UTI in Kidney Tx

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قطب علمی آموزشی نفرولوژی مرکز تحقیقات نفرولوژی

Case

A 45 YO Woman Kidney Tx 2 mo ago reffered with U/A with

WBC Many, RBC 6-7, U/C E Coli >100000, Cr 0/9

No Symptoms & Signs in Urinary System.

What is next decision?

UTI

Most common infection after kidney Tx [1-4] & associated with Bacteremia, Acute T cell-mediated rejection, Impaired allograft function, & allograft loss, increased risk of hospitalization & death [2,4-7]. Morbidity & mortality from UTI can be caused by recurrent &/or severe sepsis.

Definition

Asymptomatic bacteriuria in the transplant >100000 bacteria CFU/mL of U/C with no local or systemic symptoms.

Simple cystitis >100000 CFU/mL on U/C with local urinary symptoms, such as **dysuria**, **frequency**, or **urgency**, but **no systemic symptoms**, (**fever or allograft pain**).

Complicated >100000 CFU/mL on U/C with **fever & either one of the following**: **allograft pain, chills, malaise or bacteremia with the same organism in urine**, or **biopsy** with findings consistent with **pyelonephritis**.

Recurrent UTI is **three or more episodes of UTI in one year** [3].

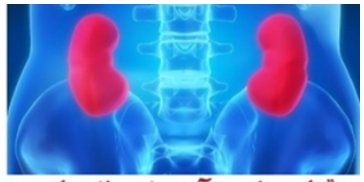
EPIDEMIOLOGY

UTI occurs in 25% of kidney Tx recipients within one year of transplant [3,4,7] & accounts for 45% of infectious complications [1].

Asymptomatic bacteriuria, uncomplicated UTI, & complicated UTI comprise 44, 32, & 24% of cases, respectively [3,4,7].

Recurrent UTI occurs in 7% of patients & is associated with an increased risk of allograft loss & death [8].

Risk factors [3,4,6]:



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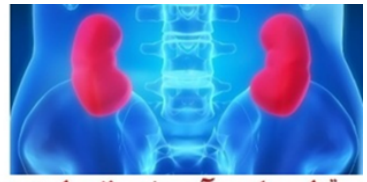
Female sex/ Advanced age/ Recurrent UTI prior to transplant/ VUR/Urethral catheterization/ Ureteral stent placement/ Deceased-donor kidney transplant/ History of ADPKD/ DGF/ Immunosuppression/ Incomplete treatment/ Multiple Hospitalization

PATHOGENESIS of U



Uropathogenic bacterial ascending.

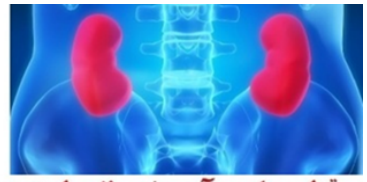
Pathologic invasion (aided by bacterial virulence structures, P fimbriae & adhesion) [9].

Absence of a sphincter predispose KTx to pyelonephritis.

Stents, kidney cysts in ADPKD [3,4,6,10].

And occasionally seeding of the kidney from bloodstream or surgical site infection.

MICROBIOLOGY



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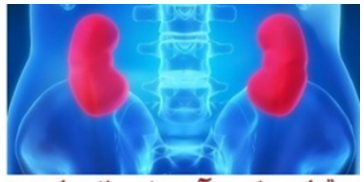
Gram-negative organisms (56 to 90%)

Escherichia coli dominant organism [2,3,7,11,12].

Others Pseudomonas aeruginosa, Enterobacter cloacae,

Klebsiella pneumoniae, & Klebsiella oxytoca.

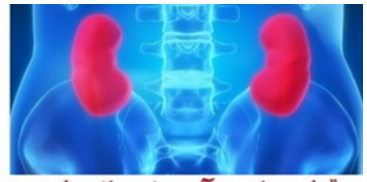


The widespread use of antibiotic in KTx has led to increased rate of resistance to ciprofloxacin & trimethoprim-sulfamethoxazole [2,12].

Enterococcus species has emerged as an important pathogen & now accounts for 24 to 33% of UTIs [1-4,7].

