Drug-Induced Kidney Disease (DIKD)

Thitinat D.

Take Home Messages

- The initial diagnosis of DIKD typically involves detection of elevated Scr and BUN.
- DIKD is best prevented by avoiding the use pf potentially nephrotoxic agents for patients at increased risk for toxicity. When these drugs cannot be avoided hydration may be used to reduce potential nephrotoxicity.
- Acute Tubular injury/necrosis (ATN) is the most common presentation of DIKD in hospitalized patients (e.g. AMG, radiocontrast media, cisplatin, AmphoB and osmotically active agents).
- ACEIs and NSAIDs are associated with hemodynamically mediated kidney injury by decreasing in glomerular capillary hydrostatic pressure.
- Acute allergic interstitial nephritis (AIN) is observed up to 27% of kidney biopsies for patients with unexplained AKI. Typically AIN present ~ 14 d after initiation of therapy and may include fever, maculopapular rash, eosinophilia, arthralgia, pyuria, hematuria, proteinuria and oliguria.

DIKD

- Manifestations may include acid-base abnormalities, electrolyte imbalances, urine sediment abnormalities, proteinuria, pyuria, and/or hematuria.
- The most common manifestation of nephrotoxicity is a decline in GFR and a corresponding rise in Scr concentrations.
- Nephrotoxicity is often reversible if one discontinues the use of the offending agent, but in some cases it may evolve into AKI and may even progress to stage 5 CKD.
- In the outpatient setting, nephrotoxicity is recognized by malaise, anorexia, vomiting, shortness of breath or edema and hypertension.

DIKD

- Laboratory tests:
  - An abrupt (within 48 hours) reduction in kidney function defined as:
    - An absolute increase in Scr of ≥ 0.3 mg/dL
    - A percentage increase in Scr of ≥ 50% (1.5-fold from baseline) within 7 days or
    - A reduction in urine output (documented oliguria of < 0.5 mL/kg/hr for more than 6 hours)
- Other diagnostic tests:
  - Urinary excretion of N-acetyl-β-glucosaminidase, γ-glutamyl transpeptidase, glutathione S-transferase, and IL-18
  - Neutrophil gelatinase-associated lipocalin (NGAL) protein may be detected in the urine within 3 hours of ischemic injury
  - Kidney injury molecule-1 (KIM-1) in the urine within 12 hours
  - IGFBP7, TIMP-2

Tubular epithelial cell damage

Acute tubular injury/necrosis
- Aminoglycoside antibiotics
- Radiographic contrast media
- Cisplatin, carboplatin
- Ifosfamide
- Amphotericin B
- Cyclosporine, tacrolimus
- Adefovir, cidofovir, tenofovir
- Pentamidine
- Foscarnet
- Zoledronate

Osmotic nephropathy
- Mannitol
- Dextran
- IV immunoglobulin (sucrose)
- Hydroxyethyl starch

Hemodynamically mediated kidney injury

- Angiotensin-converting enzyme inhibitors
- Angiotensin II receptor blockers
- SGLT-2 inhibitors
- NSAIDs
- Cyclosporine, tacrolimus
- OKT3

Obstructive nephropathy

Crystal nephropathy
- Acyclovir
- Sulfonamides
- Indinavir, atazanavir
- Foscarnet
- Methotrexate
- Ascorbic acid, ethylene glycol, orlistat

Nephrolithiasis
- Sulfonamides
- Triamterene
- Indinavir, atazanavir

Nephrocalcinosis
- Oral sodium phosphate solution

Glomerular disease

Minimal change disease
- NSAIDs, COX-2 inhibitors
- Lithium
- Pamidronate
- Interferon-α and β

Membranous disease
- NSAIDs
- Penicillamine
- Captopril

Focal segmental glomerulosclerosis
- Pamidronate
- Interferon-α and β
- Lithium
- Sirolimus
- Anabolic steroids
- Tyrosine kinase inhibitors

Tubulointerstitial disease

Acute allergic interstitial nephritis
- Penicillins
- Ciprofloxacin
- NSAIDs, cyclooxygenase-2 inhibitors
- Proton pump inhibitors
- Loop diuretics

Chronic interstitial nephritis
- Cyclosporine
- Lithium
- Aristolochic acid

Papillary necrosis
- NSAIDs, combined phenacetin, aspirin, and caffeine analgesics

Renal vasculitis, thrombotic microangiopathy, thrombosis, and cholesterol emboli

Vasculitis and thrombosis
- Hydralazine
- Propylthiouracil
- Allopurinol
- Penicillamine
- Gemcitabine
- Mitomycin C

Methamphetamines
- Cyclosporine, tacrolimus
- Adalimumab
- Bevacizumab

Cholesterol emboli
- Warfarin
- Thrombolytic agents