Urosepsis

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Case Presentation

A 48-year-old male with history of type II diabetes presented to the Emergency Department with abdominal pain for 4 days associated with dysuria, left sided flank pain, and decreased oral intake. In the Emergency Department his presenting vital signs included a heart rate of 175/min, blood pressure of 81/51 mmHg, respiratory rate of 30/min, and SpO_2 of 98% on supplemental oxygen at 5 L/min via nasal cannula. Physical exam was significant for an acutely ill appearing male with left sided costovertebral angle tenderness. Initial labs showed an elevated WBC at 14.2 K/μL with a differential showing 91% PMNs, elevated lactic acid of 6.8 mmol/L and elevated creatinine at 1.5 mg/dL. Urinalysis showed 2+ leukocyte esterase with microscopy showing many bacteria. A CT scan abdomen pelvis revealed an obstructing kidney stone within the proximal left ureter along with hydronephrosis and perirenal fat stranding of the left kidney.

Question

What is the appropriate management for this patient with septic shock from a urinary source?

Answer Prompt administration of antimicrobials and adequate source control by addressing obstruction and relieving sequestered infection.

All patients with sepsis from a urinary source should be treated with rapid resuscitation, early appropriate antimicrobial agents and elimination of infection sources that are not accessible to the blood stream. This patient received 3 L of lactated ringers in the Emergency Department without improvement in vital signs and repeat lactic acid of 2.5 after 3 h. Within the first 2 h of presentation two sets of peripheral blood cultures were drawn and 1 g of Ceftriaxone was administered intravenously. The patient was taken to the interventional radiology suite for placement of a left nephrostomy tube and decompression of hydronephrosis. He was then transferred to the intensive care unit, where a central line was placed and vasopressor support was initiated with a goal mean arterial pressure target of 65 mmHg. On day 2 of hospitalization the patient's blood cultures returned positive for gram negative bacilli and ultimately both urine and blood cultures were speciated as E. coli. He was continued on ceftriaxone and was able to be weaned off of vasopressor support on day 3 of his hospitalization and was transferred out of the ICU to the general medical ward the next day.

Principles of Management

Diagnosis

Urosepsis is commonly encountered in the ICU, accouting for over 30% of sepsis cases worldwide [1]. The main causes of urosepsis are indwelling urinary catheters and urologic interventions (stone treatment, prostate biopsies, and endoscopic urethral stricture treatment) [2]. Any patient who has undergone recent urological intervention is at particularly high risk of developing urosepsis within 24 h following intervention. Additional risk factors include other indwelling foreign objects (ureteric stents, nephrostomy tubes, nephrolithiasis) within the urinary tract and history of previous urinary tract infection [3].

In general the diagnosis for urosepsis can be made in a noncatheterized patient if two of the following are present: fever, urgency, costovertebral or suprapubic tenderness, pyuria, or radiologic evidence of urinary tract infection (pyelonephritis, abscess formation, etc.). In addition if a fluid collection (abscess, phlegmon, hydronephrotic kidney) within the urinary tract is sampled and has a positive gram

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stain or culture this is indicative of a urinary tract infection. Diagnosis for chronically catheterized patients also includes frank pus expression, greater than 10 WBC/uL, or leukocyte esterase/nitrate positivity [3, 4].

Early imaging on presentation is essential to eliminate the possibility of urinary tract obstruction or contained infection. Urinary tract obstruction and contained infection (abscess, phlegmon, hydronephrotic kidney) usually require procedural intervention to attain source control. Imaging can include renal ultrasound or CT scan (Fig. 59.1). Of the two, CT with IV contrast has been shown to be more sensative in detecting abnormalities that may require intervention compared to ultrasound [5]. CT scans without contrast have decreased sensitivity for detecting abscess and phlegmon development.

