Chapter

Emphysematous Urinary Tract Infections

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Abstract

Emphysematous urinary tract infections are severe necrotizing infections of the urinary tract. The descriptive term emphysematous is used for the gas location site: pyelonephritis, pyelitis, and cystitis. Most cases occur in adult females. Diabetes mellitus constitutes the most commonly associated comorbidity and a risk factor for necrotizing infections. Pathogenesis still needs to be fully understood. *Escherichia coli* is the most common microorganism, followed by *Klebsiella pneumonia, Proteus mirabilis*, and *Pseudomonas aeruginosa.* Bacteremia occurs in more than half of cases. The treatment includes resuscitation, glycemic control, and antimicrobial therapy, followed by early drainage. Emphysematous cystitis is the most common and frequently least morbid gas-forming urinary tract infection. Using minimally invasive image-guided procedures for drainage of gas and abscess is a conservative strategy with renal preservation, while emergency nephrectomy is considered the last option. Mortality rates have a direct correlation between the computed tomography findings and the modalities of treatment.

Keywords: necrotizing urinary tract infection, emphysematous urinary tract infections, emphysematous pyelonephritis, emphysematous pyelitis, and emphysematous cystitis

1. Introduction

Emphysematous urinary tract infections are severe necrotizing infections characterized by the presence of gas. Classification is based on the gas location site and extent: emphysematous pyelonephritis is gas in the renal parenchyma and the surrounding tissues; emphysematous pyelitis is gas only in the collecting system; emphysematous cystitis is gas within the bladder wall and lumen. The coexistence of emphysematous pyelonephritis (EPN) and emphysematous cystitis (EC) is uncommon. The cases of pneumaturia in which gas develops in the urinary tract through some fermenting microorganism were described in 1898 [1]. Other researchers have confirmed that the mixed acid fermentation of glucose by microorganisms is the primary pathway of gas formation [2]. The term emphysematous pyelonephritis was first used in 1962, with the first series of cases included from 1989 to 1962 [3]. The diagnostic challenge in these infections is that clinical manifestations do not distinguish the severity of necrotizing infections. The diagnosis depends on detecting gas in or around the kidney, collecting system, or bladder. The best diagnostic method

is computed tomography (CT) to confirm EPN [4]. Empiric antimicrobial therapy should primarily target *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Pseudomonas aeruginosa*. The current trend in using minimally invasive procedures for EPN is to perform a percutaneous intervention or internal drainage in most patients [5]. The case series EPN from 1980 to 2011 showed a mortality rate of 18% [4].

2. Emphysematous pyelonephritis

EPN is a severe necrotizing infection characterized by gas in the renal parenchyma and the surrounding tissues. The term EPN was first used in 1962 with a report of a female with a tender mass in the right flank. Her abdomen X-ray revealed gas surrounding and infiltrating the right kidney. Retrograde pyelogram showed that renal calyces and pelvis are compressed and displaced medially by a gaseous inflammatory process [3].

2.1 Epidemiology

Most reported cases of EPN occur in adult patients. The incidence is higher in females than males, with a preponderance (3:1) and mean age of 56.6 years. Diabetes mellitus (DM) constituted the most commonly associated comorbidity and a risk factor for EPN, with an incidence of 85% [4, 6, 7]. Other comorbidities include urolithiasis, a previous history of treated pyelonephritis, and chronic kidney disease [6]. To date, few cases of EPN have been reported in pediatric patients. Risk factors for pediatric: neurogenic bladder, ureteropelvic junction obstruction, obstruction due to ectopic ureter, renal stone, nephro-urological congenital malformation, congenital ureterocele, and acquired immunodeficiency [8]. The left kidney is most commonly affected in 52–67%, on the right side in 25–37.7%, and bilateral in 10.2–15.3% [4, 6, 7, 9].

