Acute Renal Infection in Adult, Part 2: Emphysematous Urinary Tract Infection—What the Radiologist Needs to Know

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Abstract

Renal emphysema, as described by Kelly and MacCallum in 1898, refers to the spontaneous generation of gas within the renal parenchyma and surrounding tissues. Since its initial description, it has become apparent that the spectrum of radiologically visible renal and perirenal gas includes three distinct clinical entities: (1) emphysematous pyelonephritis, a necrotizing infection associated with gas formation in the renal parenchyma, (2) emphysematous pyelitis, in which gas is confined to the renal pelvis and calyces, and (3) gas-forming perinephric abscess. In this article, we will review gas-forming infections of the urinary system in terms of radiological features, clinical manifestations, predisposing factors, and appropriate management guidelines.

Keywords
► emphysematous cystitis
► emphysematous pyelonephritis
► urinary infection

Introduction

The striking radiological appearance of the presence of air within the parenchyma of solid organs or the walls of hollow viscera may result from infective as well as noninfective entities. Common noninfective causes of gas in organs may be due to ischemic cell death followed by necrosis and fistulation from the bowel, or due to iatrogenic or traumatic causes.[1]

Radiologically visible gas associated with infection is generally thought to consist of carbon dioxide and nitrogen secondary to the fermentation of glucose by some species of bacteria. There is a reduced rate of glycolysis at the tissue level in diabetic patients that results in increased glucose concentrations within the interstitial fluid, which feed bacterial metabolism. There are other factors that contribute to the production of gas or slowed removal of gas in tissues. Depressed cell-mediated immune response, local tissue necrosis, and the presence of arteriosclerosis are implicated as important factors in gas-producing infection.[1,2]

In most gas-forming infections, prognosis depends on early diagnosis and early treatment. Hence, appropriate radiological imaging with prompt accurate interpretation plays an important role in the diagnosis and management of these diseases.

Initial presentation of most emphysematous infections may be insidious, but they may progress to severe life-threatening conditions later in the course of the disease. Though plain radiography and ultrasonography (USG) are the initial imaging choices for almost all abdominal pathology, computed tomography (CT) remains the gold standard for diagnosing all emphysematous infections. CT is excellent in detecting gas and excluding the differential diagnosis.

In this article, we will review gas-forming infections of the urinary system in terms of radiological features, clinical manifestations, predisposing factors, and appropriate management guidelines.

Emphysematous Renal Infection: Terminological Distinction

Renal emphysema, as described by Kelly and MacCallum[3] in 1898, refers to the spontaneous generation of gas within the renal parenchyma and surrounding tissues. Since its initial

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description, it has become apparent that the spectrum of radiologically visible renal and perirenal gas includes three distinct clinical entities: (1) emphysematous pyelonephritis (EPN), a necrotizing infection associated with gas formation in the renal parenchyma, (2) emphysematous pyelitis (EP), in which gas is confined to the renal pelvis and calyces, and (3) gas-forming perinephric abscess (**►Fig. 1**).

The common causes of gas in the urinary tract are summarized in **►Table 1** after Joseph R C et al.[4] EP is a relatively less severe condition with a lower mortality rate and lesser association with diabetes as compared with EPN.[4] Radiology reports need to exercise caution in terminology and not label this milder form as EPN.

The incidence of gas within renal abscesses is rare in the absence of factors such as diabetes. The occurrence of gas within infarcted renal cell carcinoma following embolization therapy is a recognized entity and is related to tissue necrosis rather than infection.

Relevant Clinical Issues

Diabetes is a predisposing factor in all the emphysematous infections that occur in the urinary tract. More than 90% cases of EPN occur in diabetic patients, with 10% incidence of bilateral disease.[4] Underlying poorly controlled diabetes is present in up to 90% of patients who develop EPN compared with only 50% of patients with EP who have diabetes.[4]

While attempting to explain the *pathogenesis* of emphysematous urinary tract infections (UTIs), it is assumed that high glucose concentration within the tissues acts as a favorable substrate for organisms to produce carbon dioxide through facultative anaerobic glycolysis. However, this assumption cannot adequately account for the large number of nondiabetic patients with emphysematous infections. In nondiabetic patients, urinary albumin is proposed to be the substrate for gas production by urinary pathogens. Another theory suggests that an impaired host response, involving vascular compromise and impaired catabolism within the tissues, predisposes patients to gas production within these tissues.[3] The pathogenesis is not yet fully understood, but a multifactorial etiology of impaired host responses with sugar or protein fermentation seems to be a plausible explanation for the production of gas within the affected tissues.

