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High risk and low prevalence diseases: Infected urolithiasis

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ABSTRACT

Introduction: Infected urolithiasis is a serious condition that carries with it a high rate of morbidity and mortality.
Objective: This review highlights the pearls and pitfalls of infected urolithiasis, including presentation, diagnosis, and management in the emergency department based on current evidence.
Discussion: Although urolithiasis is common and the vast majority can be treated conservatively, the presence of a concomitant urinary tract infection significantly increases the risk of morbidity, to include sepsis and mortality. Identification of infected urolithiasis can be challenging as patients may have symptoms similar to uncomplicated urolithiasis and/or pyelonephritis. However, clinicians should consider infected urolithiasis in toxic-appearing patients with fever, chills, dysuria, and costovertebral angle tenderness, especially in those with a history of recurrent urinary tract infections. Positive urine leukocyte esterase, nitrites, and pyuria in conjunction with an elevated white blood cell count may be helpful to identify infected urolithiasis. Patients should be resuscitated with fluids and broad-spectrum antibiotics. Additionally, computed tomography and early urology consultation are recommended to facilitate definitive care.
Conclusions: An understanding of infected urolithiasis can assist emergency clinicians in diagnosing and managing this potentially deadly disease.

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1. Introduction

This article series addresses high risk and low prevalence diseases that are encountered in the emergency department (ED). Much of the primary literature evaluating these conditions is not emergency medicine focused. By their very nature, many of these disease states and clinical presentations have little useful evidence available to guide the emergency physician in diagnosis and management. The format of each article defines the disease or clinical presentation to be reviewed, provides an overview of the extent of what we currently understand, and finally discusses the pearls and pitfalls using a question-and-answer format. This article will discuss acute infected urolithiasis. This condition's low prevalence but high morbidity and mortality, as well as its variable and atypical patient presentations and challenging diagnosis, makes it a high risk and low prevalence disease.

1.1. Definition

Infected urolithiasis refers to a concomitant or superimposed urinary tract infection (UTI) in the setting of a ureteral stone and is considered a type of complicated UTI [1]. A positive urine culture (>100,000 colony forming units) with a single uropathogen in a patient with a ureteral stone is generally accepted as the definition of infected urolithiasis, though no universally accepted criteria exist [2]. However, in the ED setting, features such as positive nitrites and pyuria on urinalysis along with clinical features to include fever and costovertebral angle (CVA) tenderness are more helpful in the diagnosis of infected urolithiasis, as urinary culture data are not immediately available. Infected urolithiasis may also cause near-complete or complete obstruction which can be identified radiographically, and this may progress to obstructive pyelonephritis (renal infection and systemic illness) and pyonephrosis (purulence within the collecting system) [3]. Though most patients with uncomplicated urolithiasis can be treated conservatively, those with ureteral stone infections, to include those with and without complete obstruction, obstructive pyelonephritis, and pyonephrosis, must be treated aggressively given the significant risk of sepsis and mortality [2-4]. In this article, infected ureterolithiasis, infected urolithiasis, ureteral stone infection, and infected ureteral stone are used interchangeably.

1.2. Pathophysiology

The formation of a ureteral stone is multifactorial and may involve increased urinary calcium, urate, and oxalate; decreased citrate

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excretion; disturbances in urinary pH and volume; anatomic abnormalities; suboptimal nutrition; and warm working environment with associated dehydration [4-6]. Ureteral stone formation and UTIs are likely risk factors for each other, as patients with a higher urinary pH and bacterial colonization (particularly with urease-producing organisms) both precipitate and propagate new and existing stones [5,7]. Specifically, these bacteria promote the breakdown of urea into ammonia, which further reacts to create an alkaline environment suitable for kidney stone formation and superimposed infection [7]. Additional theories for the pathophysiology of secondary infections in the setting of urolithiasis include biofilm formation on pre-existing stones, especially when the urothelial barrier is disrupted [7]. If left untreated, complications in addition to non-infected stones (i.e., obstructive uropathy) include ascending infection, progression to bacteremia, and sepsis/septic shock.

1.3. Epidemiology

Ureteral stones are a relatively common disease process, with a 12-month incidence of 2.1%, of which 54.1% are males [8]. Furthermore, the lifetime risk of ureteral stones approaches 15% [9]. Infections in the setting of ureteral stones occur in 4% to 34% of patients based on positive urine cultures, and patients who have a history of ureteral stones are also at a higher lifetime risk of developing a UTI compared to the general population (18.7% versus 14.1%) [2,10-12]. In patients with a ureteral stone infection and sepsis or septic shock, the mortality rate ranges from 8.8% to 27.3%, which depends on the degree of obstruction and timing of surgical intervention [13,14]. In a study of 209 patients with septic shock secondary to a urinary source, approximately 11% had an anatomic obstruction, with this cohort demonstrating a 27.3% hospital mortality, compared to 11.2% of patients without an obstruction [15]. Thus, infected urolithiasis imposes a significantly higher mortality rate compared with the overall mortality rate of 0.2% in all patients with ureteral stones [16].

