Original article

Emphysematous pyelonephritis: A review of its pathophysiology and management

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Abstract

Emphysematous pyelonephritis is a urologic emergency characterized by an acute necrotizing, perinephric, and parenchymal infection caused by gas-forming uropathogens. It is considered a rare entity, with greater incidence in developing countries. Even though its pathogenesis is not fully understood, there are several well-identified factors involved in the spectrum of elements that result in the production of gas in the renal parenchyma. Various poor outcome factors associated with a high mortality rate have been described in different cohorts. The treatment of those patients can typically be divided into medical management, medical management plus endoscopic or percutaneous drainage, and emergency nephrectomy. Nevertheless, given that there are very few guidelines or treatment algorithms, there is no consensus on the management of patients with emphysematous pyelonephritis.

Keywords:
Emphysematous pyelonephritis, sepsis, outcome factors.

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Introduction

Emphysematous pyelonephritis is a urologic emergency characterized by an acute necrotizing, parenchymal, and perinephric infection caused by gas-forming uropathogens.[1] The majority of authors of the different reviews categorize it as "life-threatening", warranting special attention, given its potential mortality attributable to septic complications and the variable clinical nature characteristic of this type of patient.[1-2] In recent decades, the implementation of septic patient management algorithms and less aggressive diversion treatments, has resulted in a general overall mortality rate of 21%, compared with the 43-78% rate in the 1970s and 1980s, when the only treatment was emergency nephrectomy.[3]

Historic perspective

Kelly and MacCallum described the first case of gas-forming kidney infection in 1898 and terms such as "renal emphysema" and "pneumonephritis" were used to describe that gas-forming infection.[2] In 1962, Schultz and Klorfein proposed the term "emphysematous pyelonephritis" as the preferred name, thus emphasizing the relation between the infectious pathology and the formation of gas.[2-3] Many researchers suggested that the term "emphysematous pyelonephritis" should be applied only to the formation of gas in the renal parenchyma or perinephric space, but other authors, such as Huang and Tseng stressed the fact that the pathology encompassed the presence of gas in the collecting system, as well.[1]

Epidemiology

There are no epidemiologic studies to specify the prevalence of emphysematous pyelonephritis because it is considered a rare entity. It is not unusual to find anecdotal case reports on said pathology in journals from developed countries, but there is a marked contrast with the reviews of case series from developing countries, such as the studies by Wan et al., with 38 patients in 7 years, and Huang and Tseng, with 46 patients in 8 years.[1,3] Their studies are the most representative, given that not only do they describe the presentation of the pathology, but they also correlate the most important clinical and radiologic data with the mortality rate. There are currently new case reports, such as the study by Aswathaman et al.,[4] with 41 patients evaluated over a 6-year period, and the analysis by Kapoor et al.[5] with 39 patients and a 4-year time frame. Modeled after the studies by Wan and Huang, they aimed to establish management guidelines in accordance with the results of the different treatment modalities, depending on the initial clinical, biochemical, and radiologic aspects. In Mexico, Olvera et al.[6] conducted a multicenter study in which they reported the experience of 3 tertiary care centers in the management of patients with emphysematous pyelonephritis, with a total of 62 patients, within the time frame of 2005 to 2012.

Risk factors

Emphysematous pyelonephritis is more frequent in women, with a 6:1 ratio. The mean patient age at disease presentation is 55 years.[1-2] The predisposition to females is thought to

be related to the higher incidence of urinary tract infections in that sex. The left kidney is more commonly affected (67%) than the right (23%), and bilateral presentation is the rarest of all, with a frequency of 5 to 6%.[2]

Diabetes mellitus is the most frequently associated risk factor, presenting in up to 85% of the cases.[1-2] Close to 95% of the patients with emphysematous pyelonephritis that have diabetes mellitus, have poor glycemic control. High glucose levels in uncontrolled diabetic patients have been postulated to inhibit leucocytic function, worsening the response to an infection. [2-4] In addition to diabetes, many patients present with urinary tract obstruction associated with numerous anatomic and functional urinary tract pathologies that do not allow adequate urine flow. One of the most common causes of obstruction is urolithiasis. The risk for developing emphysematous pyelonephritis secondary to urinary tract obstruction is 25 to 40%.[1-2] For example, hydronephrosis increases the pyelocaliceal pressure, compromising renal circulation, causing inadequate flow of the gas that is formed, with the consequent formation of gas bubbles that expand and result in tissue damage.[7]