EPN in *renal transplant recipients* is rare, with only 22 such cases reported in literature reviews.[5,6] Though rare, it carries

Table 1 Causes of gas in the urinary tract

Infection:
Kidney: emphysematous pyelonephritis, emphysematous pyelitis, renal abscess, perinephric abscess, and emphysema, and less commonly infracted renal cell carcinoma
Bladder: emphysematous cystitis
Iatrogenic: surgical or following endoscopic procedures
Penetrating trauma
Enterourinary fistulae

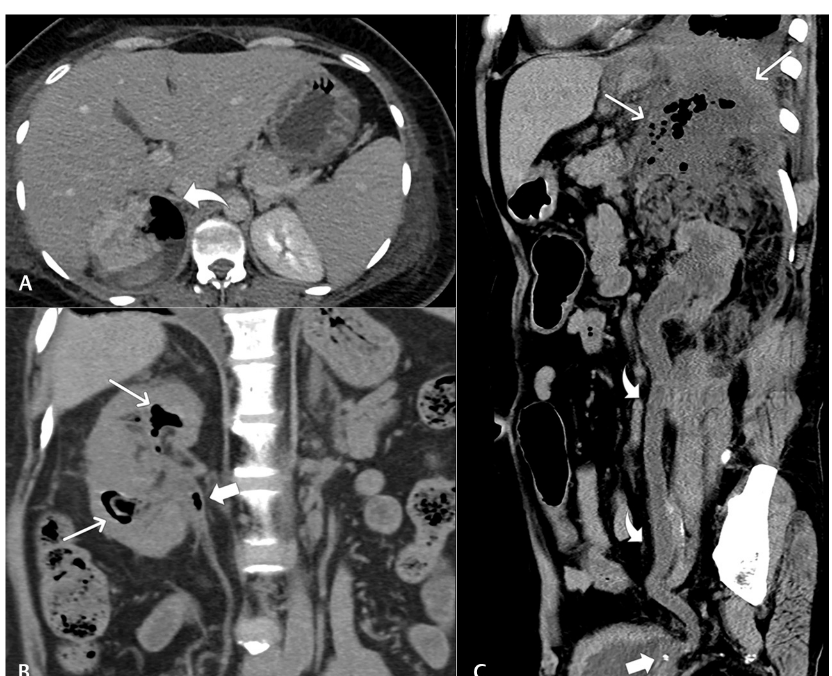

Fig. 1 (**A**) Emphysematous pyelonephritis. Axial computed tomography (CT) in the nephrogram phase of a diabetic 62-year-old man shows an abscess at the upper pole of the right kidney destroying the parenchyma with an air–fluid level (*curved arrow*) (**B**) Emphysematous pyelitis. Plain coronal CT reconstruction of a diabetic 54-year-old lady shows air within the calyces, which are clubbed due to papillary necrosis (*long arrows*) along with air in the pelvis (*short arrow*). (**C**) Gas-forming perinephric abscess. Plain CT of a 71-year-old nondiabetic man undergoing chemotherapy for multiple myeloma with curved reconstruction through the left ureter shows an obstructed left kidney due to a calculus at the vesicoureteric junction (*short stout arrow*), dilated ureter (curved arrows), and an abscess with air extending from the upper pole of the left kidney to the left subdiaphragmatic region (*thin arrows*).

the devastating possibility of graft loss and is associated with high mortality. Radiologists who are involved in renal allograft evaluation should therefore carefully look for the presence of air in renal parenchyma in transplant patients presenting with signs and symptoms of pyelonephritis. Renal transplant recipients are treated with extended courses of immunosuppressive medications that create a milieu favorable to UTI.[7] This is compounded by diabetes being one of the leading causes of end-stage renal disease, thereby amplifying the potential for developing emphysematous infection.[8-10]

EP usually accompanies *urinary tract obstruction* most commonly caused by calculi.[11] The combination of diabetes and urinary obstruction is associated with mortality in up to 71% of cases.[12]

Though less common, there have been anecdotal case reports mentioning EPN in *immune-competent nondiabetic patients* without the setting of urinary tract obstruction.[13] Such cases warrant highlighting radiological demonstration of gas in the renal parenchyma, where clinically the disease may remain unsuspected.