2. Discussion

2.1. Presentation

Patients with infected ureteral stones present with a variety of signs and symptoms, many of which overlap with non-infected stones and pyelonephritis. The classic presentation is fever, chills, dysuria, urinary frequency, malodorous urine, and flank pain [2]. This is often associated with nausea and vomiting in a patient with a prior history of kidney stones and recurrent UTIs [2]. Pain is often episodic in nature and may progress from the flank to the lower abdomen as the stone progresses distally [6]. Physical examination may demonstrate fever, dehydration, and costovertebral angle (CVA) tenderness [2]. If left untreated, or if arriving in a delayed fashion, patients may appear ill and present with sepsis and shock.

2.2. ED evaluation

As previously mentioned, there are no universally accepted criteria for the diagnosis of infected urolithiasis. However, a combination of laboratory findings may assist in their identification. Patients should at the minimum undergo a urinalysis with culture, with pyuria, positive nitrites, positive leukocyte esterase, and large blood suggesting an infected stone [2,5,15,17]. A complete blood cell count and C-reactive protein (CRP) may demonstrate inflammatory changes (i.e., elevated white blood cell count [WBC]), and renal function assessment may reveal acute kidney injury (AKI) (i.e., elevated creatinine from baseline), which, if present, is likely multifactorial to include nausea and vomiting, obstructive uropathy, and end-organ dysfunction in the setting of sepsis and shock [2,15]. Specifically, in the evaluation for infected urolithiasis, the positive likelihood ratio (LR+) and negative likelihood ratio (LR-) for leukocytosis are 2 and 0.6 respectively; the LR+ for elevated CRP and positive nitrites are 2 and 36, respectively; and the LR+ for a urinalysis with >5 WBCs/high power field (hpf) is 4 [2,15]. AKI has a LR+ and LR- of 2 and 0.8, respectively [15]. In addition to laboratory studies, computed tomography (CT) should be obtained to help confirm the presence and location of the stone and to facilitate surgical planning [17-18]. Guidelines for specific CT protocols are controversial but may include CT abdomen and pelvis with intravenous (IV) contrast, without contrast, and urography (with and without contrast) [17-18]. However, CT protocols should be tailored to the patient, and IV contrast should be used when there is concern for a perinephric abscess or alternative intra-abdominal process such as appendicitis or cholecystitis [18]. Additionally, 'low-dose' or 'stone-protocol' CTs are less helpful in the identification of a stone and its complications in larger patients (body mass index >30) [18].

2.3. ED management

Patients with infected urolithiasis are at high risk for progression to sepsis and have a significantly increased risk of mortality [3,13-14,19]. These patients should receive broad-spectrum antibiotics covering gram negative and urease-producing organisms, especially if there is obstruction [7,10]. Additional coverage for methicillin-resistant *Staphylococcus aureus* (MRSA) should be considered in patients with risk factors (i.e., recent hospitalization, known carrier, recent instrumentation of the urinary tract, immunocompromised status, etc.) or those who are critically ill. Early urologic consultation is recommended for evaluation for surgical intervention including decompression [7,17]. While CT imaging will assist with operative planning, it should not delay urologic consultation. Additional supportive and symptomatic measures to include fluid resuscitation, analgesia, and anti-emetic therapies are recommended.

3. Pearls and pitfalls

3.1. What are significant risk factors for infected urolithiasis?

The presence or history of ureteral stones is an independent risk factor for the development of a UTI, with a large retrospective study demonstrating a hazard ratio (HR) of 5.67 (95% confidence interval [CI] 4.52–7.18) [10]. Furthermore, a single-center prospective observational study of 360 patients with acute nephrolithiasis found the prevalence of concomitant UTI to be 7.8% [2]. The highest reported association of UTIs and urolithiasis was 34.1% in a 10-year Taiwanese study [20]. However, patients with a history of UTIs, especially if recurrent, also have an increased risk of kidney stone formation [11]. The true causality (i.e., stone causing infection or infection causing stone) is controversial [11,21]. Though all stone types are at risk for concomitant UTI, literature suggests concomitant infections are more common in females (31.6% versus 15.6% in males), large (>5 mm) stones, multiple stones (41.4% versus 16.1% for a single stone), and staghorn stones (48.4% versus 19.8% in non-staghorn stones) [15,22]. In particular, staghorn stones are associated with urease-producing bacteria that further promote the crystallization and branching of the stone [22]. With respect to stone composition, patients who form urate and calcium oxalate stones have a much higher risk of developing an infection, with a HR of 6.87 (95% CI 2.82–16.72) and 6.36 (95% CI 4.82–8.40), respectively [10]. In addition to stone quantity, size, and composition, patients aged <40 or > 60 years old are more likely to develop an infection, though the reason for this bimodal pattern is unclear [22]. Other typical risks factors for UTI remain even in the presence of a ureteral stone, including diabetes, urinary catheterization, hypertension, and solitary kidney [3,11,22].