Gram-positive bacteria such as Staphylococcus saprophyticus, Streptococcus species, & Corynebacterium urealyticum can rarely cause UTI [13].

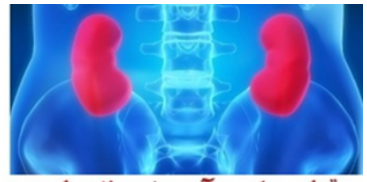
SCREENING



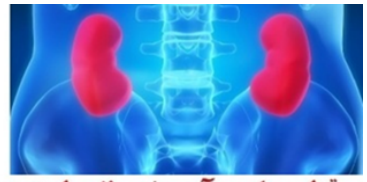
It is important to detect potential UTIs as early as possible among Tx recipients, particularly those who are within three months of Tx. Untreated UTI that occurs within three months postTx is associated with an increased risk of allograft rejection [4].

A U/A & U/C at 2, 4, 8, & 12 weeks postTx Should be obtained [19].

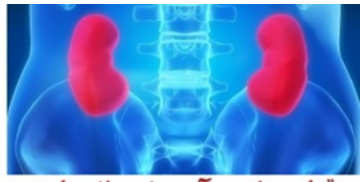
PREVENTION



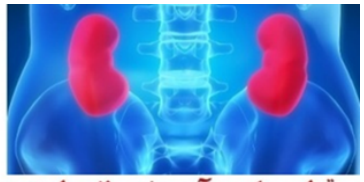
UTIs are associated with significant morbidity Tx, especially if they occur early after Tx. To prevent UTIs, administer prophylactic antibiotics. A meta-analysis of six randomized trials in 545 kidney Tx recipients demonstrated that TMP-SMX prophylaxis was associated with a reduced risk of sepsis & bloodstream infection (RR 0.13, 95% CI 0.02-0.7) & bacteruria (RR 0.41, 95% CI 0.31-0.56) [21]. Prophylaxis did not reduce graft loss or mortality.



Administer one double-strength tablet of trimethoprim-sulfamethoxazole (160 mg of the trimethoprim component) daily. Concerns have been raised about resistance [1,12].

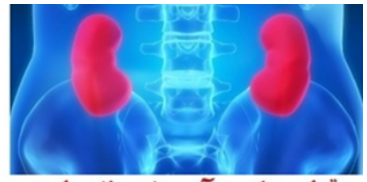


Most Tx centers continue trimethoprim-sulfamethoxazole for at least six months to one year postTx [23]. Some experts continue Co-trimoxazole prophylaxis indefinitely [24]. Co-trimoxazole also prevents opportunistic infections, such as Pneumocystis pneumonia.



In truly allergics to Co-trimoxazole, provide cephalexin 500 mg orally bd for 3 months for the few who are unable to take Co-trimoxazole [21].

CLINICAL MANIFESTATIO



Simple cystitis – Dysuria, frequency, urgency, hematuria, & suprapubic pain.

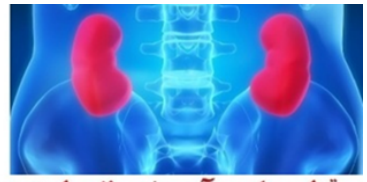
Complicated UTI – Fever, allograft pain, chills, &/or malaise & may also nausea & fatigue.

It may be difficult to distinguish complicated UTI from acute rejection. Fever tends to be more commonly associated with UTI and is rarely seen during allograft rejection unless the patient has been nonadherent with their immunosuppressive therapy. Tenderness directly over the allograft is also more commonly observed with complicated UTI.

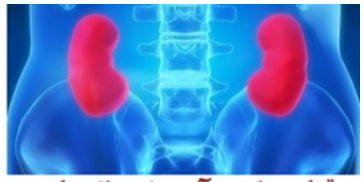
DIAGNOSIS

Asymptomatic bacteriuria is diagnosed by screening U/C & is defined by the presence of >100000 CFU/mL of bacteria.