Microbiology

The most frequently found causal microbiologic agent is *Escherichia coli* (*E. coli*), which has been identified in 70 to 75% of cultures of urine, blood, and pus.[1-2]

Tseng et al. conducted a study that attempted to identify specific virulence factors in the *E. coli* strains that were key in the formation of gas and the presentation of emphysematous pyelonephritis. They compared *E. coli* isolated in patients with non-emphysematous pyelonephritis with *E. coli* isolated in patients that had emphysematous pyelonephritis.[7] They found no significant gas-producing factors in the comparison of the two groups. Likewise, the virulence factors evaluated were very similar in both groups, with the exception of a decrease in the "papG II" gene and a decrease in the "usp" gene in the emphysematous pyelonephritis group, but with borderline results. Those authors concluded that the most important factors for the presentation of emphysematous pyelonephritis were those of the hosts, themselves (diabetes mellitus, poor glycemic control, and urinary tract obstruction), as opposed to specific bacterial virulence.[7-8]

After *E. coli*, the most frequently found microorganisms were: *Klebsiella pneumoniae* (20-30%), *Proteus mirabilis* (10%), group D *Streptococcus*, and coagulase-negative *Staphylococcus*. Other microorganisms have been found, but much less frequently, such as: *Clostridium septicum, Cryptococcus neoformans, Candida albicans*, and *Pneumocystis jirovecii*. [1-3]

Pathophysiology

The pathogenesis of emphysematous pyelonephritis is not well-understood, and several factors are involved in a spectrum of elements that result in the production of gas in the renal parenchyma. Said gas can be focal or diffuse and can be located solely in the collecting system or can also affect the perinephric or pararenal spaces.[1,2,7]

The most widely accepted elements that play an essential role in the pathogenesis of emphysematous pyelonephritis are:[1-2]

- High glucose levels.

- The presence of gas-forming microorganisms.
- Alterations in the vasculature that condition deficient blood irrigation.
- Alterations in the immune system of the patient.
- The presence of obstruction to the flow of urine due to an anatomic, functional, or pathologic alteration.

There are several theories about the pathophysiology of emphysematous pyelonephritis:

- The introduction of gas through trauma, fistulas, or invasive urinary procedures (Figure 1). This theory is the least accepted, given that the presentation of the disease due to any of those situations would be rare. However, there have been documented cases of emphysematous pyelonephritis in patients with histories of renal trauma and kidney hematomas, albeit its appearance was also favored by other factors.[2,7]

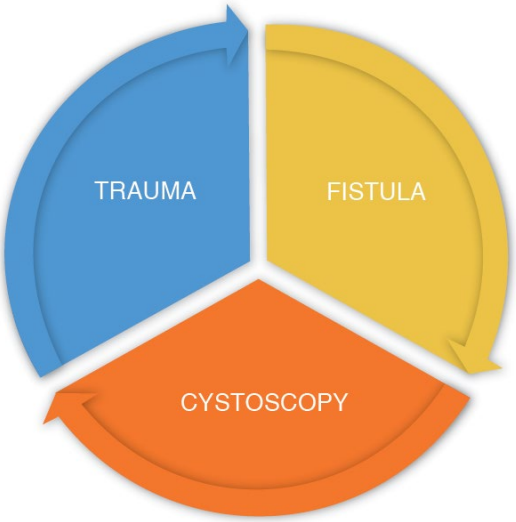

Figure 1. Theory 1. The solution of urinary tract continuity, with the consequent entrance of air, has been stipulated as a probable origin of EPN, but that does not explain the origin in the majority of cases.

- A second theory involves glucose fermentation. It is posited that the renal medulla is normally hypoxemic, especially in diabetic patients or those with some type of pre-existing kidney damage, creating a greater decrease in oxygen pressure and an increase in anaerobic metabolism. That situation is taken advantage of by gas-forming bacteria, such as *E. coli*, to ferment glucose and consequently produce lactate, carbon dioxide, and hydrogen (Figure 2).[1-2] Other identified gases are nitrogen, oxygen, traces of ammonia, methane, and carbon monoxide.[7] The transport of the gas produced by the rapid catabolism leads to the accumulation of tissular gas. That accumulation gradually expands, creating gas bubbles. In some cases, the infectious process and production of gas are so severe that they can spread to the entire retroperitoneal region. There have been reported cases of extension to the spermatic cord, scrotum, and even intraperitoneal air dissection.[2,7]

