Complicated Urinary Tract Infections

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Continuing Education Activity

Urinary tract infections (UTIs) are among the most common presenting causes of sepsis in hospitals, and urinary tract infections have a wide variety of presentations. Some are simple UTIs that can be managed with outpatient antibiotics and lead to almost universally good outcomes. On the other end of the spectrum, florid urosepsis in a patient with comorbidities can be fatal. There are several risk factors that can complicate urinary tract infections and lead to treatment failure, repeat infections, or significant morbidity and mortality. It is vitally important to determine if the patient's infection may have resulted from one of these risk factors and whether the episode is likely to resolve with first-line antibiotics. Complicated urinary tract infections are those that carry a higher risk of treatment failure, and typically require longer antibiotic courses and often additional workup. Complicated urinary tract infections include those that occur: in males, in pregnant females (including asymptomatic bacteriuria), as a result of obstruction, hydronephrosis, renal tract calculi, or colovesical fistula, in immunocompromised patients or the elderly, due to atypical organisms, after instrumentation or in conjunction with medical equipment such as urinary catheters, in renal transplant patients, in patients with impaired renal function, or after prostatectomies or radiotherapy. Additionally, urinary tract infections that recur despite adequate treatment are complicated. This activity reviews the evaluation and management of complicated urinary tract infections and highlights the role of interprofessional team members in collaborating to provide well-coordinated care and enhance outcomes for affected patients.

Objectives:

- Describe the criteria of a complicated urinary tract infections.
- Outline populations in whom all urinary tract infections are complicated.
- Summarize management considerations for patients for patients with complicated urinary tract infections.
- Explain the importance of improving coordination amongst the interprofessional team to enhance care for patients affected by complicated urinary tract infections.

Earn continuing education credits (CME/CE) on this topic.

Introduction

Urinary tract infections (UTIs) are among the most common causes of sepsis presenting to hospitals. UTIs have a wide variety of presentations. Some are simple UTIs that can be managed with outpatient antibiotics and carry a reassuring clinical course with almost universal good progress, and on the other end of the spectrum, florid urosepsis in a comorbid patient can be fatal. UTIs can also be complicated by several risk factors that can lead to treatment failure, repeat infections, or significant morbidity and mortality with a poor outcome. It is vitally important to determine if the presenting episode is the result of these risk factors and whether the episode is likely to resolve with first-line antibiotics.[1][2][3][4]

It is important to properly define a complicated UTI as infections which carry a higher risl of treatment failure as these typically require longer antibiotic courses and sometimes additional workup.

In a clinical context that is not associated with treatment failure or poor outcomes, a simple UTI, or simple cystitis, is an infection of the urinary tract that occurs due to appropriate susceptible bacteria. Typically this is an infection in a nonpregnant immune competent female patient. Pyuria and/or bacteriuria without any symptoms is not a UTI and may not require treatment. An example would be a patient with a Foley catheter or an incidental positive urine culture in an asymptomatic non pregnant immune competent female.

The normal female urinary tract has a comparatively short urethra, and therefore, carries an inherent predisposition to proximal seeding of bacteria. This anatomy increases the frequency of infections. Simple cystitis, a one-off episode of ascending pyelonephritis, and occasionally even recurrent cystitis in the right context can be considered as simple UTI, provided there is a prompt response to first-line antibiotics without any long-term sequela.

Any urinary tract infection that does not conform to the above description or clinical trajectory is considered a complicated UTI. In these scenarios, one can always find protective factors that failed to prevent infection or risk factors that lead to poor resolution of sepsis, higher morbidity, treatment failures, and reinfection.[5][6][7]

Examples of a complicated UTI include:

- Infections occurring despite the presence of anatomical protective measures (UTI in males are by definition considered complicated UTI)
- Infections occurring due to anatomical abnormalities, for example, an obstruction, hydronephrosis, renal tract calculi, or colovesical fistula
- Infections occurring due to an immune compromised state, for example, steroid use, post chemotherapy, diabetes, elderly population, HIV)
- Atypical organisms causing UTI
- Recurrent infections despite adequate treatment (multi-drug resistant organisms)
- Infections are occurring in pregnancy (including asymptomatic bacteriuria)
- Infections are occurring after instrumentation, nephrostomy tubes, ureteric stents, suprapubic tubes or Foley catheters
- Infections in renal transplant patients
- Infections are occurring in patients with impaired renal function
- Infections following prostatectomies or radiotherapy

Etiology

Most cases of urinary tract infections are due to the colonization of the urogenital tract with rectal and perineal flora. The most common organisms include *Escherichia coli, Enterococcus, Klebsiella, Pseudomonas,* and other *Enterococcus* or *Staphylococcus* species. Residential care patients, diabetics and those with indwelling catheters or any form of immunocompromise can also colonize with *Candida*.

Epidemiology

Cohorts with more risk factors show an increased incidence of urinary tract infections. Risk factors include female anatomy, increasing age, diabetes, obesity, and frequent intercourse (although UTI is not defined as a sexually transmitted infection).

Simple UTI (nonpregnant immune competent female) have been estimated to occur with as high a frequency as 0.7 infections per person per year. Fifty percent of females will have at least one UTI at some stage in life.

Complicated UTI incidence is associated with specific risk factors. For example, there is a 10% daily risk of developing bacteriuria with indwelling bladder catheters, and up to a 25% risk that bacteriuria will progress to a UTI.

Bacteriuria occurs in up to 14% of diabetic females but does not tend to occur with a higher frequency in diabetic males.

The incidence of asymptomatic bacteriuria in pregnant females is similar to that in nonpregnant females (2% to 7%) but tends to progress to symptomatic UTI in as many as 40% of pregnant women.

Asymptomatic bacteriuria also tends to increase with age in females and is present in up to 80% of the elderly female population. It is rare among younger healthy males but can be present in up to 15% of older males.

UTIs are the most common infections in renal transplant patients. Up to 25% of these patients will develop a UTI within the first year after a transplant.

Increased incidence of UTI has been described in patients using Dapagliflozin (SGLT2i). [8]

History and Physical

Despite the frequency of which urinary tract infections present to a hospital, UTI (especially complicated UTI) remain a clinical entity causing considerable confusion, diagnostic uncertainty, and a source of significant inappropriate antibiotic prescriptions.

Symptoms (increased urinary frequency, urgency, hematuria, dysuria, suprapubic or flank pain) are the most important clinical criteria for initially diagnosing a UTI. There must also be an appropriate clinical scenario in which infection of the urogenital tract is the most likely explanation for these symptoms. In this situation, it is appropriate to start empiric treatment with first-line antibiotics. A urine sample should also be sent for microscopy and culture before starting treatment, although that is not always possible. The urine sample would almost always show an abnormal red cell or white cell count and bacteria.

Severe complicated urinary tract infections can present as severe undifferentiated sepsis or even septic shock.

Furthermore, urinary tract infections may present with nonspecific grumbling symptoms, atypical presenting features (delirium in the elderly), signs mimicking an acute abdomen, be a trigger for precipitating diabetic emergencies such as diabetic ketoacidosis (DKA), and even present without any symptoms (asymptomatic bacteriuria in pregnancy).

Evaluation

A good quality urine specimen is vital in making the diagnosis. However, treatment must not be delayed if the clinical scenario is strongly suggestive of a urinary tract infection.[9][10][11]

Most patients can provide a high-quality midstream urine sample with appropriate instructions. If that is not possible, a catheterized urine sample (indwelling catheter or a straight in-out catheter) may be used. Catheter insertion is not without some risk, and this must be weighed against the diagnostic advantage of having a urine specimen for analysis and culture. In general, obtaining a urine specimen for culture is recommended whenever possible and feasible.

Different normal white cell ranges depend on the urine sample, and the results should be interpreted accordingly.

Often, urine samples in prostatitis may not be diagnostic, especially if the patients have already been partially treated. A pre-prostate and post-prostate massage urine sample (also known as the four-glass test or even the shortened 2-glass test) can improve the diagnostic yield.