UTI - signs or symptoms of UTI should undergo testing with a urine dipstick, urine microscopy, & U/C. In addition, B/C should be obtained in a complicated UTI



Urine dipstick that is positive for leukocyte esterase, nitrites, blood, & protein & urine microscopy that shows pyuria (ie, at least 10 WBC/HPF urine). The diagnosis is established by a positive U/C with >100000 CFU/mL in the presence of associated clinical findings. Among patients with UTI, 9% have positive B/C[3].



Patients with negative U/C should be tested for C. urealyticum (A slow-growing organism with potent urease activity that requires selective media for isolation) [25]. They have alkaline urine (pH >7), pyuria or microscopic hematuria, presence of struvite crystals, obstructive uropathy, & encrusting cystitis or pyelitis [13].

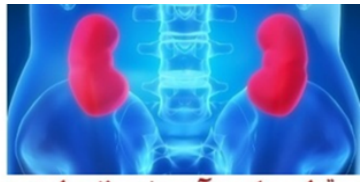
They are resistant to the oral antibiotics & requires vancomycin [13,25].

DIAGNOSIS

Selected patients require imaging [26]. Perform an ultrasound of the kidney allograft, native kidney, & bladder for patients who

- Are within one month of transplant or
- Have a history of nephrolithiasis or
- Have had two or more prior episodes within the same year

In ADPKD may require CT-PET scan [10,27]. The interpretation of imaging for ADPKD is challenging. Such patients typically have innumerable cysts.



Avoid contrast to prevent nephrotoxicity but ontrast imaging studies can identify **urinary tract strictures**, **stones**, & **complex cysts**.

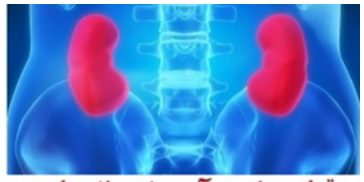
-If the CT is also unrevealing, **VCUG** can be performed to identify **VUR**.

-Urodynamic studies can also be performed to identify bladder dysfunction or outflow tract obstruction.

-Flexible cystoscopy may be required to detect abnormalities in the urethra or bladder [26].

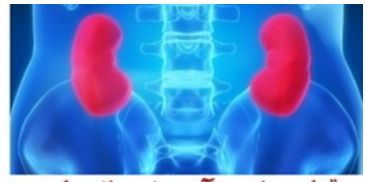
DIAGNOSIS

The major DD is acute rejection. Fever & allograft tenderness are suggestive of UTI, whereas increased Cr in the presence of new or worsening proteinuria & hypertension suggest acute rejection. Among patients who have characteristics of acute rejection, perform a kidney biopsy.



In ADPKD, infected or hemorrhagic cysts may mimic pyelonephritis of the native kidney. Such patients generally have flank pain & CV angle tenderness rather than the allograft.

TREATMENT



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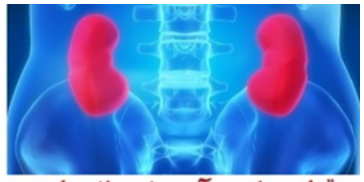
Asymptomatic bacteriuria

Treat asymptomatic bacteriuria within 1 to 3 months of Tx to prevent symptomatic UTIs, which have been associated with an increased risk of acute allograft rejection [4, 16].

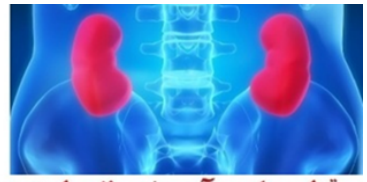


Selec an oral antibiotic & administer for five days. Ciprofloxacin 250 bd, amoxicillin 500 tid, or nitrofurantoin 100 mg qid (eGFR] >30 mL/min/1.73 m2).

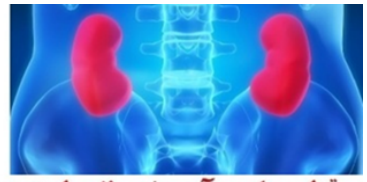
Dosing must be adjusted in reduced GFR. Historically, nitrofurantoin was contraindicated in GFR <60 mL/min.

However, studies in nontransplant patients have shown that nitrofurantoin can be safely and effectively used in patients with a creatinine clearance of ≥30 mL/min [29-32].