2.2 Pathogenesis

The pathogenesis of EPN is not yet fully understood; it could be different between patients with diabetes and no diabetics. The cases of pneumaturia in which gas develops in the urinary tract through some fermenting microorganisms were described in 1898 [1]. Mixed acid fermentation of glucose by microorganisms is the primary pathway of gas formation. Emphysematous infection in the urinary tract requires four critical conditions to develop: (1) the presence of gas-forming bacteria or fungi, (2) high local tissue glucose level, (3) impaired tissue perfusion, and (4) an inadequate immune response [2].

A urinary tract obstruction is seen in 75% of patients. It is attributable to ureteric calculi, renal papillary necrosis, ureteric stricture, and fungal bezoar [7]. Urolithiasis may be the most important contributing factor in the pathogenesis of EPN among no patients with diabetes [5]. Accumulating the gas in unrelieved urinary tract obstruction can raise pelvicalyceal pressure. Further impairing renal circulation results in poor tissue perfusion and infective parenchymal destruction [7].

A gross examination of nephrectomy specimens shows multiple abscesses in the renal parenchyma. On microscopic examination: blurred corticomedullary differentiation, congested medulla, patchy areas of hemorrhage, empty spaces, acute inflammatory cell infiltration in the surrounding areas, vasculitis, extensive necrosis, microscopic abscesses, glomerulosclerosis, arteriosclerosis, intrarenal vascular thrombi, and infarcts, or papillary necrosis [10–12].

2.3 Clinical presentation

The clinical manifestation and urinalysis do not distinguish the different types and severity of pyelonephritis. In EPN, the mean duration from the onset of symptoms to diagnosis ranged from 4 to 11 days [12]. Clinical manifestations of EPN include fever and rigors in 74.7%, flank pain in 70.4%, acute renal failure in 45.2–80%, pneumaturia in 35%, and shock in 24.6%. Septic shock at admission indicates a poor prognosis. A palpable tender kidney has been identified as one of the poor clinical prognostic parameters requiring prompt intervention and intensive monitoring. Approximately 40.4% of the patients require admission to the intensive care unit [4, 6, 11, 13].

2.4 Diagnosis

Laboratory findings demonstrate leukocytosis in 70.9% and thrombocytopenia in 25.8% [14]. Urinalysis results are positive for pyuria and hematuria [4, 7, 15]. Urine culture identified *E. coli* as the most common infective microorganism, followed by *K. pneumoniae, Proteus* sp., *Pseudomonas* sp., *Candida albicans*, *and Enterococcus* sp., among others [4–6, 9, 15, 16]. Polymicrobial infections are found in 10–23.5% [10, 16]. Extended-spectrum β–lactamase-producing Gram-negative pathogens are found in 39% of the cases [7]. Bacteremia occurs in more than half of cases (54–75%). The blood culture is positive for the same microorganism identified in the urine. *E. coli* and *K. pneumoniae* are the most common microorganisms in blood cultures [4, 6, 9, 10].

The diagnosis depends on detecting gas in or around the kidney. The best diagnostic method is CT to confirm EPN, which also aids in staging the EPN and underlying urinary tract obstruction. While the accuracy rate for ultrasonography is 67.9% and for X-ray film of the abdomen is 53.2% [4, 7].

Classification of EPN is based on radiological imaging. The most commonly used is the CT scan classification system Huang-Tseng. This classification established the location and extent of gas or abscess in the renal parenchyma and surrounding tissues. The classification focused on the radiological severity, prognosis, and management: class 1, gas in the collecting system; class 2, gas in the renal parenchyma without extension to extrarenal space; class 3A, an extension of gas or abscess to perinephric space; class 3B, an extension of gas or abscess to pararenal space; and class 4, bilateral involvement or solitary kidney with EPN [9].

2.5 Treatment

There are different treatment options and effective ways of initial management of EPN, which improves survival and helps preserve renal function. Employing different measures, which include aggressive resuscitation, glycemic control, and parenteral antimicrobial therapy followed by early drainage of the infected fluid, as well as gas and release of urinary tract obstruction [7].

