Drug Induced Nephropathy

Stephanie Mahooty, DNP
Acute Kidney Injury (AKI)

Defined as:
- Abrupt (within 48 hours) reduction in kidney function due to a rise in the serum creatinine by ≥0.3 mg/dL or
- Documented oliguria of <0.5 mL/kg/h for more than 6 hours.
- Classified as prerenal, postrenal and intrinsic renal injury
- Intrinsic renal injury can be glomerular, microvascular, interstitial or tubular.
Epidemiology

- Drugs cause approximately 20% community and hospital acquired episodes of AKI.
- The incidence of drug-induced nephrotoxicity is as high as 66% among older adults.
- One of the leading cause of AKI
- It can be costly, require multiple interventions, and hospitalization.
Risk Factors

- Age, sex
- Pre-existing CKD
- Hypoalbuminemia-hepatic failure with ascites, nephrotic, heart failure
- Sepsis
- Diabetes mellitus
- Dehydration and intravascular volume depletion
- Exposure to multiple nephrotoxins
Pathologic Mechanisms

- Intraglomerular hemodynamics - ACEi/ARBs/NSAIDs/Calcineurin inhibitors (cyclosporin, tacrolimus)

- Tubular cell toxicity - aminoglycosides, amphotericin B, cisplatin, beta lactams, quinolones, rifampin, sulfonamides, vancomycin, acyclovir, and contrast agents.

- Inflammation - Numerous drugs have been known to cause
Pathologic Mechanisms

- Crystal nephropathy-ampicillin, ciprofloxacin, sulfonamides, acyclovir, ganciclovir, methotrexate, and triamterene. Can result from chemo due to uric acid deposition

- Rhabdomyolysis-statins

- Thrombotic microangiopathy-antiplatelets, ticlopidine, cyclosporine, mitomycin-C, quinine
Drugs With Nephrotoxicity Potential

• Non-steroidal anti-inflammatory drugs—most common causes of drug-induced renal injury
• Angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers
• Antimicrobial agents—aminoglycosides, sulfmethoxazole-trimethoprim, sulfa based antibiotics, Vancomycin, Ciprofloxacin.
• Antivirals—acyclovir, foscarnet, antiretroviral drugs
• Anti fungal—amphotericin B
Drugs With Nephrotoxicity Potential

- Chemotherapeutic agents-cisplatin, ifosfamide, MTX, bisphosphonates
- Radiocontrast agents-
- Immunosuppressive agents-tacrolimus and cyclosporine
- Miscellaneous-Lithium, acetaminophen, proton-pump inhibitors, statins, osmotic agents-e.g, mannitol,
Vancomycin (VCM)

- Vancomycin is a glycopeptide antibiotic
- Used first line to treat MRSA
- VCM nephrotoxicity is generally due to acute tubular necrosis or acute interstitial nephritis.
- Risk factors for the development of nephrotoxicity with VCM involves trough levels >15 mg/L, long duration of therapy, and concomitant administration of other nephrotoxins (e.g., aminoglycosides)
Case Study

- 69 year old Native American Male had prolong hospitalization secondary to vancomycin toxicity and subsequent acute kidney injury. He put his foot in hot water to take a bath, due to his neuropathy he did not realize how hot it was and developed a blisters along lateral part of his foot and over toes 3 and 4. He then developed an ulcer. Was treated with silver silvadene, apparently got worse.

- Hospitalized: 4/15-5/3

- PMH: Acute on chronic kidney disease stage 3, insulin-dependent DM, severe PVD, degloving injury secondary to thermal burn in 4/2016 of his left foot, peripheral neuropathy, chronic pain, major recurrent depression, nonhealing left foot ulcer-distal fifth metatarsal, osteomyelitis left foot, hyperlipidemia, hypertension, hypothyroidism, chronic pancreatitis, BPH
Case Study

- Medications prior to hospitalization: Levothyroxine, pantoprazole, fluoxetine, glimepiride, pregabalin, calcium, cyanocobalamin, cholecalciferol, ranitidine, Tamsulosin, fentanyl patch, morphine sulfate SR, detemir insulin, doxepin HCL, metformin HCL, silver sulfadiazine cream

- Inhouse Medications:
  1. Zosyn: 4/15-17
  2. Rocephin: 4/18-25
Case Study

- LABS:
  4/05 creatinine 0.87 eGFR >60
  4/14 creatinine 1.12
  **4/23 creatinine 4.6, 4/26 creatinine 4.7 eGFR 12** sodium 140, potassium 4.0 bicarbonate 21, WBC 15.8 from 12.6, hgb 11 hgb A1c 9.7
  4/30 creatinine 3.8 eGFR 15

  Wound cultures grew out group b strep and methicillin-susceptible staphylococcus aureus

  5/3 creatinine 3.6 eGFR 16

Year later: creatinine 1.13 mg/dL, eGFR > 60 mL/min, hgb A1c 11.1%, UPCR 1.0

- IMAGING: 4/27 MRI done, significant osteomyelitis of third and second toes.
- 2/4/ renal u/s showed cyst in right kidney, otherwise unremarkable.