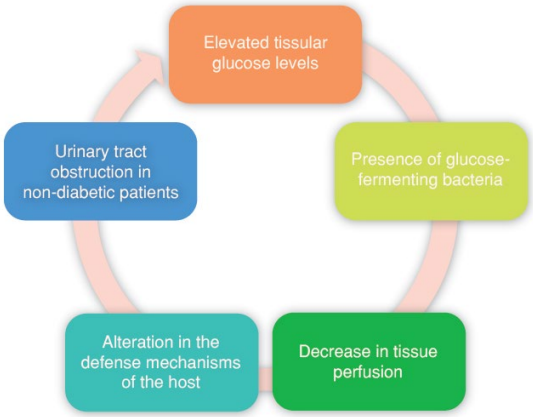

Figure 2. High glucose levels, low tissular glucose levels, low oxygenation levels, and obstruction are the essential basic elements in the pathophysiology of emphysematous pyelonephritis.

- A third theory points toward the production of gas through the necrotic tissue that resulted from the inflammatory and infectious process, as well as the destruction of the parenchyma, favored by the expansion of gas and the poor vascular supply.[2,7]

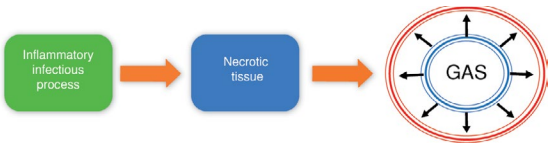

Figure 3. The inflammatory and infectious process destroys the renal parenchyma, forming necrotic tissue that produces gas during its formation and expands, necrotizing even more tissue and perpetuating the cycle.

Clinical picture

Almost all the patients present with fever, vomiting, lumbar pain, and dysuria. Sometimes symptomatology is vague and very nonspecific.[2-4] The duration of prodromal symptoms can vary from days to weeks. Less common symptoms include dyspnea, crepitation, and pneumaturia,[8-10] and there can also be an altered state of alertness and signs consistent with septic shock. Bacteremia presents in more than 50% of the cases of emphysematous pyelonephritis.[10] There have been atypical cases in which symptoms mimic those of bowel obstruction, cases of symptoms of gas extension to the pancreas and vertebral discs, and cases of post-transplantation kidney graft involvement.[10-15]

Biochemical profile and outcome factors

Biochemically, there are signs of leukocytosis (70-80%), thrombocytopenia (15-20%), altered acid/base balance in gasometric tests, acute kidney dysfunction, hyperglycemia, gross hematuria, microscopic hematuria, and proteinuria.[1-6]

Urine culture results are always positive and *E. coli* is the most frequent microorganism identified. *Klebsiella* and *Proteus* bacteria are detected less frequently.[3-6] Cultures with mixed bacterial growth and even cultures with no bacterial growth have been reported.[8-9]

Various risk factors directly related to mortality have been studied in different cohorts. The presence of diabetes mellitus has been clearly identified as a risk factor for the development of the disease, but numerous studies do not identify it as a significant predictive risk factor for mortality associated with emphysematous pyelonephritis.[16-18] Similarly, in relation to greater mortality, there is no well-established association with nephrolithiasis, *E. coli* or *Klebsiella* infection, age above 50 years, female sex, a history of urinary tract infections, or alcoholism.[13-16]

Systolic blood pressure below 90 mmHg, altered state of consciousness, increased serum creatinine levels, thrombocytopenia, hyponatremia, need for hemodialysis, and the performance of emergency nephrectomy have been found to be associated with greater mortality.[1-6,17-19] Type I disease, as classified by Wan et al., was associated with worse outcome due to a fulminant clinical course and more extensive parenchymal damage.[3] Likewise, the use of medical therapy, alone, was related to worse outcome.[17-19]

In several studies, thrombocytopenia was one of the most consistent poor outcome factors[1-6] due to disseminated intravascular coagulation that especially presents in the more severe cases. Many of them have prolonged

coagulation times and increases in serum fibrinogenic degradation products. Altered state of consciousness can arise from central nervous system dysfunction secondary to poor perfusion or to metabolic factors.[5-6] Shock is a sign of cardiovascular system collapse. All those signs represent dysfunction of the hematologic, renal, central nervous, and cardiovascular systems. [1-6,17-19]

Table 1. Poor outcome factors associated with a higher mortality rate found in the most significant case series.