3.2. What are the signs and symptoms associated with infected urolithiasis?

The signs and symptoms of infected urolithiasis often overlap with those of pyelonephritis and uncomplicated urolithiasis. However,

reported fever (relative risk [RR] 6.6, 95% CI 3.1–13, LR+ 5), dysuria (RR 4.4, 95% CI 1.8–11, LR+ 2), chills (RR 3.0, 95% CI 1.3–6.7, LR +3), urinary frequency (RR 2.5, 95% CI 1.1–5.5, LR+ 2), and malodorous urine (RR 2.7, 95% CI 0.5–8.4, LR+ 3) are symptoms most strongly associated with infected urolithiasis [2]. Though common on presentation, other symptoms such as urinary urgency, hesitancy, hematuria, nausea, and vomiting are not associated with a significantly higher risk of infected urolithiasis [2]. Elevated temperature (>37.9 °C) is the strongest sign associated with infected urolithiasis, with a LR+ of 15 and odds ratio (OR) of 3.1 (95% CI 1.8–13.6) [2,23]. CVA tenderness possesses a RR of 2.7 (95% CI 1.0–8.1) though the LR+ is only 1 [2]. Other examination findings including suprapubic tenderness are less helpful in predicting infected urolithiasis [2].

3.3. What laboratory testing can assist in the diagnosis, and what are the keys to the urinalysis?

A urinalysis with urine culture is essential in the diagnosis of an infected kidney stone. Given their importance, patients should be given instruction for providing a clean-catch or catheterized urine sample if unable to provide a clean-catch sample to prevent contamination, which can occur in up to 54.9% of samples [24]. Particular attention should be given to female, pregnant, and obese patients who are at the highest risk for providing a contaminated urine sample [24].

The American Urological Association (AUA) does not provide specific guidance on the interpretation of a urinalysis in patients with urolithiasis but does have a strong recommendation based on a Grade B level of evidence to obtain a urine culture if there are concerns for superimposed infection based on clinical or laboratory findings [17]. Due to its importance, clinicians should ensure that urine cultures are obtained in patients with suspected infected urolithiasis rather than relying on institutional automated reflex protocols. Pyuria and positive leukocyte esterase suggest the presence of a concomitant infection, though individually, these markers have only moderate sensitivities and specificities. For the identification of a single organism with 100,000 colony forming units on urine culture, literature suggests positive leukocyte esterase has both a sensitivity and specificity of 86% and a LR+ and LR- of 6 and 0.2, respectively [2]. Specificity and LR+ increase to 98% and 24, respectively, with the presence of large leukocyte esterase [2]. Pyuria, defined as >5 WBCs/hpf, demonstrates a sensitivity and specificity of 86% and 79%, respectively [2]. This correlates with a LR+ and LR- of 4 and 0.2, respectively [2]. Increasing pyuria, with cutoffs of >10 WBCs/hpf, >15 WBCs/hpf, and > 20 WBCs/hpf are associated with increasing specificities of 87%, 91%, and 93%, respectively [2]. At these cutoffs, the LR+ is 6, 8, and 9, respectively, although the LR- are minimally affected (0.2, 0.3, and 0.3, respectively) [2]. Positive nitrites demonstrate a sensitivity and specificity of 43% and 99%, respectively, correlating with a LR+ of 36 and LR- of 0.6; subsequently, a urine specimen with positive nitrites has an exceedingly strong probability of resulting in a positive urine culture in the setting of urolithiasis [2,15].

Serum inflammatory markers including WBC count above 10–11.3 $\times 10^9$/L and CRP above 3.5 mg/L are also non-specific indicators that may predict infected urolithiasis [2,15]. Specifically, one study demonstrated that leukocytosis above 10.9 $\times 10^9$/L has a LR+ and LR- of 2 and 0.6, respectively, and another study found that 70% of patients with obstructive and infected urolithiasis had CRP elevations above 3.5 mg/L [2,16]. These studies, however, should be used in conjunction with urinalysis findings and clinical presentation such as fever [2,15]. Other laboratory studies including creatinine elevation are less helpful [16]. Ultimately, a urine culture is essential for diagnosing infected urolithiasis and should be obtained and followed closely regardless of patient disposition and the initial urinalysis results. Subsequently, ED physicians are encouraged to ensure that the primary care physician, admitting physician, and/or urologist are aware of pending culture results.

3.4. What is the utility of ultrasound versus CT?

The use of ultrasound in the evaluation for urolithiasis has been advocated to avoid radiation exposure. Specifically, in younger adults with renal colic, ultrasound alone may be adequate in its diagnosis, especially if the stone is >5 mm [25-26]. In these patients, hydronephrosis, especially if moderate to severe, is suggestive of urolithiasis; however, unless directly visualized, ultrasound cannot confirm the actual presence of urolithiasis [25]. Most studies demonstrate modest accuracy in the diagnosis of urolithiasis, with a meta-analysis of nine studies demonstrating a sensitivity and specificity of 70.2% and 75.4%, respectively, correlating with a LR+ and LR- of 3 and 0.4, respectively [26]. However, the sensitivity of ultrasound for the diagnosis of renal infections is limited at only 56.6%, with a normal appearing kidney being a common finding [27-28]. Ultrasound literature regarding the identification of urolithiasis complications including superimposed infections is extremely sparse. Ultrasound, however, may be more useful in determining disease progression of an infected stone to pyonephrosis, or development of pus in the setting of a urinary obstruction [29-30]. In these cases, ultrasound has a LR+ and LR- of 30 and 0.1, respectively [31]. However, the challenges for identifying a stone as the etiology of pyonephrosis or pyelonephritis remain [31].

