergent nephrectomy, to a more conservative approach including intravenous antibiotics and/or percutaneous drainage (Aswathaman *et al.*, 2008). A systematic review of 210 patient cases noted that mortality was significantly lower in those patients treated with antibiotics and percutaneous drainage as compared to nephrectomy (Somani *et al.*, 2008). Our patient had Class II/III disease with two risk factors: thrombocytopenia and presented with severe sepsis. The

diagnosis was made within hours of presentation and she was treated successfully with intravenous antibiotics, percutaneous drainage, strict glucose control and monitored with serial imaging. Early diagnosis is essential, as delays have been associated with increasing complications and higher mortality (Huang and Tseng, 2000). However, a month later she continued to have worsening renal function and underwent left laparoscopic radical nephrectomy.

For patients with EPN, the duration of antibiotic treatment has not been clearly defined. Our patient was continued on parenteral antibiotics for more than two weeks in the hospital, then discharged on intravenous and oral antibiotics for another two weeks. She defervesced after 13 days of treatment but continued to experience occasional chills. A repeat CT showed mild improvement and decrease in the size of the abscesses. After nephrectomy, she was continued on intravenous antibiotics and then transitioned to oral therapy for an additional week on discharge. Some patients remain on antibiotic therapy after intervention and the duration reported ranges from 10 days to 30 days depending on severity of the illness (Arsene *et al.*, 2014). Oral antibiotics may be continued afterwards for one to three months (Best *et al.*, 1999; Jain *et al.*, 2000; Laway *et al.*, 2012; Tahir *et al.*, 2000). There are currently no established guidelines for recommended duration of antibiotics for EPN.

Early diagnosis of EPN is essential as it carries a high mortality. Patients with uncontrolled diabetes and urinary tract obstruction are particularly at risk. Prompt computed tomography is essential to establish the diagnosis. Early resuscitation, broad antimicrobial therapy and percutaneous drainage are the mainstays of initial therapy. A strong clinical suspicion is required, as EPN may have an atypical presentation (Ali and Barlas, 2010) and may masquerade as an ordinary urinary tract infection.

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Author's Contributions

Tasnim F. Imran: Concept data acquisition, literature search, composing manuscript, selecting images, revision.

Frederick Yick: Literature search, composing, manuscript, editing of images, table.

Ahmed H. Qavi: Literature search, manuscript, editing images.

Sundar Dhamotharan: Critical revision of manuscript.

Steven J. Sperber: Editing, composition, critical revision of manuscript.

Ethics

Patient consent was obtained prior to publication.

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