2.5.1 Antimicrobial therapy

Empiric antimicrobial therapy should primarily target *E. coli*, *K. pneumoniae*, *P. mirabilis*, *P. aeruginosa*, and *Enterococcus* sp. Third-generation cephalosporins are recommended as initial treatment. Carbapenems are the empiric therapy of choice in patients, with histories of prior hospitalization, antibiotic use, those needing emergency hemodialysis or developing disseminated intravascular coagulation, and

clinically unstable patients irrespective of CT findings (low/high risk) [16, 17]. There has yet to be a consensus on the duration of antimicrobial therapy for ENP. At the time of discharge, the duration of treatment could reach ≥4 weeks [18].

2.5.2 Minimally invasive procedures

Using minimally invasive image-guided procedures for drainage of the gas and abscess is a conservative strategy with renal preservation. In 1986, EPN was successful management by percutaneous drainage (PCD) under fluoroscopic guidance and medical management [19]. This report was followed by CT-guided interventional drainage. PCD tube placement is best done with CT guidance. Monitoring response to PCD, CT was done 4 to 7 days later to ascertain the location of the catheter and assess the abscess resolution. Catheters were removed when follow-up scans indicated complete resolution. Antimicrobial therapy with PCD was associated with improved survival rates [20]. The PCD and relief of urinary tract obstruction (if it exists) combined with antimicrobial therapy is the choice for class 1 or 2 of the CT scan classification system Huang-Tseng. However, for extensive classes, 3 or 4 may be attempted too [9].

Other alternative intervention strategies include JJ stent insertion or percutaneous nephrostomy insertion. [6] The preference for placing JJ stents as the choice of drainage procedure is because it can be performed endoscopically [15]. The current trend in using minimally invasive procedures for EPN is to perform a percutaneous intervention or internal drainage in most patients [5].

2.5.3 Open surgical drainage

Available evidence has suggested that if antimicrobial therapy with PCD is not improving the patient's condition, open surgical drainage must be considered before considering a nephrectomy [4]. Perinephric and extensive pararenal abscesses are other indications for open surgical drainage with the placement of large caliber tubes. Opening the Gerota fascia in cases of perinephric collections is a crucial and rewarding step to drain the gas and infected fluid [7].

2.5.4 Emergency nephrectomy

Since the early series reported, the immediate nephrectomy has been a subject of controversy [10, 12]. More recently, kidney preservation should be the primary goal in treating EPN when the differential renal clearance is >10% because the preserved kidneys maintained their function during the follow-up [13, 17]. Emergency nephrectomy is considered the last option. Furthermore, it is reserved only for patients with extensive EPN and fulminant courses or for patients who can not be stabilized despite aggressive resuscitation or by failure percutaneous measures. [5, 7, 9] Considering these indications, the number of patients requiring emergency nephrectomy is 6% [5–7, 17].

2.6 Mortality

Mortality rates had a direct correlation with the CT findings and the modalities of treatment. Patients with extensive EPN class 3B or 4 of the CT scan-classification system Huang-Tsengn had a high mortality rate of 45% [11]. The mortality rate approached 46% among patients who received medical treatment only [12]. Using

minimally invasive procedures with medical treatment showed a mortality rate of 18.8% [4, 5]. Risk stratification of the lethality of the EPN based on the prognostic scoring system reaches an overall mortality rate of <6%. A score of 1–8 is very low risk, a score of 9–15 is low-risk, a score of 16–20 is intermediate risk, and a score of >20 is high risk. A higher prognostic score was associated with mortality. Identifying prognostic indicators and risk stratification allow prompt and appropriate medical and surgical treatments [6].

The factors associated with mortality: systolic BP <90 mm Hg at admission, decreased platelet count <100,000/mm^3, urine culture for *E. coli*, hyponatremia, radiological severity with higher CT grade at admission, higher creatinine levels, and emergency nephrectomy [5, 14]. Over 54% of patients with septic shock died from EPN [4]. Early risk stratification, intensive management, and prompt treatment according to a protocol can reduce mortality even further in patients with EPN [17].

3. Emphysematous pyelitis

Emphysematous pyelitis (gas only in the collecting system-class1) is classified into mild class EPN with a better prognosis. In this class, conservative management should be considered [4].