CT of the abdomen and pelvis is the imaging study of choice to identify the location and size of urolithiasis, evaluate for infectious complications, and perform operative planning. However, CT is not a functional test of urinary drainage but is rather an anatomical evaluation of the urinary tract and other abdominal organs. The AUA has a strong recommendation to obtain a non-contrast CT in patients who may need percutaneous nephrolithotomy and a conditional recommendation to obtain a non-contrast CT in patients who may benefit from shockwave lithotripsy or ureteroscopy [17]. Generally, large stones (>10-15 mm), stones that have failed conservative management (failure to pass spontaneously within 4–6 weeks), patients with intractable pain, proximal stones, and infected stones should be evaluated for urologic intervention [32]. Furthermore, the American College of Radiology Appropriateness Criteria suggests that CT imaging (with and/or without IV contrast) in patients with suspected renal infection and a history of stone or obstruction is usually appropriate and demonstrates a sensitivity of 97% [18]. Though the diagnosis of infected urolithiasis can be made based on history, examination, and laboratory evaluation, clinicians should maintain a low threshold to obtain a CT in the ED to identify stone characteristics and facilitate urologic interventions [18]. Clinicians should also consider the use of contrast when suspecting infectious complications (i.e., pyelonephritis, pyonephrosis, abscess), to exclude alternative etiologies of flank pain (i.e., appendicitis), and facilitate urologic interventions [18].

3.5. What antibiotics are necessary, and what are the major treatment considerations?

Generally, broad-spectrum antibiotics should be administered to patients with suspected infected stones given their risk for progression to sepsis, though neither the AUA nor IDSA make specific recommendations [11-12,17]. Antibiotics should target gram-negative rods and urease-producing organisms (Table 1). Meta-analysis data demonstrate that the most common organisms associated with infected urolithiasis are *E. coli*, *Klebsiella*, *Enterococcus* species (spp), *Proteus*, and *Pseudomonas* [7,11]. In infected struvite stones, *Proteus* spp. are common, but additional consideration must be given to urease-forming species such as *Staphylococcus*, *Providencia*, and *Serratia* [11]. Initial empiric therapies include ceftriaxone in patients without concern for *Pseudomonas* and cefepime or piperacillin-tazobactam for patients with *Pseudomonas* risk factors [1,33-34]. These include the use of an indwelling catheter or nephrostomy tube, immunosuppression, recurrent UTIs, and dementia [35]. Vancomycin, daptomycin, or linezolid should be added in critically ill patients or if the etiology is suspected to be secondary to MRSA

Table 1
Example antibiotic regimens for infected urolithiasis. Antibiotic regimens should be tailored based on local antibiograms and urine culture sensitivities [5,36-39].

Population	Potential organisms	Example regimens
Critically ill	*Pseudomonas, E. coli, Klebsiella, Proteus, Providencia, Serratia*	-Meropenem 1-2 g IV q8h or -Piperacillin-tazobactam 3.375–4.5 g IV q6-8h* or -Cefepime 2 g IV q12h*
	MRSA, *Enterococcus* spp.	-Vancomycin 15–20 mg/kg IV q8-12h or -Daptomycin 8–10 mg/kg IV q24h** or -Linezolid 600 mg IV q12h**
Non-critically ill, requiring hospitalization	*E. coli, Klebsiella, Proteus, Providencia, Serratia*	-Ceftriaxone 1 g IV q24h or -Ciprofloxacin 400 mg IV q12h or -Levofloxacin 750 mg IV q24h or -Piperacillin-tazobactam 3.375–4.5 g IV q6-8h
	Enterococcus spp.	-Ampicillin 2 g IV q6h or -Vancomycin 15–20 mg/kg IV q8-12h or -Daptomycin 8–10 mg/kg IV q24h** or -Linezolid 600 mg IV q12h**
Outpatient	*E. coli, Klebsiella, Proteus*	-Cefpodoxime 200 mg PO BID for 10–14 days or -Amoxicillin-clavulanate 875–125 mg PO BID for 10–14 days or -Ciprofloxacin 500 mg PO BID for 7 days or -Levofloxacin 750 mg PO for 5 days
	Enterococcus	-Amoxicillin 500 mg PO TID for 5 days or -Fosfomycin 3 g PO once

IV – intravenous, mg – milligrams, kg – kilograms, BID – twice a day, TID – three times a day, PO – oral.

* Prior urine cultures should be reviewed for a history of extended-spectrum β-lactamase (ESBL)-producing organisms, as their presence may preclude the use of cephalosporins and/or penicillins; meropenem (if resistance only to ertapenem), carbapenems combined with a β-lactamase inhibitor (i.e., meropenem-vaborbactam), cefiderocol, and ceftazidime-avibactam should be considered in conjunction with urology and infectious disease consultation [37].