Blood cultures are also useful in more severe septic presentations. A positive blood culture can sometimes also help corroborate a urine sample result and reduce the suspicion of contamination.

Other microbiology and culture specimens can be directed if there is multifocal sepsis.

Radiological investigations are not helpful in the initial diagnosis of most infections limited to the genitourinary tract, as there should be sufficient clues from the history, physical examination, and laboratory results. Ultrasound and CT scans may sometimes be useful or even critical for diagnosing perinephric abscess, urinary retention, hydronephrosis and obstructive pyelonephritis from stones in septic patients. All patients who fail to respond to appropriate broad-spectrum antibiotics should undergo imaging to exclude complications such as abscesses, urinary retention, calculi, gas, obstructive uropathy and hydronephrosis.

All patients who present with a complicated UTI, even the first presentation of ascending pyelonephritis in nonpregnant immune competent females, should undergo a renal tract ultrasound at a minimum to evaluate for anatomical abnormalities, hydronephrosis or lesions. Since there is no reliable clinical method to rule out urinary obstructions in complicated UTIs (such as a stone), it is the responsibility of the treating physician to do so with ultrasound or CT.

Treatment / Management

As UTI can present with severe, life-threatening sepsis and multiorgan involvement. Resuscitation often precedes definitive treatment. The severely septic patient might need aggressive fluid resuscitation as well as broad-spectrum antibiotics administered in the emergency department. Antibiotic choice should always be according to local guidelines.[12][13][14][15]

Patients presenting with septic shock may not respond to fluid resuscitation alone, and there should be a low threshold to consider vasopressor support in light of a poor initial response to fluids.

On the other hand, nonseptic stable patients may be treated as outpatients.

Broad-spectrum, empiric antibiotics should always be switched to a targeted narrow-spectrum antibiotic, if possible, once culture results are

available. Initial broad-spectrum choices tend to be penicillins or beta-lactams, cephalosporins, fluoroquinolones, and carbapenems (especially if dealing with an extended-spectrum beta-lactamases (ESBL) organism). The specific choice will depend on the individual hospital's microbiological spectrum and antibiogram.

Patients who present with repeat infections may also be initially treated as per their previous urine culture results until new cultures are available. Imaging to look for a source of infection such as an abscess or stone should be done with relapsing infections that involve the same organisms.

In most cases, treatment response should be evident in 24 to 48 hours. A poor response may indicate inappropriate antibiotic selection, polymicrobial infections, atypical infections, hydronephrosis, obstructing stone causing pyonephrosis, complications such as a perinephric abscess or emphysematous UTI, fluid collections such as urinary retention or anatomical lesions leading to poor response (nephrocalcinosis acting like an infective nidus, obstructive urinary tract lesions, or fistulas). A Foley catheter, to guarantee good bladder drainage, is often recommended for these patients if they are septic and have increased post-void residual volumes.

Failure to respond to appropriate antibiotics should suggest a possible obstructive component such as obstructive pyelonephritis. In such cases, a renal ultrasound or non-contrast CT scan should be done for diagnosis and immediate surgical drainage performed if an obstructed, infected kidney is found (either double J stenting or a percutaneous nephrostomy).

Prophylactic antibiotics are seldom recommended due to rapid bacterial resistance patterns developing. When the clinical situation requires prophylaxis, nitrofurantoin is usually the preferred agent.

Patients with permanent Foley catheters or suprapubic tubes should avoid prophylactic antibiotics and should only be treated when symptomatic. More frequent changes of urinary catheters is recommended in chronically cahteterized patients with reurrent infections.

Mandelamine is a twice-daily medication that, in acid urine, is converted to formaldehyde which is a potent urinary antiseptic. This can be useful in patients with persistently elevated post-void residuals instead of prophylactic antibiotics.