4. Coexistence of emphysematous pyelonephritis and emphysematous cystitis

The coexistence is an uncommon presentation that has been reported rarely [11]. Patients with EC can progress ascending emphysematous infections, and 10.2% may subsequently develop EPN, which could significantly increase the associated morbidity and mortality of these infections [21–23].

5. Emphysematous cystitis

Emphysematous cystitis (gas within the bladder wall and lumen) is the most common and frequently the least morbid gas-forming urinary tract infection.

5.1 Epidemiology

The incidence of EC is unknown since the number of EC might be underdiagnosed, as imaging studies are not routinely used in patients with urinary tract infections. The main risk factors for EC are DM in 70%, chronic kidney disease, neurogenic bladder, recurrent urinary tract infection, and urinary stasis secondary to bladder outlet obstruction [21, 23].

5.2 Anatomopathological findings

A pathological assessment of involved bladder tissue might show bladder wall thickening with vesicles of varying size. Microscopic findings showed multiple gas-filled vesicles predominantly within the bladder mucosa lined by flattened fibrocytes and multinucleated giant cells [24].

5.3 Clinical presentation

Patients can be asymptomatic in 7%, with diagnosis incidental to abdominal imaging for other concurrent illnesses [23]. Symptoms of acute cystitis are nonspecific and usually mild; dysuria, urinary frequency, and urinary urgency occur in approximately 50% of patients. Fever may be observed in approximately 30–50%. Other symptoms may be present, such as abdominal pain and hematuria [22].

5.4 Diagnosis

E. coli is the most common cause of EC in 40.4%, followed by *Klebsiella pneumonia*, *Enterobacter aerogenes*, *P. mirabilis*, and *Streptococcus* spp. Extended-spectrum β–lactamase-producing Gram-negative pathogens are identified in 36.5% [21]. EC is diagnosed by: radiological studies, through direct visualization on cystoscopy, and during laparotomy, on tissue from bladder biopsy or autopsy. Most cases are diagnosed using simple plain films of the abdomen, 84%. CT detects cases of EC that are not apparent on plain abdominal films. CT accurately defines the extent and severity of EC and allows an assessment of ascending infection [23].

5.5 Treatment

Most patients are treated successfully with glycemic control, antimicrobial treatment, urethral catheterization, and hydration [21, 23]. The severity of the EC determines the surgical method. Surgical involved cystectomy, partial cystectomy, or debridement. Surgery is required in patients exhibiting a poor response to initial medical management or those with severe necrotizing infection.

5.6 Mortality

The overall death rate of EC is 7%. Among the patients that die are the following associated conditions: septic shock, late presentation, perforation of the bladder, and nonresponse to medical therapy [22, 23].

6. Case report

A 51-year-old man was admitted to the hospital with malaise, left flank pain, fever, chills, and dysuria lasting 5 days. He has a history of 20 years with diabetes mellitus and hypertension, receiving insulin, metformin, and telmisartan therapy. On physical examination, he had a 103/52 mm Hg blood pressure with mild left costovertebral angle tenderness. Laboratory values revealed impaired renal function with a serum creatinine of 3.2 mg/dL and blood urea of 198.5 mg/dL. Procalcitonin of 12.9 ng/ml, white blood cell counts of 19×10^9/L, HbA1c 9.7%, D-dimer of 1707 ng/ml, and glycosuria. An urgent abdominal CT scan showed class 3B, CT scan-classification system Huang-Tseng with an extension of gas or abscess to pararenal space (**Figure 1**) and EC. Initial empiric antimicrobial therapy with ertapenem started. On day 1 of admission, the patient was transferred to the intensive care unit after open surgical drainage of gas, an abscess of 80 mL, and placement of large caliber tubes. At the time of admission, he was intubated with a blood pressure of 95/51 mm Hg and vasopressor support. The sequential organ failure assessment (SOFA) score was 8, with an estimated