Emphysematous Pyelonephritis

EPN represents a severe life-threatening infection of the renal parenchyma with gas-forming bacteria. Diabetes is a predisposing factor. Urinary collecting system obstruction from pathological conditions such as stone disease, urothelial neoplasm, and sloughed papilla are associated factors. Patients present clinically with varying degrees of renal failure, lethargy, acid-base irregularities, and hyperglycemia. Rapid progression to septic shock may be seen. *Escherichia coli* is the causative bacterial source in approximately 70% of cases, with *Klebsiella*, *Candida*, *Pseudomonas* species isolated less frequently. EPN carries an overall mortality rate of approximately 60% when treated with antibiotics only and a rate of 30 to 50% when nephrectomy is performed.[14,15]

Imaging

Conventional radiography may demonstrate gas bubbles overlying the renal fossa or may show a diffusely mottled kidney with radially oriented gas corresponding to the renal pyramids (►**Fig. 2E**).

Ultrasound findings of EPN include echogenic foci within the renal parenchyma representing air with posterior “dirty shadowing” caused by reverberation artifacts. This can be differentiated from the posterior acoustic shadowing of intrarenal calculi, which have an echo-free shadow distal to the calculus. If fluid collections are present, there may be ring-down artifacts from air bubbles trapped within fluid collections. In severe cases in which there is a significant

