Drug Induced Nephropathy Cases

1. **H.H., 43 y.o., 80 kg male being treated for gram-negative septic shock**
   - Admitted to hospital 6 days ago, and has spent the last 3 days intubated in the ICU because of hypotension, respiratory failure, and altered mental status. On admission, H.H. was started on ceftriaxone 2 g IV daily, gentamicin 140 mg IV q8h.
   - Admission labs:
     - BUN 13 mg/dL (5-20)
     - SCr 0.9 mg/dL (0.5-1.2)
     - Serial, blood, urine, and sputum cultures were positive for Acinetobacter baumanii sensitive to ceftriaxone and gentamicin.
   - Current medications
     - Ceftriaxone 2 g IV daily
     - Gentamicin 140 mg IV q8h.
     - Norepinephrine IV 18 mcg/min
     - Pancuronium 0.02 mg/kg IV q3h
     - Famotidine 20 mg IV q12h
     - Lorazepam IV 2 mg/hr
   - Today (hospital day 7) vital signs:
     - Temp 101.5 F (38.6 C)
     - BP 90/40 mmHg
     - Pulse 135 beats/min
     - Respirations 20 breaths/min
   - Labs:
   - BUN 67 mg/dL
   - SCr 5.4 mg/dL
   - WBC 16,700 cells/mm3
   - Urinalysis:
     - Many WBC (0-5)
     - 3% RBC casts (0-1%)
     - Granular casts
     - Osmolality 250 mOsm/kg (400-600)
   - Serum gentamicin with last dose:
     - Peak 15 mg/dL (target 6-10)
     - Trough 9.1 mg/dL (target <2)

   a) Circle the renal parameters that are abnormal.

   b) What drug is most likely associated with the abnormal renal labs?

c) What information did you use to arrive at your assessment?

2. J.S., 50 y.o. female with cellulitus

- In hospital blood and wound cultures were positive for methicillin-sensitive *Staphylococcus aureus*
- Received 2 full days nafcillin 2 g IV q4h and then was discharged home on dicloxacillin 500 mg PO QID x 14 d
- 10 days post discharge, J.S. returned to the ER complaining of fever diffuse rash, hematuria, and reduced urine output
- Labs:
    - BUN 39 mg/dL (5-20)
    - SCr 2.3 mg/dL (0.5-1.2)
    - WBC count 18,500 cells/mm^3 (4,000-9,000)
        - 18% eosinophils
    - Urinalysis:
        - elevated specific gravity, WBC, RBC, eosinophiluria

a) What renal parameters are abnormal?

b) What type of renal dysfunction is most likely present?

c) What signs and symptoms are consistent with your assessment of J.S.?

d) What would be your therapeutic recommendation/plan?

3. A.B. has chronic kidney disease

- The renal nurse practitioner calls you and explains:
  - A.B. was prescribed Septra DS i tab po BID x 14 days for a community acquired MRSA skin and soft tissue infection
  - A.B. has completed the course of antibiotics, and today's SCr level is 2.0 mg/dL
  - Her baseline SCr is usually around 1.5 mg/dL

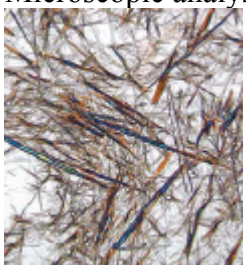
a) What do you think is going on?

b) What types of drug induced nephropathy can Septra cause?

c) How would you go about determining what type of renal injury the A.B. is experiencing?

4. **W.M. is a 60 year old male admitted to hospital with altered mental status, a temperature of 38.3°C with seizure-like activity.** His medications included efavirenz, emtricitabine, tenofovir, and pravastatin. Empirical treatment with intravenous acyclovir (10 mg/kg) and antibiotics was initiated. Two hours after the administration acyclovir, his urine became cloudy and white in the proximal portion of the Foley catheter, with clear urine distally.

   A urinalysis showed:
   Specific gravity 1.025
   pH 5.0
   Ketones, albumin, blood detected.

   Microscopic analysis of the urine reveal the following:
    (birefringent needle-shaped crystals)

   His serum creatinine increased from 0.7 to 1.1 mg/dL.

   a) What is your assessment of the situation?

   b) What signs and symptoms are consistent with your assessment?

   c) What drug most likely resulted in the renal injury?

   d) How would you recommend managing W.M.?

Drug Induced Nephropathy Cases
(Answers)

Case #1 (From Koda-Kimble & Young's applied therapeutics. 10th ed. Philadelphia, PA; Lippincott Williams & Wilkins 2013)

a) Abnormal renal lab parameters:
BUN, SCr
Urinalysis:
Many WBC
RBC casts
Granular Cases
Hypo-osmolar

b) Gentamicin

c) Gentamicin is a well-known nephrotoxic drug. Mechanism of renal injury is typically acute tubular necrosis.
Granular casts (muddy brown casts) are hallmark for tubular necrosis.
Urine hypo-osmolar (gentamicin nephrotoxicity usually presents as impaired urine concentrating ability.)
Timeframe of 7 days is consistent with expected time frame of gentamicin nephrotoxicity (5-10 days.)
Trough concentrations high. High trough known to be associated with gentamicin nephrotoxicity

Case #2

a) Abnormal renal parameters:
BUN, SCr
Urinalysis: elevated specific gravity, WBC, RBC, eosinophiluria

b) Acute allergic interstitial nephritis

c) AIN triad: fever, rash, eosinophilia/eosinophiluria (only present 10% of cases present with all three signs)
Onset typically within 2 weeks of starting drug. May be shorter with previous exposure.
75% of AIN cases due to drugs. Of the drug induced cases, 1/3 related to antibiotics.

d) Discontinue dicloxacillin
Supportive measures
Corticosteroids can be considered in this patient to shorten duration and extend renal tissue recovery
Since this is an immune-mediated/allergic reaction, highly likely that adverse effect will recur with repeat drug exposure. Therefore document as an allergy and avoid prescribing patient penicillins.

Case #3

a) Septra induced renal effect/toxicity

b) Trimethoprim – pseudo renal failure
Sulfamethoxazole – acute allergic interstitial nephritis, crystalluria

c) Pseudo-renal failure: SCr should return to baseline within a few days of stopping the drug.
Isolated increase in SCr (that is BUN concentration remains in normal range)

AIN – sustained increase in SCr for prolonged time period
Systemic symptoms, fever, rash
Increased eosinophils in blood
Urinalysis: eosinophils, WBC casts

Crystalluria
Crystals in urine under microscope
Decreased serum creatinine with proper patient hydration (short serum creatinine recovery time)

Case #4

a) Crystalluria

b) Crystals on microscopic urine analysis.
Urine cloudy and white in proximal portion of catheter post acyclovir administration.
Acyclovir known to cause crystalluria.
Slight increase in SCr

c) Acyclovir

d) Hydration to dissolve crystals and to dilute acyclovir in renal tubules to prevent re-crystallization. Acyclovir can be continued with proper hydration