Empiric Antimicrobial Administration

Selection and early administration of an antimicrobial agent that can effectively treat the infective pathogen is essential to the optimal management of a patient with urosepsis. This should ideally be done after the specimens of urine, blood, and other possible sources of infection are taken. Obtaining specimens for culture must not delay the initial antibiotic administration >45 min [2]. It is paramount that the antimicrobial selected not only effectively targets the suspected infectious agent but also that it penetrates the urologic system (i.e. is excreted by the kidneys).

Pathogens that cause urosepsis are primarily gram negative. This is different from sepsis overall, which is dominated by gram-positive bacteria. The most frequent pathogen, Escherichia coli, is encountered in almost half of urosepsis cases. Other frequent pathogens are Klebsiella spp., Pseudomonas aeruginosa, Enterococcus, and Enterobacter spp. [2].

When selecting an initial antimicrobial prior to the identification of the offending organism it is important to consider local susceptibilities, previous patient colonization, recent antimicrobial administration or recent hospitalization (both lead to increased chance of resistant organisms), foreign body presence, and patient specific circumstances (cystic kidney, acute kidney injury, etc.).

For a patient with no risk factors for development of resistant organisms ceftriaxone or another third generation cephalosporin may be administered. Fluoroquinolones (namely ciprofloxacin and levofloxacin) were previously recommended for first line therapy as often as third generation cephalosporins for treatment of urosepsis however fluroquinolone resistance, particularly in E. coli, have made these agents less appealing [6]. Patients that are colonized and have been previously treated for E. coli and K. pneumoniae are at risk for extended spectrum beta-lactamase (ESBL) producing organisms. In these patients, empiric treatment with the carbapenem class of antibiotics is preferred. In the patient with previous history of vancomycin resistant enterococcus (VRE), linezolid is the preferred agent. Aminoglycosides, long a mainstay in the treatment of urinary sepsis because of their concentration within the urinary collective system, have fallen out of favor due to the risk of renal toxicity. For the patient with previous fungal colonization of their urinary source and concern for fungal urinary sepsis, empiric treatment with fluconazole or amphotericin B deoxycholate are the preferred antifungals because of their urinary tract penetration. Echinocandins and other azoles, as well as amphotericin B lipid formulas do not have good urinary tract penetration and should be avoided [7].

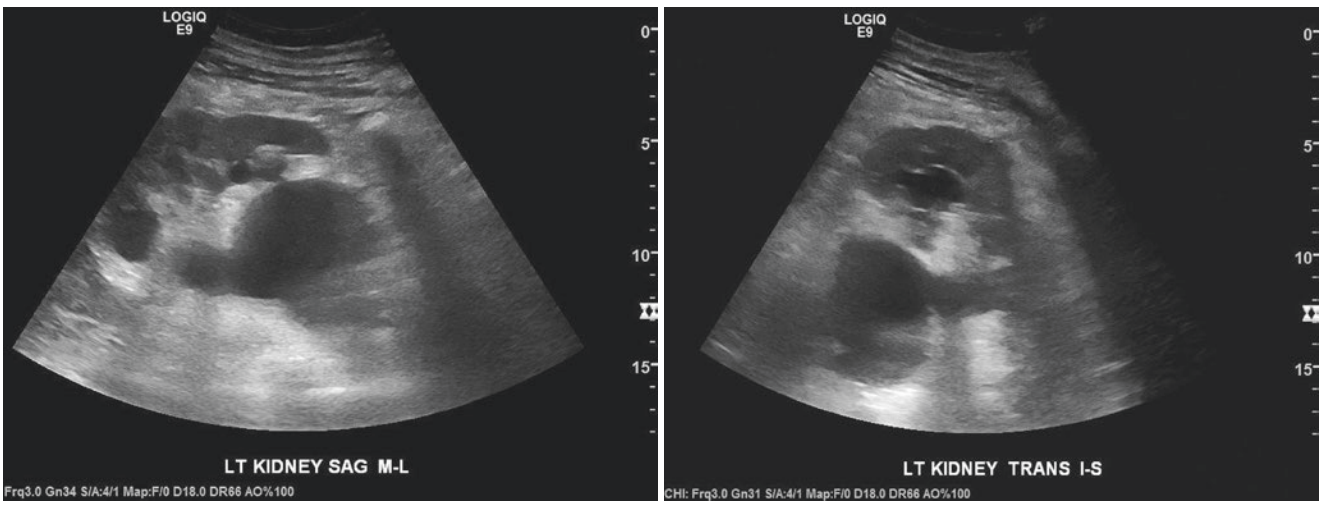

Fig. 59.1 Ultrasound images showing massive dilation of the renal pelvis and collecting system (hydronephrosis) due to ureteral obstruction