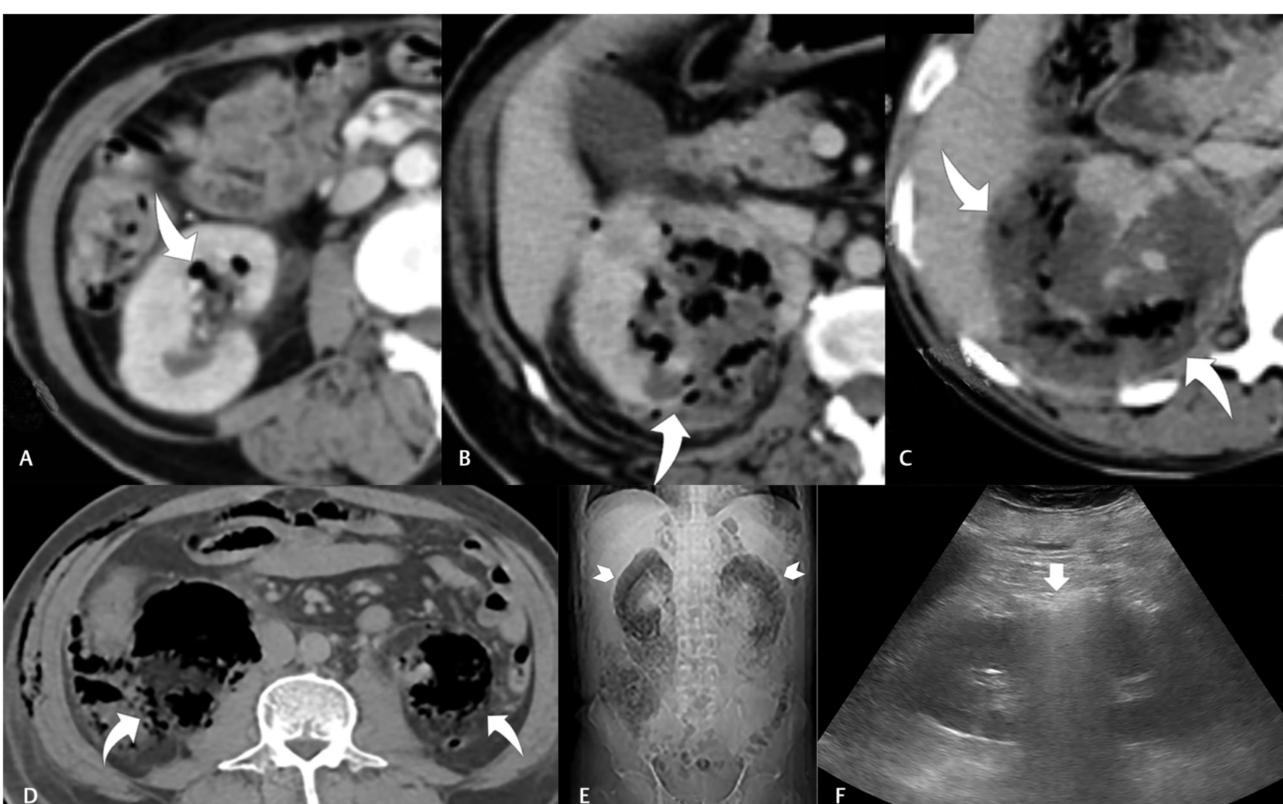

Fig. 2 (**A**) Axial computed tomography (CT) in the nephrogram phase shows class 1 emphysematous pyelonephritis (EPN) with gas in the right renal collecting system (*arrow*) of a 63-year-old nondiabetic woman. (**B**) Axial CT in the nephrogram phase shows Class 2 EPN with gas in the parenchyma of the upper pole of the right kidney in a 73-year-old diabetic man (*arrow*). **C.** Axial plain CT in a 46-year-old diabetic man shows a class 3 EPN with the presence of gas in the right perinephric spaces (*arrow*). (**D**) Class 4 EPN. Axial plain CT section in a 48-year-old poorly controlled diabetic man who had a fatal outcome within 48 hours of hospitalization shows the presence of air in both renal fossae (*arrows*). (**E**) Plain X-ray of the abdomen (anteroposterior view) outlines the kidneys with gas (*arrowheads*). (**F**) Ultrasonography long section through the left kidney of a 67-year-old diabetic woman reveals air within and around the midportion with dirty shadowing (*arrow*).

amount of air within the perinephric space, the artifact may completely obscure the kidney[16] (►Fig. 2F).

CT confirms the presence and extent of parenchymal gas. Gas may be seen in the renal parenchyma, at the subcapsular or perinephric location, or within the collecting system (**►Fig. 2A, B**). Perinephric extension of disease suggests a grave prognosis. Extension of disease to the perinephric space with gas is important to report as it increases mortality to 80%. In the majority of cases, the renal function is impaired and hence a contrast-enhanced CT is best avoided. A plain CT reliably allows the identification of the level and cause of obstruction when present. Contrast-enhanced CT, whenever performed, reveals renal enlargement, asymmetric parenchymal enhancement, delayed excretion, and areas of focal tissue necrosis or abscess formation. CT has been used to classify the disease into the following three patterns that roughly correlate with the stages in progression of the disease: (1) mottling areas of low attenuation that extend radially along the pyramids, (2) more extensive disease with involvement of the perinephric space, and (3) extension of air into the retroperitoneum. Gas may be occasionally visualized in the renal vessels.[5]

Nuclear scintigraphy does not have a role in diagnosis. However, it is helpful in quantifying renal function prior to planned surgery.

Factors for Prognostication

Michaeli et al concluded that age, sex, site of infection, serum urea nitrogen level, and blood glucose level were not the prognostic factors, and the best combination of characteristics of EPN with favorable outcome was that of a patient with nonobstructive unilateral disease receiving combined medical and surgical treatment within a short interval of symptom onset.[17] In an attempt to prognosticate emphysematous renal infection, they suggested a system of classification as follows: stage I limited gas within the kidneys and perirenal tissues, stage II extensive gas in the renal parenchyma and perirenal tissues, and stage III gas in the perinephric spaces, or bilateral EPN. However, they did not find any prognostic significance of the preceding classification.