Wan, et al.[3] *1998*	*Huang and Tseng* [1] *2000*	*Falagas, et al.*[19] *2007*	*Aswathaman, et al.*[4] *2008*	*Kapoor, et al.*[5] *2009*	*Olvera, et al.*[6] *2014*
Thrombocytopenia (p= .001)	Short time of symptom onset before diagnosis (p= .002)	Exclusive use of medical treatment OR 2.85 (p= .02)	Thrombocytopenia (p= .001)	Altered state of consciousness (p= <.001)	Age OR .11 (p= .009)
Compromised kidney function (p= .0003)	Thrombocytopenia (p= <.01)	Bilateral emphysematous pyelonephritis OR 5.36 (p= .001)	Shock (p= .028)	Thrombocytopenia (p= .01)	Raised creatinine levels OR 1.53 (p= .009)
Microscopic hematuria (p= .029)	Compromised kidney function (p= .05)	Huang & Tseng type 1 emphysematous pyelonephritis OR 2.53 (p= .02)	Altered state of consciousness (p= .007)	Compromised kidney function (p= .01)	Need for emergency nephrectomy OR 6.12 (p= .03)
Wan type 1 emphysematous pyelonephritis (p= .002)	Altered state of consciousness (p= < .01)	Thrombocytopenia OR 22.68 (p= <.001)	Need for emergency hemodialysis (p= .028)	Hyponatremia (p= .002)	
	Shock (p= .01)	Systolic pressure below 90 mmHg (p= .01)		Destruction of more than 50% of the renal parenchyma (p= <.0001)	
		Raised creatinine levels (p= .05)		Early nephrectomy (p= .01)	
		Creatinine above 2.5 mg/dl (p= .01)			
		Altered state of consciousness (p= .01)			

Radiologic diagnosis

Diagnosis is confirmed through radiologic studies. Abdominal x-ray can identify tissular gas distributed in the parenchyma that appears as gaseous shadows over the compromised kidney (Image 1).[2] That finding is often confused with intestinal gas. A collection of gas in the shape of a half moon over the upper pole of the kidney is more specific.[1-2]As the infection advances, the gas extends into the perinephric space and the retroperitoneum.

Ultrasound can show strong, localized echoes that suggest the presence of intraparenchymal gas.[1-2]

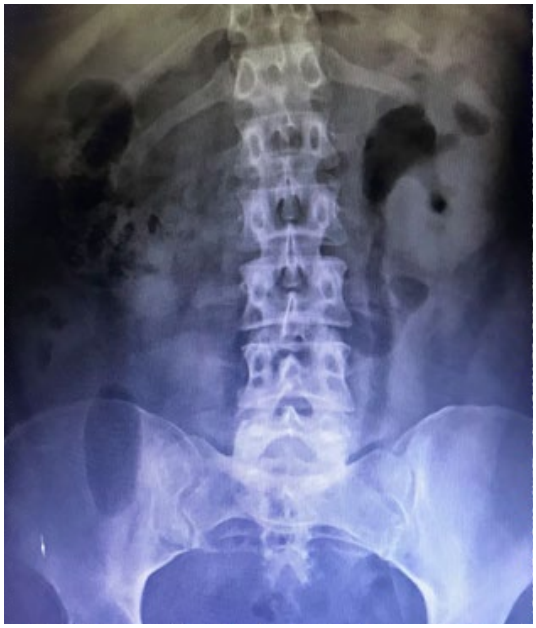

Image 1: a) Plain abdominal x-ray clearly showing the presence of gas in both kidneys, extending to the ureters.

Computed tomography is the diagnostic imaging study of choice for defining the extension of the emphysematous process and can aid in treatment selection. The absence of fluid in the tomographic images or the presence of striated or mottled gaseous patterns with accumulated gas bubbles or septa appear to be associated with rapid destruction of the renal parenchyma and a mortality rate of 50 to 60%.[1-3] The presence of fluid in the renal or perinephric space with gas in bubbles or between the septa in the collecting system and the presence of striated or mottled gaseous patterns are associated with a mortality rate under 20%.[1-3] Obstructions are identified in about 25% of the cases. Some authors think kidney scintigraphy should be performed.[2, 20]

There are 3 radiologic classifications for patients with emphysematous pyelonephritis (Table 2). Michaeli[1] was the first to classify the disease according to findings in plain abdominal x-ray and intravenous pyelography. Wan et al.[1,3]conducted a study on a cohort of 38 patients and categorized them into two groups according to tomographic findings. In 2000, Huang and Tseng[1-2] published a new classifi-

cation based on a more detailed tomographic description and related to the treatment for each of the patients.