Procedures/Surgery

In order to attain source control of urinary infections caused by obstruction it is necessary to relieve the obstruction. Interventions for relieving obstruction include foley catheter insertion, ureteral stents, nephrostomy tubes, surgical drainage, and nephrectomy. The choice of intervention depends on the location of the obstruction. For post-vesicular obstruction, foley catheter placement may relieve the obstruction. However if the obstruction is ureteral, nephrostomy tube placement or retrograde ureteral stent is necessary.

Evidence Contour

Several aspects regarding the diagnosis and management of urosepsis remain without consensus.

Empiric Antibiotic Choice

Given the importance of targeting the correct offending bacteria species within the first hours of onset of sepsis, it is essential to select the correct antimicrobial empirically, prior to culture data being available. Some data is available from previous studies regarding the most efficacious empiric antibacterial agent. One study compared empiric intravenous doripenem (a carbapenem) vs. intravenous levofloxacin (a fluoroquinolone) as the treatment of complicated urinary tract infections and found cure rates comparable at approximately 80% each [8]. Another study compared ertapenem (a carbapenem) and ceftriaxone (a third generation cephalosporin) in patients with complicated UTI and found equitable microbiological responses [9]. Thus, evidence supports using local susceptibility patterns for antimicrobial selection.

Indications for Imaging

Frequently in patients with a high degree of clinical suspicion for pyelonephritis no imaging is necessary. However, in the septic ICU patient, imaging should be considered. Computed tomography (CT) provides the most complete anatomic evaluation of the genito-urinary tract. However, there are no studies showing difference in outcomes between patients imaged with CT scan versus ultrasound, which is also frequently used in this patient population [5]. Ultrasound is the less expensive test, has high sensitivity for hydronephrosis from an intervenable obstruction, and spares the patient of radiation exposure. However, this modality often requires an experienced operator or dedicated ultrasound technician to be available (may be difficult in the evening/weekend hours) and may provide suboptimal images in patients who are obese [10]. Studies evaluating initial use of CT or ultrasound in the patient with sepsis from a urinary source are needed.

Intervention Method

Relief of obstruction is critical for source control in patients presenting with urinary sepsis with underlying obstruction (stricture, nephrolithiasis, etc) (Fig. 59.2). This can be achieved via ureteral stent placement or percutaneous nephrostomy tube placement. While retrograde ureteral stent