Huang et al[9] offered a classification with prognostication as follows:

- Class 1: gas in the collecting system only termed EP (**►Fig. 2A**).
- Class 2: gas in the renal parenchyma without extension to the extrarenal space (**►Fig. 2B**).
- Class 3:
  - A: Extension of gas or abscess to the perinephric space.
  - B: Extension of gas or abscess to the pararenal space (**►Fig. 2C**).
- Class 4: bilateral EPN or solitary kidney with EPN (**►Fig. 2D, E**).

They found that though there were no significant differences in the clinical features among the preceding radiological classes, a tendency toward higher mortality rate and failure rate of percutaneous catheter drainage (PCD) were observed in classes 3 and 4. Classes 1 and 2 responded well to PCD and relief of the urinary tract obstruction combined with antibiotic treatment. Risk factors of poor prognosis were thrombocytopenia, acute renal function impairment, disturbance of consciousness, severe proteinuria, and shock. Of their class 3 and 4 patients, 85% with less than two of the aforementioned risk factors could be successfully treated with PCD combined with antibiotic treatment. The patients with two or more of the aforementioned risk factors had a significantly higher failure rate and poor outcome (92 vs. 15%; $p < 0.001$). Nephrectomy provided the best outcome for extensive EPN.

It was assumed in the past that high tissue glucose levels may be a risk for EPN to develop and cause a fulminant course in patients with diabetes as it provides gas-forming microbes with a microenvironment more favorable for growth and rapid catabolism.[18,19] However, Huang et al found no correlation for prognostic outcome between EPN and HbA1c level, the presence of diabetic retinopathy, or urinary tract obstruction.[9] Interestingly, age also did not seem to influence prognosis in EPN in their study.

Wan et al[20] divides EPN into two types, which have a prognostic significance: type 1, which is characterized by parenchymal destruction with streaky or mottled gas collections but no fluid collections (**►Fig. 3**), andtype 2, which is characterized by bubbly or loculated gas within the parenchyma or collecting system with associated renal or perirenal fluid collections (**►Fig. 4**). Type I or the dry type has a 69% mortality rate versus 18% for type II, which represents a favorable immune response. Transformation from type I to type II has been observed following conservative treatment.

Emphysematous Pyelitis

The term *emphysematous pyelitis* (EP) is used to describe the presence of gas limited to the renal excretory system. There is lesser association with diabetes. It is also a less severe form of disease than EPN. Although the urothelium may be primarily involved, the gas is usually secondary to coexistent bacterial infections of the kidney or urinary bladder, with *E. coli* being the most commonly cultured bacteria.

Clinical manifestation of EP is nonspecific, similar to the clinical presentation of uncomplicated acute pyelonephritis. Roy et al[21] reported on five patients who were eventually diagnosed with EP, and all had a 1-week history of fever and chills at presentation. These symptoms were associated with a localizing upper-quadrant tenderness. Four of the patients had dysuria, and one had pyuria. Macroscopic hematuria was found in one patient.

In our experience, all our cases of EP presented with fever, frequency, and dysuria, and frank hematuria was rare. They were conscious, oriented, and with a preserved sense of well-being in most instances. Authors' institutional experience with EP shows that antibiotic therapy alone appears to be sufficient with no risk of mortality. Urinary tract obstruction was not seen in most cases.

In conventional radiography, gas is seen lining and outlining the ureters and pelvicalyceal system. USG typically shows high-amplitude shadowing along the nondependent surfaces