** Prior urine cultures should be reviewed for a history of vancomycin-resistant *Enterococci* which will dictate the necessity for daptomycin or linezolid [38].

[1,33-34]. Alternative broad-spectrum antibiotics that may be considered include carbapenems with anti-pseudomonal activity (i.e., meropenem) and aminoglycosides [1]. Antibiotic selection, however, should ideally be performed in conjunction with urology and based on the local antibiogram.

There are no robust data regarding antibiotics as an outpatient, given that outpatient management of infected urolithiasis is only recommended with caution in select stable patients without complete obstruction, immunosuppression, or major comorbidities; when admission is not feasible; and close urologic follow-up can be ensured. In these cases, it may be reasonable to choose an antibiotic regimen similar to that used for complicated UTIs, such as fluoroquinolones (i.e., ciprofloxacin, levofloxacin), later-generation cephalosporins (i.e., cefpodoxime), or broader spectrum penicillins (i.e., amoxicillin) if *Enterococcus* is suspected (Table 1) [36]. Outpatient antibiotics should be tailored based on previous culture data, if available, as well as local sensitivities.

3.6. What are the major complications of infected urolithiasis?

Progression to sepsis and septic shock is a significant concern for patients with infected stones with rates reported as high as 20–50% [3,19]. Similarly, the risks for bacteremia (3.4 times risk), hospital length of stay (4.5 days longer), and in-hospital mortality (27.3%) are significantly increased in patients with a UTI with an obstructive process [17]. In patients with concomitant infection and obstruction, mortality is 2.6 times higher if surgical decompression is not performed [13]. AKI may occur in up to 31% of patients with infected urolithiasis, which is likely multifactorial to include obstructive uropathy and propensity for progression to systemic illness (i.e., sepsis) [13,15]. Unfortunately, even after endourologic intervention, patients with infected urolithiasis remain at elevated risk for postoperative fever and sepsis [40-41]. To the authors' knowledge, there is minimal to no literature regarding any increased risk of bleeding, urinary extravasation, ureteral stricture, abscess formation, or other significant complications in infected versus non-infected urolithiasis at the time of this manuscript and are areas for further research.

3.7. Which patients benefit from consultation and further intervention beyond antibiotics?

In general, all patients with an infected stone should undergo urologic consultation in the ED for surgical management [7]. In patients with infected stones causing obstruction, the AUA has a strong recommendation for urgent collecting system drainage with stent or nephrostomy tube placement [17]. Additionally, in patients with stone disease with residual fragments and infection, the AUA has a moderate recommendation for endoscopic intervention [17]. Timely decompression, typically defined as <2 days from admission, has demonstrated mortality benefits in a large multivariate study [42]. This study demonstrated the odds of death increased by 29%, with an OR of 1.29 (95% CI 1.03–1.63), in patients who had delays in surgical decompression [42]. In a recent Japanese study evaluating 1363 patients with obstructive pyelonephritis both with and without sepsis, the total mortality rates increased when comparing decompression at 1–2 days (1.5%), 3–4 days (2.0%), and ≥ 5 days (2.5%) [43]. Furthermore, a retrospective study including patients with severe infection and urolithiasis found a 19% mortality rate in patients not treated with surgical decompression, compared to 8.8% in patients undergoing surgical decompression, highlighting the importance of early urologic consultation [13]. Only select patients who are too unstable or have stones in anatomically challenging locations, such as the inferior renal pole, should be considered for non-surgical management [17].

Common urologic interventions in the management of urolithiasis include shockwave lithotripsy, ureteroscopy, percutaneous nephrolithotomy (PCNL), and placement of stents to include ureteral stents and nephrostomy tubes [17]. In patients without significant stone burden (i.e., <20 mm), shockwave lithotripsy (external high-energy waves directed at the stone) or ureteroscopy (endoscopic stone manipulation) are generally first-line procedures [17]. In larger stones, patients often require PCNL, in which the renal pelvis is accessed through the kidney for stone access [17]. Ureteral stents are placed in cases of ureteral injury, strictures, and concern for unsuccessful fragment clearance but are not always required [17]. Similarly, nephrostomy tube placement is an alternative to ureteral stents when urgent drainage is required and may be used in conjunction with PCNL, particularly if repeat PCNL is planned [17]. Laparoscopic or open surgeries may be required in rare cases in patients who have failed less invasive interventions and/or with large complex stones requiring reconstructive surgery [17].

3.8. Which patients can potentially be discharged?

No consensus admission criteria exist for either uncomplicated or infected urolithiasis. However, patients with significant stone burden (i.e., >10–15 mm or multiple stones), solitary kidney, intractable symptoms (nausea, vomiting, and pain), urinary extravasation, severe renal function impairment, and clinical instability (i.e., sepsis or septic shock) should be admitted to the hospital with urologic consultation [5]. In the setting of a concomitant infection, patients with significant

Table 2
Infected urolithiasis pearls.