Table 2. Radiologic classifications of emphysematous pyelonephritis. [1]

Classification	*Radiologic study*	*Class*
Michaeli[1]	Abdominal radiography and intravenous pyelogram	I. Gas in the renal parenchyma or the perinephric tissue. II. Gas in the kidney and surrounding tissues. III. Gas extended through the fascia or bilateral disease.
Wan[1,3]	Computed tomography	I. Renal necrosis with the presence of gas, but no fluid. II. Gas in the parenchyma, associated with fluid in the renal parenchyma, perinephric space, or collecting systems.
Huang and Tseng[1-2]	Computed tomography	1. Gas in the collecting system (Image 2). 2. Gas solely in the renal parenchyma (Image 2). 3A. Gas extended into the perinephric space (Image 3). 3B. Gas extended into the paranephric space (Image 3). 4. Gas in a single kidney or bilateral disease (Image 4).

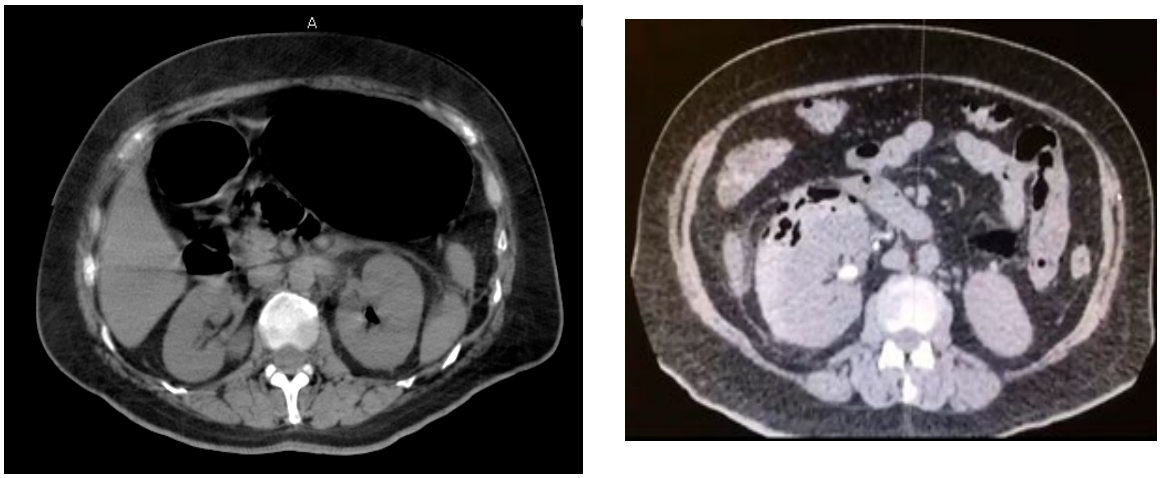

Image 2: a) Huang 1.- The presence of gas in the collecting system of the left kidney. b) Huang 2.- The presence of gas in the renal parenchyma.

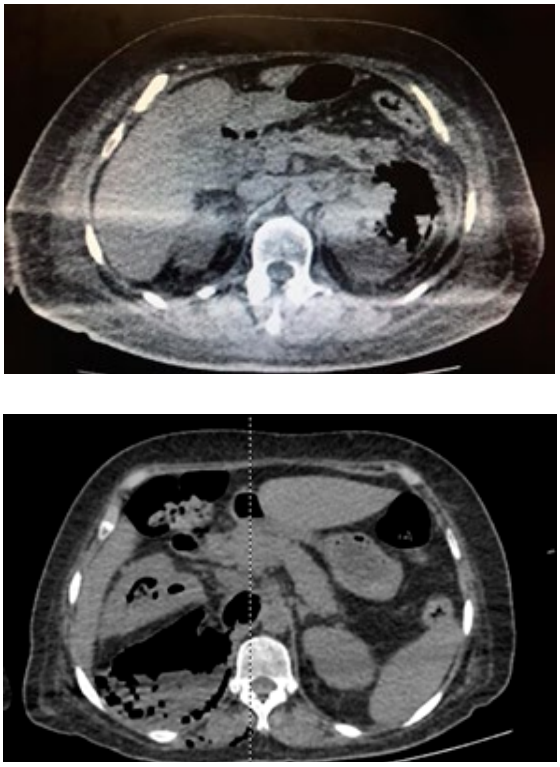

Image 3: a) Huang 3a.- The presence of gas in the perinephric space. b) Huang 3b.- The presence of gas in the pararenal space.