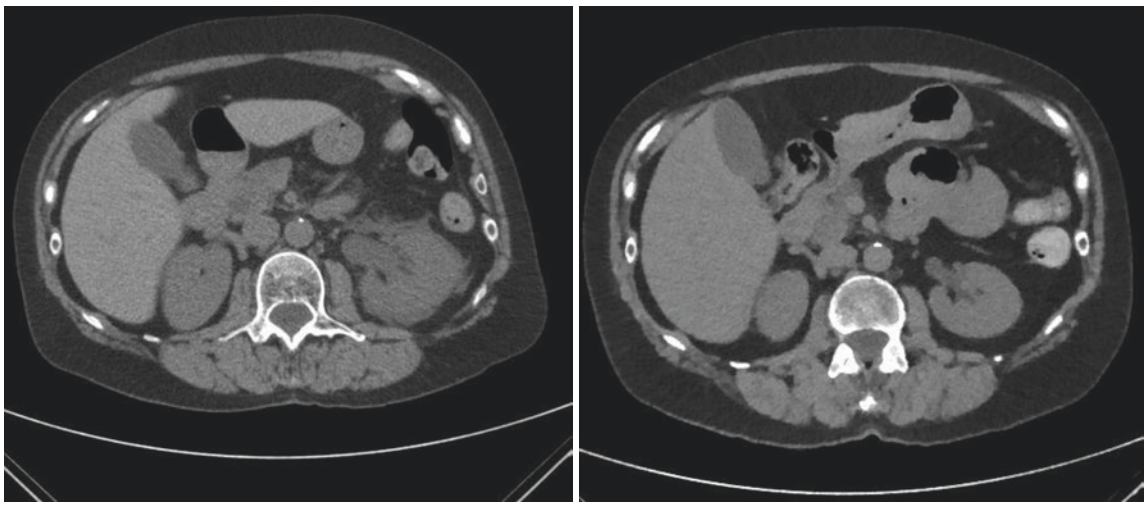

Fig. 59.2 Non-contrast CT of the abdomen showing collecting system dilation with perinephric stranding in the panel on the left. On the right, CT shows resolution following relief of obstruction

placement provides more definitive relief of the obstruction, it requires general anesthesia which may not be feasible in the presence of shock or hemodynamic instability. One study from Peare *et al* investigating 42 patients with obstructive calculi and sepsis revealed similar success rates between the two modalities in regards to WBC normalization and fever trend [11]. Percutaneous nephrostomy does provide adequate drainage in over 90% of patients. The rate of major complications secondary to nephrostomy tube placement, namely hemorrhage, varied from 2% to 5% of cases depending on operator experience [12].

However, there is data suggesting that retrograde ureteral stent placement may offer some benefits. In that same study by Pearle, retrograde stent placement was found to reduce length of hospital stay when compared to patients who received nephrostomy placement (4.5 vs. 3.2 days). This similarity in outcomes with reduction of hospital stay length may argue that when feasible, retrograde ureteral stent placement should be preferred [11, 12].

References

1. Brunkhorst FM. Epidemiology, economy and practice—results of the German study on prevalence by the competence network sepsis (SepNet) [in German]. Anasthesiol Intensivmed Notfallmed Schmerzther. 2006;41:43–4.
2. Tandogdu Z, Bjerklund Johansen TE, Bartoletti R, Wagenlehner FME. Management of the urologic sepsis syndrome. Eur Urol Suppl. 2016;15:102–11.
3. Nicolle L. Urinary tract infection. Crit Care Clin. 2013;29:699–715.
4. Calandra T, et al. International sepsis forum definition of infection in the ICU Consensus Conference. The international sepsis forum consensus conference on definitions of infection in the intensive care unit. Crit Care Med. 2005;33:1538–48.
5. Demertzis J, et al. State of the art: imaging of renal infections. Emerg Radiol. 2007;14:13–22.
6. Grabe M, Bjerklund-Johansen TE, Botto H, et al. Guidelines on urological infections. Eur Assoc Urol. Website. http://www.uroweb.org/gls/pdf/15_U.
7. Pappas PG, et al. Clinical practice guidelines for the management of candidiasis: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis. 2009;48:503–35.
8. Naber KG, et al. Intravenous Doripenem at 500 milligrams versus levofloxacin at 250 milligrams with an option to switch to Oral therapy, for treatment of complicated lower tract infection and pyelonephritis. Antimicrob Agents Chemother. 2009;53(9):3782–92.
9. Wells WG, et al. Treatment of complicated urinary tract infection in adults: combined analysis of two randomized, double-blind, multicentre trials comparing ertapenem and ceftriaxone followed by appropriate oral therapy. J Antimicrob Chemother. 2004;53(Suppl. S2):ii67–74.
10. Demertzis J, et al. State of the art: imaging of renal infections. Emerg Radiol. 2007;14:13–22.
11. Pearle M, et al. Optimal method of urgent decompression of the collecting system for obstruction and infection due to ureteral calculi. J Urol. 1998;160:1260–4.
12. Ramsey S. Evidence-based drainage of infected hydronephrosis secondary to ureteric calculi. J Endourol. 2010;24(2):185–9.