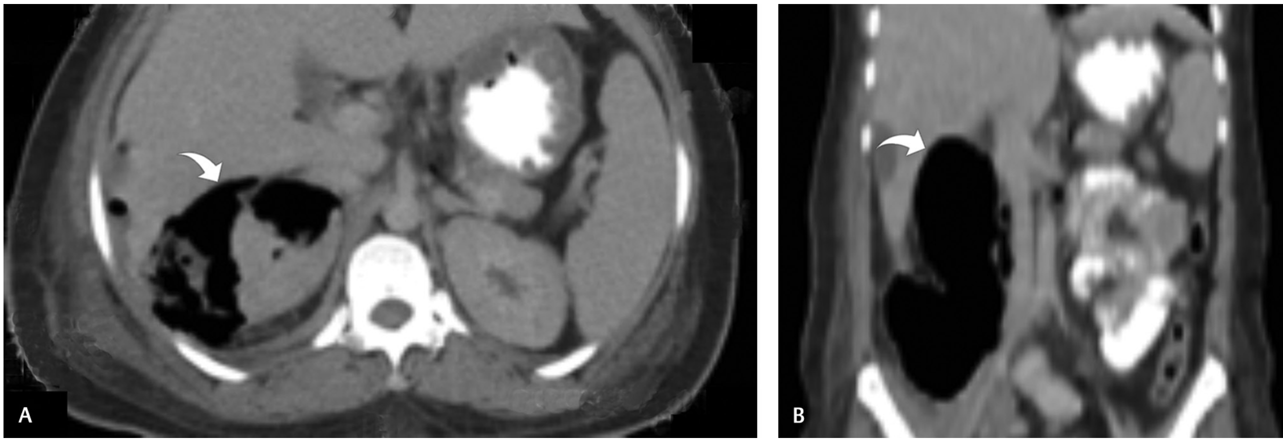

Fig. 3 Wan type 1 emphysematous pyelonephritis. (**A**) Axial and (**B**) coronal planes of a 66-year-old diabetic man reveal the presence of gas at the upper pole of the right kidney and renal fossa with destruction of renal parenchyma but without fluid collection (*arrows*).

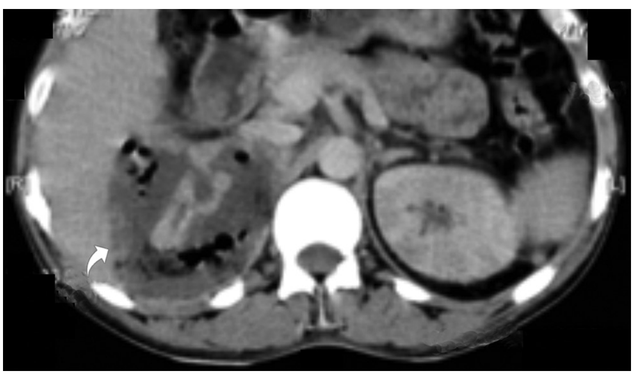

Fig. 4 Wan type 2 emphysematous pyelonephritis. Axial computed tomography (CT) in the nephrogram phase of a 55-year-old diabetic lady reveals destruction of the right renal parenchyma and replacement with fluid and gas within and around the kidney. Nephrectomy was required as there was no response to antibiotics and drainage procedures.

with posterior dirty acoustic shadowing. CT best delineates gas within the collecting system and helps reliably identify stones (**►Figs. 1B and 2A**). More importantly, CT helps exclude the presence of renal or perirenal collections, frank abscesses, or EPN. Potential noninfectious sources of gas within the collecting system that should be excluded from patient history include reflux of air during instrumentation and the presence of an anastomotic surgery to the bowel.

Emphysematous Cystitis

This entity was known to exist in animals as well as man in late 1800. It was reported in living human being first in 1932.[22] Bailey in 1961 suggested that EC be used to describe gas collection in the bladder wall and lumen secondary to infecting microorganisms. He suggested that primary Pneumaturia and EC can be considered as the same entities.[23] There are reports of emphysematous ureteritis, nephritis, and adrenalitis coexisting with cases of bladder emphysema, with reported increased mortality in cases of renal and adrenal involvement.[24] EC represents an uncommon rare form of acute inflammation of the bladder mucosa and underlying musculature. Clinical symptoms of dysuria, increased urinary frequency, and hematuria are common. Though specific clinically, the presence of pneumaturia is rare. Diabetes, female sex, chronic UTI, bladder outlet obstruction, and a neurogenic bladder are predisposing factors. There are reports of occurrence of EC in infants.[25] Frequently, isolated gas-producing bacteria include the coliform bacteria *E. coli-Enterobacter* aerogenes, although *Clostridia* and fungal species are occasionally identified.