Treatment

Treatment for patients with emphysematous pyelonephritis can generally be divided as follows:[1-4,6]

- Medical management (MM)
- MM + Endoscopic or percutaneous drainage
- Emergency nephrectomy

Resuscitation maneuvers, opportune administration of intravenous fluids, correction of acid/base and fluid and electrolyte imbalances, glycemic control, and early intravenous administration of antibiotics are the basis of treatment in patients with emphysematous pyelonephritis.[4] It is important to maintain systolic blood pressure above 100 mmHg, whether by the administration of intravenous solutions or the use of inotropic agents, if necessary.[3,6,19-21] There are meta-analyses that compare adverse effects on mortality, identifying patients with systolic pressure of 90 mmHg as having poor outcome, compared with patients with an initial systolic pressure above 100 mmHg.[21-23] Some patients may even require ventilation support.

Due to the fact that Gram-negative bacteria continue to be the most common causal agents, antibiotic treatment should be directed at those types of microorganisms as targets, which is why aminoglycosides, B-lactamase inhibitors, cephalosporines, and quinolones are the antibiotics that are initially used in treating emphysematous pyelonephritis.[2-4,6,24] The necessary adjustments should be made, once the urine culture or blood culture is available, to optimize treatment.[24-25]

Comparative studies on medical therapy vs. initial surgical treatment in patients with emphysematous pyelonephritis revealed a mortality rate of 78% between 1898-1970 and 75% between 1970-1982 for medical treatment. Surgical treatment showed significant advantages in mortality with rates of 42% between 1898-1970 and 11% between 1970-1982.[1-3] As a result, emergency nephrectomy plus open drainage with medical treatment has been a well-accepted therapy since the 1980s. Nevertheless, several recent meta-analyses reported very different results with that therapy, with mortality rates of 40 to 50%.[2,4-5,19,22]

In the parenchyma, pathologic findings following nephrectomy reveal signs of abscess in formation, zones of microinfarcts and macroinfarcts, vascular thrombosis, vascular sclerosis, signs of intra-arterial infection, cavities at sites where gas is accumulated, and areas of necrosis su-

rrounded by inflammatory cells. In addition, diabetic patients are frequently identified with signs of glomerulosclerosis and papillary sloughing.[2-3,23,25-26]

Some authors state that functional tests such as kidney scintigraphy should be performed to determine kidney function, given that conservative treatment or minimally invasive diversion therapy should be considered in patients with emphysematous pyelonephritis and a functioning kidney, to preserve the renal unit.[2,18,20]

In their study published in 1986, Hudson et al.[27] reported on percutaneous kidney drainage with a pig-tail catheter in a diabetic patient with emphysematous pyelonephritis that had a high risk for death from anesthesia during the surgical procedure. The patient's clinical progression was favorable, and the later control study showed acceptable preservation of the function of that kidney. Since then, the great advances in the interventionist procedures and their materials have made it possible for percutaneous drainage to be a treatment option in those patients.[6, 27-28]

Some studies have shown successful treatments using percutaneous drainage plus medical treatment, achieving an important reduction in mortality rates.[16,27]

Additionally, the use of percutaneous drainage as an option in the treatment of emphysematous pyelonephritis aids in preserving the function of the affected kidney in approximately 70% of the cases.[27] Percutaneous drainage can be carried out in patients, especially those with very localized areas of gas or collections and that have zones of functional renal parenchyma. A tomography-guided 14 Fr pig-tail drain is generally placed, which has shown greater success than the ultrasound-guided drain.[27-28]

There are several studies that support the use of drains to preserve the kidney unit. In a systematic review of 10 studies, with a total of 210 cases, Somani et al. found that medical treatment plus nephrostomy had a lower mortality rate (13%), compared with medical therapy (50%) or emergency nephrectomy (25%), with important statistical significance ($p<0.001$).[27]

A multi-loculated abscess or an abscess with numerous collections are not contraindications for percutaneous drainage. Indeed, even more than one catheter can be used. Drainage should be kept in place until control tomography shows the initial findings are resolved, which can require more than 12 weeks.[25,27] The feasibility of washouts with antibiotic solutions through the drainage catheter has been described.[27] After percutaneous drainage insertion, some patients may still require nephrectomy. That could be the case in patients that do not respond favorably to treatment or those whose kidney scintigram shows kidney exclusion during the follow-up.[25-27]