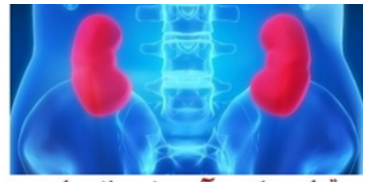
Simple cystitis



Empirically treat all Tx recipients. Obtain U/A & U/C prior to initiating antibiotics. Definitive treatment is administered once the species & antibiotic susceptibilities of the microorganism are identified.



Commonly prescribed empiric treatment includes ciprofloxacin 250 orally bd or levofloxacin 500 orally once daily, with dose adjustment based on eGFR. Cephalosporins (eg, cefpodoxime, cefdinir) are other options and may have a more favorable adverse effect profile when compared with fluoroquinolones. If Enterococcus species are suspected on the basis of past causative organisms, amoxicillin 500 tid or nitrofurantoin 100 orally twice daily (provided eGFR >30 mL/min/1.73 m2) should be added.



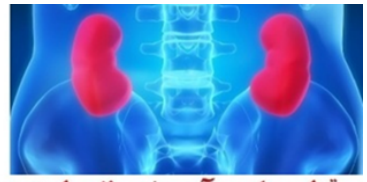
Treat simple cystitis

Earlier than six months postTx with 10 to 14 days

&

In more than six months postTx with 5 to 7 days of oral antibiotics [33].

Complicated UTI



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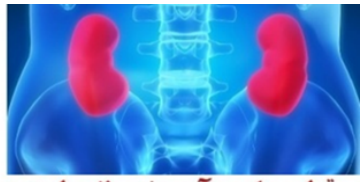
Treat all Tx recipients complicated UTI with IV antibiotics that cover both G- & G+ bacteria. Obtain U/c & B/C prior to initiating antibiotics. Empiric treatment should be followed by definitive treatment once the identity & antibiotic susceptibilities of the causative organism are known.

Empiric antibiotics should have adequate coverage against P. aeruginosa, enteric G- organisms, & Enterococcus species. Commonly prescribed treatment regimens include monotherapy with piperacillin-tazobactam 4.5 g IV every six hours or meropenem 1 g IV every 8 h, or combination therapy with vancomycin plus cefepime 1 g IV every 8 h. Adjusted according to GFR.



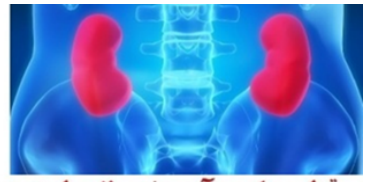
Treat complicated UTI 14 to 21 days [33]. Oral agents may be substituted for IV therapy once the patient is free of symptoms & antibiotic susceptibilities are known.

Recurrent UTI (Three or more episodes of UTI in one year)

Duration of treatment is 14 to 21 days, but, in some situations, a longer course may be necessary.

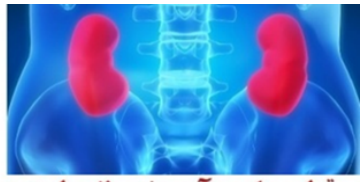
Recurrent UTIs associated with an indwelling source (such as infected cysts in native kidneys) can require up to four to six weeks of therapy. In other situations, therapy can be discontinued after a shorter period, & the patient can be transitioned to prophylactic antibiotics.

Prevention



Patients should be assessed for anatomic or functional abnormalities.

Topical estrogen for postmenopausal women may prevent recurrence [34].



Some Tx programs use methenamine hippurate (1000 mg bd) with or without ascorbic acid (1000 mg bd) for prevention of recurrent UTI in Tx recipients. A study of 38 kidney Tx recipients found that use of methenamine alone was associated with a

- 45% reduction in the frequency of UTI,
  42% reduction in the length of antibiotic use for UTI treatment, and
  59% reduction in UTI-related hospitalizations [35].

Similar findings were reported in a second study of 30 kidney transplant recipients treated with the combination of methenamine and ascorbic acid; the benefit was greatest in female patients & patients with diabetes, especially those with a glycated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