- Patients with ureteral stones are at increased risk for concomitant UTI, and patients with infected urolithiasis may decompensate rapidly and progress to sepsis and shock.
- Patients with staghorn stones, urate and calcium oxalate stones, and multiple stones are also at higher risk for superimposed infection.
- A thorough history (fever, chills, dysuria, and history of UTIs), physical examination (CVA tenderness), urinalysis, and urine culture are essential for diagnosis. Inflammatory markers (elevated WBC and CRP) can be helpful adjuncts.
- CT is recommended to identify complications and assist with preoperative planning in those with suspected infected urolithiasis.
- Specific CT protocols (abdomen/pelvis with/without contrast, urogram) should be patient-tailored, with strong consideration for contrast in patients with concern for abscess formation or other intra-abdominal processes (i.e., appendicitis).
- ED management includes broad-spectrum antibiotics covering gram-negative and urease-producing organisms, as well as MRSA in patients with risk factors.
- Urology consultation early in the patient's evaluation and management is recommended. Delays in surgical decompression for patients with infected, obstructed stones worsen outcomes.

comorbidities (i.e., older age and immunosuppression), complete obstruction, hydronephrosis, ill-appearance, inability for close follow-up, and/or inability to take oral antibiotics should also be admitted to the hospital [5,44-45]. Outpatient management of infected urolithiasis should be approached cautiously, especially given the risk of progression to sepsis. Though the literature is sparse, patients with smaller and non-obstructing stones who are well-appearing, afebrile, without significant comorbid conditions, and able to take oral antibiotics may be considered for outpatient management after consultation with urology in the ED and ensuring follow-up [5,44-45]. In these patients, close urologic and urine culture follow-up is imperative.

Table 2 provides pearls for infected urolithiasis.

4. Conclusions

Patients with urolithiasis and concomitant UTI represent a group with high morbidity and mortality. Diagnosis may be challenging as symptoms often overlap with pyelonephritis and non-infected renal colic, but elevated inflammatory markers, positive nitrites, and leukocyte esterase in febrile patients with CVA tenderness and a history of urolithiasis and UTIs should raise suspicion for an infected stone. Patients should receive broad-spectrum antibiotics, undergo CT imaging for operative planning, and be rapidly evaluated by urology. Contrast should be used if considering abscess formation or other intra-abdominal etiologies of flank pain. Early surgical decompression in patients with obstruction and infection can improve patient outcomes.

CRediT authorship contribution statement

Michael J. Yoo: Writing – review & editing, Writing – original draft, Visualization, Validation. **Jessica Pelletier:** Writing – review & editing, Writing – original draft, Visualization, Validation. **Alex Koyfman:** Writing – review & editing, Visualization, Validation, Supervision, Conceptualization. **Brit Long:** Writing – review & editing, Visualization, Validation, Supervision, Resources, Data curation, Conceptualization.

Declaration of Competing Interest

None.

