

Sterile Pyuria

Masashi Narita

Pyuria is defined as the presence of leukocytes in the urine and suggests that inflammation exists in the urinary tract. Polymorphonuclear leukocytes are the predominant cell type in urinary tract infections. Monocytes, lymphocytes and eosinophils suggest interstitial nephritis. Inflammation of the adjacent structure of prostate and urethra can also cause sterile pyuria. Noninfectious systemic diseases, structural/abnormalities of the urinary tract, and adverse effects of drugs can also produce sterile pyuria (Table 1). One common cause of sterile pyuria is that of a chronic indwelling foley catheter which may cause bladder wall irritation and subsequent low grade pyuria.

Infectious diseases with sterile pyuria include microorganisms not detected by standard bacteriological media including *Mycobacterium tuberculosis*, fungi, viruses (herpesviruses, adenoviruses, varicella-zoster virus), leptospirosis, brucellosis, and parasites (Schistosomiasis). Fastidious bacteria such as *Hemophilus influenzae* will also not be detected by routine cultures. Systemic fungal infection such as *Cryptococcus neoformans*, *Blastomyces dermatitidis* or *Coccidioides immitis* involving the prostate or epididymitis can cause sterile pyuria in the urine. Urinary tract infection treated with antibiotics may show pyuria for up to a week following discontinuation of the antibiotics. A perinephric abscess may lead to subsequent sterile pyuria.

Systemic causes of sterile pyuria include diabetic nephropathy and sickle cell disease with papillary necrosis, sarcoidosis with granulomatous nephritis, Kawasaki disease with urethral involvement, systemic lupus erythematosus with tubulointerstitial nephritis, reactive arthritis, and cyanotic congenital heart disease with glomerular and tubular dysfunction.

Structural and physiological causes of sterile pyuria include polycystic kidney disease, vesicourethral reflux, hydronephrosis, stones, retained foreign body, post transurethral resection prostate, genitourinary trauma, extreme dehydration, and hyperchloremic metabolic acidosis. Intrinsic urinary tract pathology leading to sterile pyuria include papillary necrosis secondary to obstructive uropathy, tubulointerstitial nephritis, glomerulonephritis, interstitial cystitis, renal transplant rejection, and urinary tract tumors.

Many drugs have been associated with interstitial nephritis (Table 2). Medication groups most commonly implicated in drug-induced interstitial nephritis include NSAIDS and antibiotics. Antibiotics cause acute interstitial/tubulointerstitial nephritis through two different mechanisms: a drug induced hypersensitivity process and direct action due to drug accumulation. Hypersensitivity can occur from allergic interstitial nephritis secondary to an immunocomplex allergic reaction (beta-lactams, rifampin, vancomycin), and granulomatous interstitial nephritis secondary to a cell mediated allergic reaction.

(ciprofloxacin, penicillin). The triad of rash, fever, and eosinophilia are most commonly seen in beta-lactam associated acute interstitial nephritis. Anti-staphylococcal penicillin's such as nafcillin or oxacillin are the most common culprit. The urinalysis with acute interstitial nephritis typically shows leukocyte casts in addition to leukocytes. Eosinophiluria is suggestive of acute interstitial nephritis.

Table1. Differential Diagnosis of Sterile Pyuria

Contamination during collection

Vaginal secretions
Foreskin secretions

Infectious Diseases

Urethritis
Tuberculosis and other mycobacterial infections
Viral cystitis (herpes, adenoviruses, varicella-zoster)
Leptospirosis
Hemophilus influenzae
Brucellosis
Urinary schistosomiasis
Systemic fungal infections
Partially treated urinary tract infections

Infections of structures adjacent to the urinary tract

Appendicitis
Diverticulitis
Prostatitis
Perinephric Abscess

Noninfectious Diseases

Systemic Causes
Diabetic nephropathy
Sickle cell disease nephropathy
Sarcoidosis
Kawasaki disease
Reactive Arthritis
Systemic lupus erythematosus
Cyanotic congenital heart disease

Structural and Physiologic Causes

Polyzystic kidney disease
Vesicourethral reflex
Nephrocalcinosis/urolithiasis
Retained foreign body
Transurethral resection prostate
Hydronephrosis
Genitourinary trauma
Extreme dehydration
Hyperchloremic metabolic acidosis

Intrinsic Urinary Tract Pathology

Papillary necrosis
Obstructive uropathy
Tubulointerstitial diseases
 Interstitial nephritis
 Renal transplant rejection
Glomerulonephritis
Interstitial cystitis
Renal/ureteral/bladder tumors

(Modified from Kunin CM, Urinary Tract Infections, Williams and Wilkins, 5th edition, 1997)

Table2. Drug-related Cause of Sterile Pyuria

Drug-induced tubulointerstitial nephritis
NSAIDS
Antibiotics
 Beta-lactams, sulfonamides, rifampicin, tetracyclines, isoniazid, ciprofloxacin, polymyxin, ethambutol, erythromycin, vancomycin, acyclovir, indinavir
Diuretics
 thiazides, furosemide, clorthialidone, triamterene
Anticonvulsants
 carbamazepine, phenytoin, phenobarbital, diazepam
Hypouricaemics
 alloprinol, sulfinpyrazone
Others
 lithium, omeprazole, cimetidine, aspirin, clofibrate, captopril, aldomet, azatioprine
Tubular dysfunction
 toluene
Papillary necrosis
 NSAIDS
Cystitis
 cyclophosphamide, NSAIDS, danazol, allopurinol, tranilast (anti-allergic drug)

NSAIDS: Non-Steroidal Anti-Inflammatory Drugs

Reading List

- 1.** Davison AM, Jones CH. Acute interstitial nephritis in the elderly: a report from the UK MRC Glomerulonephritis Register and a review of the literature. *Nephrol Dial Transplant*. 1998;13 Suppl 7:12-6.
- 2.** Demirkaya E, Atay AA, Musabak U, Sengul A, Gok F. Ceftriaxone-related hemolysis and acute renal failure. *Pediatr Nephrol*. 2006; May;21(5):733-6. Epub 2006 Feb 21.
- 3.** Dieter, R. S. Sterile pyuria: a differential diagnosis. *Compr Ther* 2000; 26: 150-2.
- 4.** Kunin, C. Urinary Tract Infection. Williams & Wilkins. 5th edition 1997.
- 5.** Lomaestro BM. Fluoroquinolone-induced renal failure. *Drug Saf*. 2000; Jun;22(6):479-85.
- 6.** Michel, D. M., and C. J. Kelly. Acute interstitial nephritis. *J Am Soc Nephrol* 1998; 9: 506-15.
- 7.** Ruffing, K. A., P. Hoppe, D. Blend, A. Cugino, D. Jarjoura, and F. C. Whittier. Eosinophils in urine revisited. *Clin Nephrol* 1994; 41: 163-6.