In their study conducted at 3 tertiary care centers on patients with emphysematous pyelonephritis, Olvera et al.[6] developed a management algorithm that involved the evaluation of the patient and the initial treatment according to the "Surviving Sepsis Campaign" guidelines, that emphasize initial resuscitation, broad-spectrum antibiotic therapy, and evaluation of the probable origin of infection through computed tomography. According to that algorithm, the presence or not of urinary tract obstruction, of collections or abscess formation and of hydronephrosis should be identified to consider the use of minimally invasive diversion therapies, such as double-J stents or nephrostomy, or the use of conservative medical treatment. In addi-

tion, they suggest a re-evaluation of the hemodynamic and biochemical status of the patients at 12 to 48 hours to determine whether treatment should be continued. If there is no improvement, the combination of diversion methods should be carried out, or even emergency nephrectomy, as a last resort. The importance of the study by Olvera et al. lies in their development of an algorithm based on data obtained from a Mexican population, but especially because it is the first study to apply general treatment guidelines for the septic patient as an initial model in the evaluation and therapeutic intervention of patients with emphysematous pyelonephritis. [6]

Conclusions

Emphysematous pyelonephritis is a potentially fatal disease, whose pathophysiology is due to numerous conditions that result in the lack of adequate urine flow, favoring bacterial overgrowth and the possibility of severe sepsis.

There are few significant case series that enable us to adequately identify the clinical profile of those patients or offer conclusive data that guide treatment direction.

Because there are no clinical guidelines or treatment algorithms, there is no consensus on the management of those patients. However, key points to be considered when treating patients with emphysematous pyelonephritis are: the location and distribution of gas, the degree of kidney destruction, initial hemodynamic status, and poor outcome factors.

It should be pointed out that treatment of the patient with emphysematous pyelonephritis is not static. The very nature of the septic patient implies the need for dynamic management. Therefore, we believe it is important to carry out strict follow-up and make decisions that allow an opportune change in treatment when it is required.

References

1. **Huang JJ, Tseng CC.** Emphysematous pyelonephritis: clinicoradiological classification, management, prognosis, and pathogenesis. Arch Intern Med. 2000;160(6):797-805.
2. **Ubee SS, McGlynn L, Fordham M.** Emphysematous pyelonephritis. BJU Int. 2011;107(9):1474-8.
3. **Wan YL, Lo SK, Bullard MJ, Chang PL, Lee TY.** Predictors of outcome in emphysematous pyelonephritis. J Urol. 1998;159(2):369-73.
4. **Aswathaman K, Gopalakrishnan G, Gnanaraj L, Chacko NK, Kekre NS, Devasia A.** Emphysematous pyelonephritis: outcome of conservative management. Urology. 2008;71(6):1007-9.
5. **Kapoor R, Muruganandham K, Gulia AK, Singla M, Agrawal S, Mandhani A, et al.** Predictive factors for mortality and need for nephrectomy in patients with emphysematous pyelonephritis. BJU Int. 2010;105(7):986-9.
6. **Olvera-Posada D, Armengod-Fischer G, Vázquez-Lavista LG, Maldonado-Ávila M, Rosas-Nava E, Manzanilla-García H, et al.** Emphysematous pyelonephritis: multicenter clinical and therapeutic experience in Mexico. Urology. 2014;83(6):1280-4.
7. **Tseng C-C, Wu J-J, Wang M-C, Hor L-I, Ko Y-H, Huang J-J.** Host and bacterial virulence factors predisposing to emphysematous pyelonephritis. Am J Kidney Dis Off J Natl Kidney Found. 2005;46(3):432-9.
8. **Lin W-R, Chen M, Hsu J-M, Wang C-H.** Emphysematous pyelonephritis: patient characteristics and management approach. Urol Int. 2014;93(1):29-33.