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References

[1] Dubbs SB, Sommerkamp SK. Evaluation and Management of Urinary Tract Infection in the emergency department. Emerg Med Clin North Am. 2019;37(4):707–23. https://doi.org/10.1016/j.emc.2019.07.007.
[2] Abrahamian FM, Krishnadasan A, Mower WR, Moran GJ, Talan DA. Association of pyuria and clinical characteristics with the presence of urinary tract infection among patients with acute nephrolithiasis. Ann Emerg Med. 2013;62(5):526–33. https://doi.org/10.1016/j.annemergmed.2013.06.006.
[3] Hamasuna R, Takahashi S, Nagae H, et al. Obstructive pyelonephritis as a result of urolithiasis in Japan: diagnosis, treatment and prognosis. Int J Urol. 2015;22(3):294–300. https://doi.org/10.1111/iju.12666.
[4] Bishop K, Momah T, Ricks J. Nephrolithiasis. Prim Care. 2020;47(4):661–71. https://doi.org/10.1016/j.pop.2020.08.005.
[5] Sakhaee K, Maalouf NM, Sinnott B, Clinical review.. Kidney stones 2012: pathogenesis, diagnosis, and management. J Clin Endocrinol Metab. 2012;97(6):1847–60. https://doi.org/10.1210/jc.2011-3492.
[6] Corbo J, Wang J. Kidney and ureteral stones. Emerg Med Clin North Am. 2019;37(4):637–48. https://doi.org/10.1016/j.emc.2019.07.004.
[7] Marien T, Miller NL. Treatment of the infected stone. Urol Clin North Am. 2015;42(4):459–72. https://doi.org/10.1016/j.ucl.2015.05.009.
[8] Hill AJ, Basourakos SP, Lewicki P, et al. Incidence of kidney stones in the United States: the continuous National Health and nutrition examination survey. J Urol. 2022;207(4):851–6. https://doi.org/10.1097/JU.0000000000002331.
[9] Wilcox CR, Whitehurst LA, Cook P, Somani BK. Kidney stone disease: an update on its management in primary care. Br J Gen Pract. 2020;70(693):205–6. Published 2020 Mar 26. https://doi.org/10.3399/bjgp20X709277.
[10] Brain E, Geraghty RM, Cook P, Roderick P, Somani B. Risk of UTI in kidney stone formers: a matched-cohort study over a median follow-up of 19 years. World J Urol. 2021;39(8):3095–101. https://doi.org/10.1007/s00345-020-03564-7.
[11] Ripa F, Pietropaolo A, Montanari E, Hameed BMZ, Gauhar V, Somani BK. Association of Kidney Stones and Recurrent UTIs: the chicken and egg situation. A systematic review of literature. Curr Urol Rep. 2022;23(9):165–74. https://doi.org/10.1007/s11934-022-01103-y.
[12] Jennings CA, Khan Z, Sidhu P, Navarrete O, Palladino A, Rutland E, et al. Management and outcome of obstructive ureteral stones in the emergency department: emphasis on urine tests and antibiotics usage. Am J Emerg Med. 2019 Oct;37(10):1855–9.
[13] Borofsky MS, Walter D, Shah O, Goldfarb DS, Mues AC, Makarov DV. Surgical decompression is associated with decreased mortality in patients with sepsis and ureteral calculi. J Urol. 2013;189(3):946–51. https://doi.org/10.1016/j.juro.2012.09.088.
[14] Reyner K, Heffner AC, Karvetski CH. Urinary obstruction is an important complicating factor in patients with septic shock due to urinary infection. Am J Emerg Med. 2016;34(4):694–6. https://doi.org/10.1016/j.ajem.2015.12.068.
[15] Abi Tayeh G, Safa A, Sarkis J, et al. Determinants of pyelonephritis onset in patients with obstructive urolithiasis. Urologia. 2022;89(1):100–3. https://doi.org/10.1177/03915603211035244.
[16] GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015 [published correction appears in Lancet. 2017 Jan 7;389(10064):e1]. Lancet. 2016;388(10053):1459–544. https://doi.org/10.1016/S0140-6736(16)31012-1.
[17] Assimos D, Krambeck A, Miller NL, et al. Surgical Management of Stones: American urological association/Endourological society guideline, PART II. J Urol. 2016;196(4):1161–9. https://doi.org/10.1016/j.juro.2016.05.091.
[18] Expert Panel on Urological Imaging, Smith AD, Nikolaidis P, et al. ACR appropriateness criteria® acute pyelonephritis: 2022 update. J Am Coll Radiol. 2022;19(11S):S224–39. https://doi.org/10.1016/j.jacr.2022.09.017.
[19] Hsiao CY, Chen TH, Lee YC, et al. Urolithiasis is a risk factor for Uroseptic shock and acute kidney injury in patients with urinary tract infection. Front Med (Lausanne). 2019;6:288. Published 2019 Dec 5. https://doi.org/10.3389/fmed.2019.00288.
[20] Huang WY, Chen YF, Chen SC, Lee YJ, Lan CF, Huang KH. Pediatric urolithiasis in Taiwan: a nationwide study, 1997-2006. Urology. 2012;79(6):1355–9. https://doi.org/10.1016/j.urology.2012.01.036.
[21] Borghi L, Nouvenne A, Meschi T. Nephrolithiasis and urinary tract infections: 'the chicken or the egg' dilemma? Nephrol Dial Transplant. 2012;27(11):3982–4. https://doi.org/10.1093/ndt/gfs395.
[22] Yongzhi L, Shi Y, Jia L, Yili L, Xingwang Z, Xue G. Risk factors for urinary tract infection in patients with urolithiasis-primary report of a single center cohort. BMC Urol. 2018;18(1):45. Published 2018 May 21. https://doi.org/10.1186/s12894-018-0359-y.

