Weird Science:

What’s hiding in sterile pyuria?

Dr. A. Christian Whelen
Vice President / Technical Director
Microbiology and Molecular Diagnostics
Diagnostic Laboratory Services, Inc.
Case presentation

- 5/5/2018: 33 year old female w/ PMH of familial hypercholesterolemia and Type 2 DM
- Presents to urology for evaluation of persistent pyuria and right flank pain (8 out of 10 - sharp/persistent); no fever or chills
- History of intermittent right sided pain since last year and recurrent culture-negative UTI
- CTKUB showed moderate right hydronephrosis, hydroureter, thickening of renal pelvis and proximal ureter (likely inflammation but tumor cannot be ruled out)
- Patient is on oral Cipro 250 mg
- Nocturia is about 2-3 time(s) per night; day time frequency is about once every 2 hours
Causes of sterile pyuria?

**Causes related to infection**
- Current use of antibiotics
- Recently treated urinary tract infection (within past 2 wk)
- Gynecologic infection
- Urethritis due to chlamydia, *Neisseria gonorrhoeae*, mycoplasma, or ureaplasma
- Prostatitis
- Balanitis
- Appendicitis (if the appendix lies close to a ureter or the bladder)
- Viral infection of the lower genitourinary tract
- Genitourinary tuberculosis
- Fungal infection
- Parasitic disease such as trichomoniasis or schistosomiasis

**Causes not related to infection**
- Presence or recent use of a urinary catheter
- Recent cystoscopy or urologic endoscopy
- Urinary tract stones
- Foreign body such as surgical mesh in the urethra or a retained stent
- Urinary tract neoplasm
- Pelvic irradiation
- Urinary fistula
- Polycystic kidney
- Rejection of a renal transplant
- Renal-vein thrombosis
- Interstitial nephritis or analgesic nephropathy
- Papillary necrosis
- Interstitial cystitis
- Inflammatory disease such as systemic lupus erythematosus or Kawasaki's disease
Surgery – same day (5/5/2018)

- Cystoscopy with biopsy of the bladder, right ureteroscopy and biopsy with stent placement, and right retrograde pyelogram
- Specimens removed: bladder tissues, distal and proximal ureteral tissues
- Description of pertinent findings: Inflammation in the bladder, distal ureter and proximal ureter.
- Post-operative diagnosis: Right hydronephrosis & hydroureter
- Estimated blood loss: 50 ml
Emergency Department – 5/7/2018

- Feeling unwell, patient went to ED with fever at 101.7, bilateral abdominal pain that was mild to moderate, and worsens with her dry cough.
- She has been experiencing hematuria since Foley placement.
Two more days later (5/9/2018)

- Admitted to hospital for management of sepsis due to acute cystitis with complication of indwelling foley catheter
- Urinalysis: Protein 2000 (H), WBC 51-100 (H), LE (+), RBC >100 (H)
- Treated with IV Ceftriaxone
- Follow-up with surgical path from 5/5
- Hydrate aggressively
- Order urine culture & blood culture
- Discontinue foley catheter
Labs

- **UA**: Protein 2000 (H), WBC 51-100 (H), LE (+), RBC >100 (H)

- **0.19 Procalcitonin**
  - \( \leq 0.05 \text{ ng/mL} \) is normal
  - \( > 0.1 \text{ ng/mL} \) suggests a clinically relevant bacterial infection
  - \( > 0.5 \text{ ng/mL} \) suggests a higher risk for developing severe sepsis or septic shock

- Pathology of the removed specimen showed granulation tissues consistent with infection/inflammation
Discharged after 6 days (5/15/2018)

- Gram stain, AFB stain, fungal stains all negative
- Tissue bacterial cultures negative, AFB & Fungal in progress
- Urine culture and blood cultures negative

- Returned to the ER 5/16/2018 with fever of 103.3 F, dizziness, and headache
- ID consult
Thoughts? More tests?