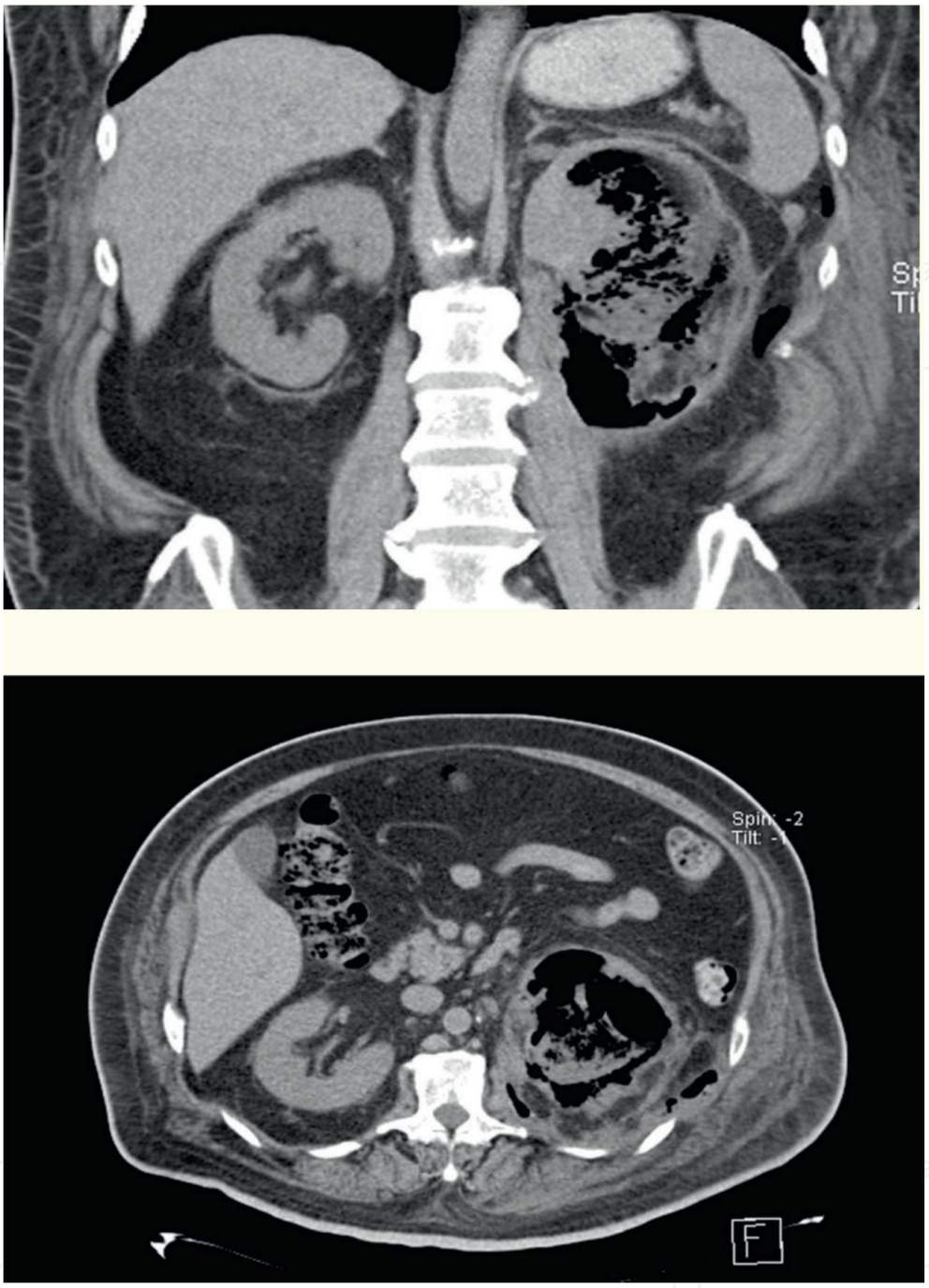

Figure 1.
CT scan of a 51-year-old male with left side class 3B ENP CT scan-classification system Huang-Tseng with an extension of gas and abscess to pararenal space. It shows an enlarged left kidney with intraparenchymal gas.