Possible noninfectious sources of pelvic air should be considered and include recent bladder instrumentation, vesicocolic or vesicovaginal fistulas, trauma, and pneumatosis cystoides intestinalis. Conventional radiography of EC characteristically shows curvilinear or mottled areas of increased radiolucency in the region of the urinary bladder, separate from more posterior rectal gas. Intraluminal gas will be seen as an air–fluid level that changes with patient position and, when adjacent to the nondependent mucosal surface, may have a cobblestone or “beaded necklace” appearance. USG will commonly demonstrate diffuse bladder wall thickening and increased echogenicity. Focal regions of high-amplitude echoes with posterior dirty acoustic shadowing into the lumen may be seen in extensive cases. CT is highly sensitive, and that allows early detection of intraluminal or intramural gas (**►Figs. 5** and **6**). It is also useful in evaluating other

Fig. 5 Axial plain computed tomography (CT) section through the pelvis of a 56-year-old postmenopausal diabetic lady shows the presence of air within the bladder forming an air–fluid level (*arrow*) without any history of catheterization, suggesting gas-forming urinary infection.

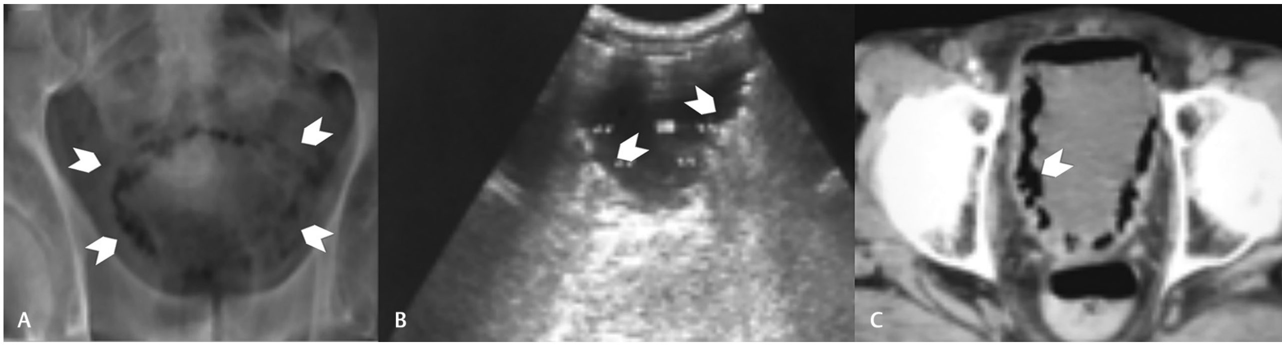

Fig. 6 Emphysematous cystitis. A 72-year-old nondiabetic male with chronic renal failure, hypertension, pain in the lower abdomen, and malena. (**A**) Plain X-ray of the abdomen (anteroposterior view) shows streaky air lucencies in the distribution of the bladder wall (*arrowheads*). (**B**) Ultrasonography shows air as echogenic foci with ring-down artifacts from the bladder wall (*arrowheads*). (**C**) Axial plain computed tomography (CT) shows gas within the bladder wall (*arrowhead*).