[23] Yilmaz S, Pekdemir M, Aksu NM, Koyuncu N, Cinar O, Akpinar E. A multicenter case-control study of diagnostic tests for urinary tract infection in the presence of urolithiasis [published correction appears in Urol res. 2012 Aug;40(4):431. Akpinar, E [added]]. Urol Res. 2012;40(1):61–5. https://doi.org/10.1007/s00240-011-0402-x.
[24] Hansen MA, Valentine-King M, Zoorob R, et al. Prevalence and predictors of urine culture contamination in primary care: a cross-sectional study. Int J Nurs Stud. 2022;134:104325. https://doi.org/10.1016/j.ijnurstu.2022.104325.
[25] Moore CL, Carpenter CR, Heilbrun ME, et al. Imaging in suspected renal colic: systematic review of the literature and multispecialty consensus. Ann Emerg Med. 2019;74(3):391–9. https://doi.org/10.1016/j.annemergmed.2019.04.021.
[26] Wong C, Teitge B, Ross M, Young P, Robertson HL, Lang E. The accuracy and prognostic value of point-of-care ultrasound for nephrolithiasis in the emergency department: a systematic review and Meta-analysis. Acad Emerg Med. 2018;25(6):684–98. https://doi.org/10.1111/acem.13388.
[27] Majd M, Nussbaum Blask AR, Markle BM, et al. Acute pyelonephritis: comparison of diagnosis with 99mTc-DMSA, SPECT, spiral CT, MR imaging, and power Doppler US in an experimental pig model. Radiology. 2001;218(1):101–8. https://doi.org/10.1148/radiology.218.1.r01ja37101.
[28] Vourganti S, Agarwal PK, Bodner DR, Dogra VS. Ultrasonographic evaluation of renal infections. Radiol Clin North Am. 2006;44(6):763–75. https://doi.org/10.1016/j.rcl.2006.10.001.
[29] Kumar LP, Khan I, Kishore A, Gopal M, Behera V. Pyonephrosis among patients with pyelonephritis admitted in Department of Nephrology and Urology of a tertiary care Centre: a descriptive cross-sectional study. JNMA J Nepal Med Assoc. 2023;61(258):111–4. Published 2023 Feb 1. 10.31729/jnma.8015.
[30] Nicola R, Menias CO. Urinary obstruction, stone disease, and infection. In: Hodler J, Kubik-Huch RA, von Schulthess GK, editors. Diseases of the abdomen and pelvis 2018–2021: Diagnostic imaging - IDKD book. Cham (CH): Springer; March 21, 2018. p. 223–8.
[31] Tamburrini S, Lugarà M, Iannuzzi M, et al. Pyonephrosis ultrasound and computed tomography features: a pictorial review. Diagnostics (Basel). 2021;11(2):331. Published 2021 Feb 17. https://doi.org/10.3390/diagnostics11020331.
[32] Pradère B, Doizi S, Proietti S, Brachlow J, Traxer O. Evaluation of guidelines for surgical Management of Urolithiasis. J Urol. 2018;199(5):1267–71. https://doi.org/10.1016/j.juro.2017.11.111.
[33] Koch GE, Johnsen NV. The diagnosis and Management of Life-threatening Urologic Infections. Urology. 2021;156:6–15. https://doi.org/10.1016/j.urology.2021.05.011.
[34] Orr A, Awad M, Johnson N, Sternberg K. Obstructing ureteral calculi and presumed infection: impact of antimicrobial duration and time from decompression to stone treatment in developing Urosepsis. Urology. 2023;172:55–60. https://doi.org/10.1016/j.urology.2022.10.010.
[35] Tumbarello M, Raffaelli F, Peghin M, et al. Characterisation and risk factor profiling of Pseudomonas aeruginosa urinary tract infections: pinpointing those likely to be caused by multidrug-resistant strains. Int J Antimicrob Agents. 2020;55(4):105900. https://doi.org/10.1016/j.ijantimicag.2020.105900.
[36] Johnson JR, Russo TA. Acute pyelonephritis in adults [published correction appears in N Engl J med. 2018 mar 15;378(11):1069]. N Engl J Med. 2018;378(1):48–59. https://doi.org/10.1056/nejmcp1702758.
[37] Tamma PD, Aitken SL, Bonomo RA, Mathers AJ, van Duin D, Clancy CJ. Infectious Diseases Society of America guidance on the treatment of extended-Spectrum β-lactamase producing Enterobacterales (ESBL-E), Carbapenem-resistant Enterobacterales (CRE), and Pseudomonas aeruginosa with difficult-to-treat resistance (DTR-P. Aeruginosa). Clin Infect Dis. 2021;72(7):e169–83. https://doi.org/10.1093/cid/ciaa1478.
[38] Miller WR, Murray BE, Rice LB, Arias CA. Resistance in Vancomycin-Resistant Enterococci. Infect Dis Clin North Am. 2020;34(4):751–71. https://doi.org/10.1016/j.idc.2020.08.004.
[39] Herness J, Buttolph A, Hammer NC. Acute pyelonephritis in adults: rapid evidence review. Am Fam Physician. 2020;102(3):173–80.
[40] Chugh S, Pietropaolo A, Montanari E, Sarica K, Somani BK. Predictors of urinary infections and Urosepsis after Ureteroscopy for stone disease: a systematic Review from EAU section of urolithiasis (EULIS). Curr Urol Rep. 2020;21(4):16. Published 2020 Mar 24. https://doi.org/10.1007/s11934-020-0969-2.
[41] Eswara JR, Shariftabrizi A, Sacco D. Positive stone culture is associated with a higher rate of sepsis after endourological procedures [published correction appears in urolithiasis. 2013 Oct;41(5):415. Sharif-Tabrizi, Ahmad [corrected to Shariftabrizi, Ahmad]]. Urolithiasis. 2013;41(5):411–4. https://doi.org/10.1007/s00240-013-0581-8.
[42] Haas CR, Li G, Hyams ES, Shah O. Delayed decompression of obstructing stones with urinary tract infection is associated with increased odds of death. J Urol. 2020;204(6):1256–62. https://doi.org/10.1097/JU.0000000000001182.
[43] Kamei J, Sugihara T, Yasunaga H, et al. Impact of early ureteral drainage on mortality in obstructive pyelonephritis with urolithiasis: an analysis of the Japanese National Database. World J Urol. 2023;41(5):1365–71. https://doi.org/10.1007/s00345-023-04375-2.
[44] Wang RC. Managing Urolithiasis. Ann Emerg Med. 2016;67(4):449–54. https://doi.org/10.1016/j.annemergmed.2015.10.021.
[45] Dielubanza EJ, Mazur DJ, Schaeffer AJ. Management of non-catheter-associated complicated urinary tract infection. Infect Dis Clin North Am. 2014;28(1):121–34. https://doi.org/10.1016/j.idc.2013.10.005.