Patients with frequent UTI recurrences, especially if already performing intermittent self catheterization, can be managed with daily bladder instillations of Gentamycin solution. The recommended dosage is to instill 30-60 cc's of a solution of 480 mg of Gentamycin in 1 Liter of Normal Saline after initially draining the bladder.[16] Gentamycin has no significant systemic absorption when used in this fashion so it can be used regardless of renal function. Interestingly, heparin bladder instillations have also shown some activity in reducing recurrent UTIs.[17]

Differential Diagnosis

- Acute pyelonephritis
- Bladder cancer
- Chlamydial genitourinary infections
- Cystitis
- Herpes simplex
- Interstitial cystitis
- Pelvic inflammatory disease
- Urethritis
- Vaginitis

Pearls and Other Issues

Diagnostic Pitfalls

Urinary tract infections are primarily a clinical diagnosis, and expert opinion should be sought before initiating treatment of an isolated positive result in an otherwise asymptomatic patient, the only exception being asymptomatic bacteria.

Quite often, clinicians end up treating the positive culture report rather than a genuine urinary tract infection. Most often, positive culture in an asymptomatic patient can be traced to a poor sampling technique.

Another confusing scenario is that of septic, delirious, elderly patient who is unable to provide a history or demonstrate adequate examination signs to help localize a septic source. Quite frequently, these patients are treated as having a presumed UTI in the absence of a clear alternative septic source.

UTI associated radiological changes can sometimes take several months to resolve and must be interpreted with care in cases of recurrent or persistent infections.

UTI must be considered as a differential diagnosis when evaluating a patient with a pelvic inflammatory disease or an acute abdomen.

Male patients with a urinary tract infection must also be screened for sexually transmitted infections.

Interstitial cystitis is frequently misdiagnosed and treated as a UTI, and must be considered as an alternative diagnosis in patients who keep presenting with cystitis symptoms without positive cultures.

"Sterile pyuria," with persistent urinary WBCs but negative standard urine cultures, could indicate tuberculosis which requires special cultures.

Bacterial infections only tend to account for 80% of all urinary tract infections, and antibiotics may sometimes prove ineffective.

Management Pitfalls

Multidrug-resistant infections are becoming a major source of in-hospital mortality and morbidity. Suppressive antibiotic regimens are sometimes used in poorly responding or resistant cases. These presentations should always be guided by a dedicated infectious disease team, as long-term suppressive antibiotics come with a unique set of complications.

Long-term antibiotic prophylaxis must also be used with caution, as it would increase the risk of resistance and change susceptibilities of colonized organisms. On occasion, residual urinary symptoms may take several months to resolve or might never resolve (especially in the case of indwelling catheters, post-prostatectomy cases, post bladder surgery, or radiotherapy), and do not always indicate a genuine urinary tract infection.

Long-term prophylaxis with nitrofurantoin is associated with hypersensitivity pneumonitis. Patients should be counseled accordingly.

It helps to identify predisposing factors for the infection and correct them if possible. For example, the diabetic patient would benefit from improving glycemic control. Renal tract anatomic abnormalities may be assessed by urology to see if an intervention is appropriate (renal calculi, BPH, ureteric strictures). Immunocompromising factors may be addressed if possible (steroids, HIV). Finally, nephrotoxic medications may be rationalized in patients with suboptimal renal functions.

Enhancing Healthcare Team Outcomes

The management of complex UTI is an interprofessional that includes a urologist, nephrologist, infectious disease expert, internist, pharmacist and the primary care provider.Complicated UTIs need to treated more carefully to serve patients with these infections and to avoid overuse and misuse of antibiotics that will ultimately result in more resistant infections in the future. Using the right antibiotic for the right duration is key. Practitioners should not hesitate to take advantage of infectious disease specialty services in these situations to help optimize antibiotic use.

Failure of a standard UTI or pyelonephritis to respond to initial treatment should suggest some other medical problem such as diabetes, sepsis, an abscess, urinary retention or an obstructing stone with a possible pyonephrosis. Bladder drainage with a Foley and appropriate imaging tests can identify these problems.

These patients need close monitoring because of potential complications. The outlook for patients with severe UTI is guarded and even those

who do recover tend to have a prolonged recovery period.[18][19][20] (Level V)

Continuing Education / Review Questions

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