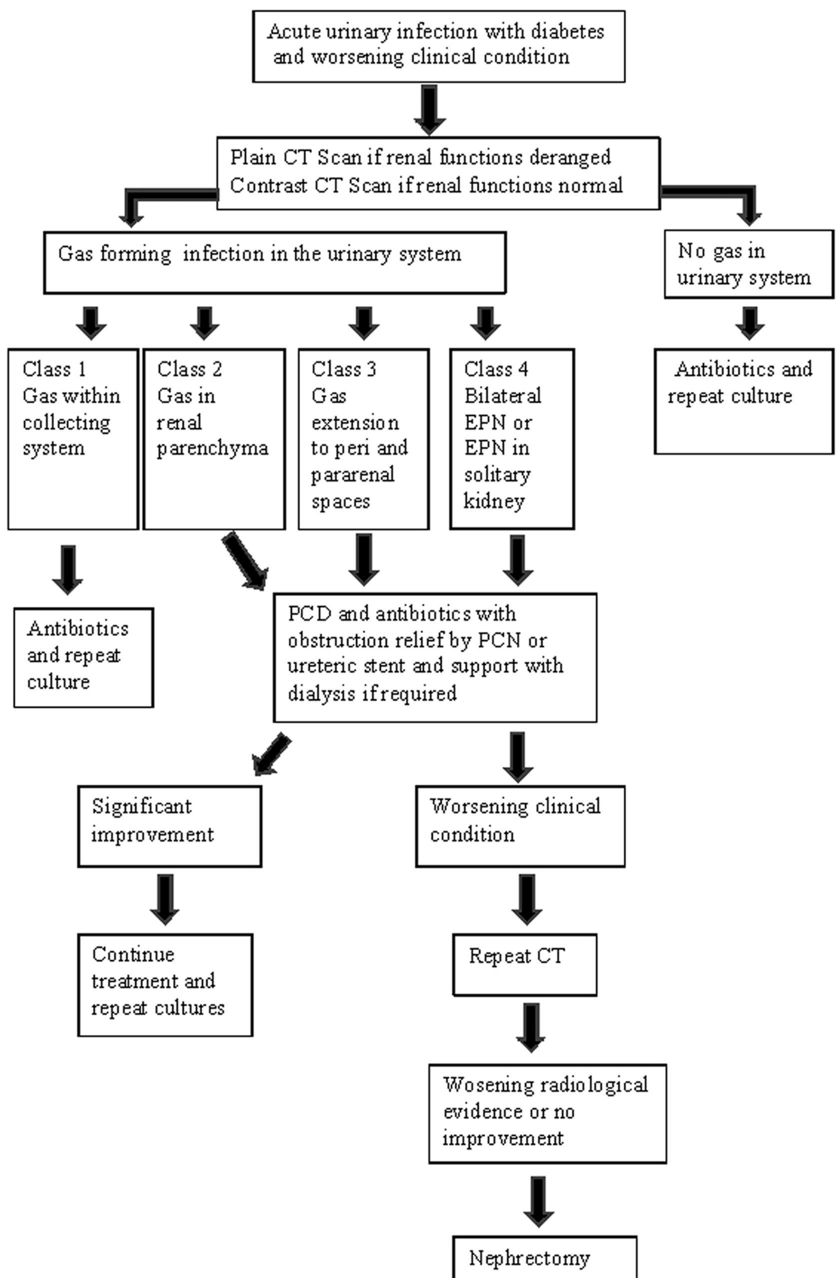

Fig. 7 Algorithm for the management of emphysematous urinary infections.

causes of intraluminal gas such as enteric fistula formation from adjacent bowel carcinoma or inflammatory disease.

Treatment for EC generally involves broad-spectrum antimicrobial therapy, hyperglycemic control, and adequate urine drainage with the correction of possible bladder outlet obstruction when present.

Current Trends in Gas-Forming Urinary Infection

►**Figure 7** gives an algorithm for the management of emphysematous urinary infections. There has been a change in the clinical scenario of EPN over the years. Earlier, EPN used to be feared as a fulminant and potentially life-threatening disease. CT scan is now widely available, with resultant early detection of even small pockets of air in the urinary system or around it. With more effective newer antibiotics and better intensive care including dialytic support services as well as skillful drainage of collections and obstructed kidneys, the outcome in these patients has improved remarkably. There is a distinct trend of managing EPN more conservatively, with favorable outcomes and impressive reductions in overall mortality. Managing EPN more conservatively has thus become the standard of care today. Only critically ill patients with class 3 or 4 disease and altered poor prognostic risk factors may require a more aggressive surgical plan.[26]

Conclusion

Gas-forming infections of the urinary tract are potentially life-threatening conditions. The initial clinical manifestation may be insidious, but rapid urosepsis will occur in the absence of early therapeutic intervention. Conventional radiography and USG are often the initial imaging modalities used to evaluate patients with common abdominopelvic complaints. In case of emphysematous infections, CT should be considered the imaging modality of choice. CT is both highly sensitive and specific in the detection of abnormal gas and well suited to reliable depiction of the anatomical location and extent of gas. Appropriate CT evaluation combined with accurate interpretation and ability to identify gas modifies treatment dramatically. In addition, knowledge of the pathophysiological characteristics and common predisposing conditions associated with gas-forming infections of the genitourinary system will aid in further diagnostic work-up, surveillance of potential complications, and evaluation of therapeutic response.

Conflict of Interest
None declared.

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