mortality of 15–20%. SOFA score was used to quantify the degree of organ dysfunction or failure present on admission and stratify for mortality prediction in intensive care unit patients. The acute physiology and chronic health disease classification system (APACHE) II score was 22, with an estimated mortality of 57.4%. This score includes weightage for age, past comorbid conditions, acute physiological parameters, emergency surgery, and reason for intensive care unit admission. APACHE II score was designed to measure the severity of disease for adult patients admitted to intensive care units. After 4 days in the intensive care unit, he was transferred back to the ward. On day 22 of hospitalization, open surgical drainage of an abscess in a pararenal space

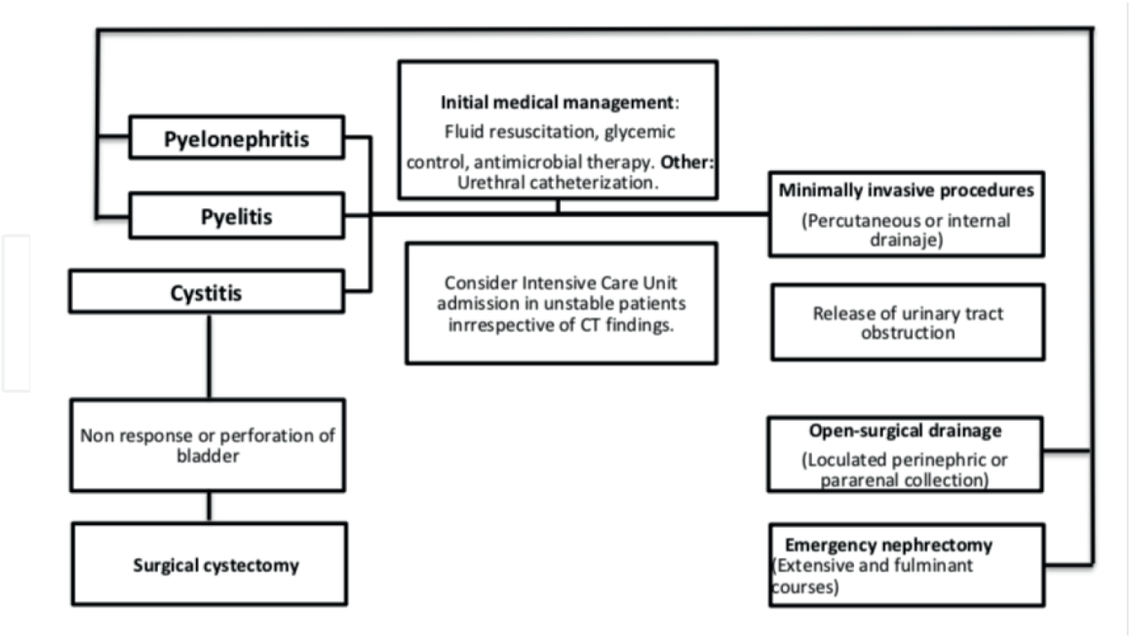

Figure 2.
Management of emphysematous urinary tract infections.

of 200 mL with debridement was realized. On day 27, a nephrectomy was performed (**Figure 2**). *E. coli* was isolated from urine and abscess with the same sensitivity pattern and positive for extended-spectrum β–lactamase. He received meropenem for 4 weeks, and his renal function gradually returned to normal. He was discharged after 44 days of hospital stay.

7. Conclusions

Emphysematous urinary tract infections are severe necrotizing infections of the urinary tract. Septic shock at admission and a palpable tender kidney have been identified as poor clinical prognostic parameters. The diagnosis depends on detecting gas in or around the urinary tract. The best diagnostic method is CT to confirm emphysematous urinary tract infections. Extended-spectrum β–lactamase-producing Gram-negative pathogens are found in high percentages of cases. This type of resistance is a global public health concern. Mortality rates had a direct correlation with the CT findings and the modalities of treatment.

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