9. **Kolla PK, Madhav D, Reddy S, Pentyala S, Kumar P, Pathapati RM.** Clinical Profile and Outcome of Conservatively Managed Emphysematous Pyelonephritis. ISRN Urol. 2012;2012. Available in: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3329657/
10. **Peng C-Z, Chen Y-C, How C-K.** Emphysematous pyelonephritis with intraperitoneal air dissection. Eur Geriatr Med. 2016;7(6):589-90. Available in: https://www.em-consulte.com/en/article/1097368
11. **Hu S-Y, Lee B-J, Tsai C-A, Hsieh M-S.** Concurrent emphysematous pyelonephritis, cystitis, and iliopsoas abscess from discitis in a diabetic woman. Int J Infect Dis IJID Off Publ Int Soc Infect Dis. 2016;51:105-6.
12. **Chauhan V, Sharma R.** Emphysematous pyelonephritis (class IIIa) managed with antibiotics alone. Hong Kong Med J Xianggang Yi Xue Za Zhi. 2015;21(4):363-5.
13. **Crouter AJ, Abraham MK, Wilkerson RG.** Emphysematous pyelonephritis in a renal allograft. Am J Emerg Med. 2017;35(3):520.e1-520.e2.
14. **Min JW, Lee SK, Ko YM, Kwon KW, Lim JU, Lee YB, etal.** Emphysematous pyelonephritis initially presenting as a spontaneous subcapsular hematoma in a diabetic patient. Kidney Res Clin Pract. 2014;33(3):150-3. Disponible en: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4714164/
15. **Sodhi KS, Lal A, Vyas S, Verma S, Khandelwal N.** Emphysematous pyelonephritis with emphysematous pancreatitis. J Emerg Med. 2010;39(1):e85-87.
16. **Olvera-Posada D, García-Mora A, Culebro-García C, Castillejos-Molina R, Sotomayor M, Feria-Bernal G, et al.** Factores pronósticos en pielonefritis enfisematosa. Actas Urol Esp. 2013;37(4):228-32. Available in: http://www.elsevier.es/es-revista-actas-urologicas-espanolas-292-articulo-factores-pronosticos-pielonefritis-enfisematosa-S0210480612003269
17. **Lu Y-C, Chiang B-J, Pong Y-H, Huang K-H, Hsueh P-R, Huang C-Y, etal.** Predictors of failure of conservative treatment among patients with emphysematous pyelonephritis. BMC Infect Dis. 2014;14:418.
18. **Khaira A, Gupta A, Rana DS, Gupta A, Bhalla A, Khullar D.** Retrospective analysis of clinical profile prognostic factors and outcomes of 19 patients of emphysematous pyelonephritis. Int Urol Nephrol. 2009;41(4):959-66.
19. **Falagas ME, Alexiou VG, Giannopoulou KP, Siempos II.** Risk factors for mortality in patients with emphysematous pyelonephritis: a meta-analysis. J Urol. 2007;178(3 Pt 1):880-5; quiz 1129.
20. **Pontin AR, Barnes RD. Current management of emphysematous pyelonephritis.** Nat Rev Urol. 2009;6(5):272-9.
21. **Fatima R, Jha R, Muthukrishnan J, Gude D, Nath V, Shekhar S, et al.** Emphysematous pyelonephritis: A single center study. Indian J Nephrol. 2013;23(2):119-24. Disponible en: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3658289/
22. **Tsu JH-L, Chan C-K, Chu RW-H, Law I-C, Kong C-K, Liu P-L, et al.** Emphysematous pyelonephritis: an 8-year retrospective review across four acute hospitals. Asian J Surg. 2013;36(3):121-5.
23. **Uruc F, Yuksel OH, Sahin A, Urkmez A, Yildirim C, Verit A.** Emphysematous pyelonephritis: Our experience in managing these cases. Can Urol Assoc J. 2015;9(7-8):E480-3. Available in: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4514496/
24. **Lu Y-C, Hong J-H, Chiang B-J, Pong Y-H, Hsueh P-R, Huang C-Y, et al.** Recommended Initial Antimicrobial Therapy for Emphysema-

tous Pyelonephritis: 51 Cases and 14-Year-Experience of a Tertiary Referral Center. Medicine (Baltimore). 2016;95(21):e3573.

25. **Bhat RA, Khan I, Khan I, Palla N, Mir T.** Emphysematous pyelonephritis: Outcome with conservative management. Indian J Nephrol. 2013;23(6):444-7. Available in: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3841514/
26. **Royle J, Williamson R, Strachan M, O'Donnell M, Jackson S, Argryopoulos T, et al.** Emphysematous Pyelonephritis Successfully Treated with Laparoscopic Nephrectomy. Br J Med Surg Urol. 2009;2(5):204-7. Available in: https://journals.sagepub.com/doi/abs/10.1016/j.bjmsu.2009.05.004
27. **Somani BK, Nabi G, Thorpe P, Hussey J, Cook J, N'Dow J, et al.** Is percutaneous drainage the new gold standard in the management of emphysematous pyelonephritis? Evidence from a systematic review. J Urol. 2008;179(5):1844-9.
28. **Nana GR, Brodie A, Akhter W, Karim O, Motiwala H.** Nephroureterectomy for emphysematous pyelonephritis: An aggressive approach is sometimes necessary. A case report and literature review. Int J Surg Case Rep. 2015;10:179-82.