**Causes related to infection**
- Current use of antibiotics
- Recently treated urinary tract infection (within past 2 wk)
- Gynecologic infection
- Urethritis due to chlamydia, *Neisseria gonorrhoeae*, mycoplasma, or ureaplasma
- Prostatitis
- Balanitis
- Appendicitis (if the appendix lies close to a ureter or the bladder)
- Viral infection of the lower genitourinary tract
- Genitourinary tuberculosis
- Fungal infection
- Parasitic disease such as trichomoniasis or schistosomiasis

**Causes not related to infection**
- Presence or recent use of a urinary catheter
- Recent cystoscopy or urologic endoscopy
- Urinary tract stones
- Foreign body such as surgical mesh in the urethra or a retained stent
- Urinary tract neoplasm
- Pelvic irradiation
- Urinary fistula
- Polycystic kidney
- Rejection of a renal transplant
- Renal-vein thrombosis
- Interstitial nephritis or analgesic nephropathy
- Papillary necrosis
- Interstitial cystitis
- Inflammatory disease such as systemic lupus erythematosus or Kawasaki's disease

NEJM 2015. 372;11
Test results thus far

- GC/CT NAAT negative
- Vaginitis Panel (Candida, BV, Trichomonas) negative
- HPV NAAT negative for high risk types
- HSV/VZV PCR negative
- Mycoplasma/Ureaplasma PCR negative
- Tissue specimens AFB & Fungal smear negative (culture in progress)
ID Case history

• Patient is a 33-year-old Filipino woman referred to infectious disease clinic for culture-negative UTI

• Past medical history significant for diabetes, hypertension, migraine headache, polycystic ovarian syndrome and treated latent tuberculosis

• Treated with Ciprofloxacin and Cefdinir (3rd Gen Oral) after discharge with no improvement

• Latent TB was treated in high school with daily INH for extended time

• Any other lab, imaging, patient management orders?
Urine AFB Smear & Culture

- **Urine AFB smear 2+**
- GenXpert (off-label): MTB detected, RIF Not Detected
- Airborne isolation
- Start 4 drug therapy: Isoniazid, rifampin, pyrizinamide, ethambutol
- Chest X-ray
- Check sputum for AFB x1, MTB PCR, if negative can d/c airborne
Extra pulmonary TB

- Lymphadenitis (most common)
- Pleural tuberculosis (second most common)
- Skeletal Tuberculosis (Pott’s disease)
- CNS tuberculosis (TB meningitis, tuberculomas)
- Abdominal tuberculosis
  - GI, peritonitis, genito urinary
- Miliary TB (disseminated)
- Tuberculosis pericarditis
BUT WAIT – there’s more:
Case 2 – Three months later: 8/16/2018

• Same ID physician is consulted on 77-year-old Asian man with PMH significant for lumbar spine fracture, history of stroke, history of bladder cancer, chronic kidney disease and more recently, acute renal failure

• No fever or chills, intermittent dysuria, no hematuria, no weight loss

• Referred to ID because patient's blood cultures for mycobacteria were reportedly positive

• ID called lab to clarify results - the blood cultures are negative so far

• The positive AFB culture was from his urine

• Thoughts?

• Tests, isolation, treatment, more questions about the history?
Case 2

- Intravesicular BCG (Bacillus Calmette-Guerin) treatment 3 months ago with urology service for bladder cancer
- Per his recollection, his overall response to treatment for his bladder cancer with excellent
- Symptomatic urinary tract infections post-BCG have been documented up to one year after treatment
- Treatment of symptomatic cystitis related to BCG is acceptable with 2 weeks of levofloxacin versus INH
- Systemic disease such as disseminated BCG would be treated with 6 months of combined treatment with isoniazid, rifampin, and ethambutol
Case 2 management

- The patient was asymptomatic with regards to urinary symptoms, so no treatment
- What would the GeneXpert result be?
- Urine cultures grew MTB complex, BCG is one of these
- Any other test of value in this case?
- Patient's MTB IGRA (QuantifERON Gold+) was negative
  - Remember BCG vaccination doesn’t interfere with IGRA
- Confirmed that positive urine culture was likely related to BCG treatment, and not extrapulmonary Mycobacterium tuberculosis infection