**DIFFERENTIAL DIAGNOSIS:**

- **Presentation:** Pulmonary Renal Syndromes (PRS) are life-threatening diseases with pulmonary hemorrhage (DAH) & renal failure (glomerulonephritis). Although pulmonary and renal involvement is the defining feature, PRS can affect many organs:
  - Acute respiratory failure or diffuse alveolar hemorrhage (DAH)
  - Inflammatory eye disease
  - Cardiovascular disease
  - Digital ischemia
  - Cutaneous palpable purpura

**PATHOPHYSIOLOGY:**

- The defining feature of PRS is the involvement of multiple organs, including the kidneys and lungs.
- Immune-mediated diseases (e.g., anti-glomerular basement membrane (GBM) disease) can lead to renal failure and pulmonary hemorrhage.
- Antibodies, such as anti-neutrophil cytoplasmic antibodies (ANCA), can cause vasculitis, leading to inflammation and organ damage.

**AUTO-ANTIBODIES:**

- **ANCA** (myeloperoxidase (MPO)) and **GBM** (crescentic GN) are associated with PRS.

**DIAGNOSIS:**

- **Labs:**
  - BMP (quantify renal injury), Coags (r/o coagulopathy)
  - CBC w differential (check eosinophil count for EGPA)
  - Auto-antibodies: ANCA antibody, Anti-GBM antibody
  - Urine: UA, Urine protein to creatinine (UPC) ratio
  - Cardiac: consider BNP, troponin if concern for EGPA
  - ESR and CRP (non-specific, ESR usually low in anti-GBM)

**Other tests:**

- CT chest to evaluate pulmonary involvement
- Bronchoscopy: confirm DAH, r/o infection
- Echocardiogram for EGPA (↓ LVEF, pericardial effusion)
- PFTs (outpatient; increased DLCO after recent DAH)
- EMG/NCS for mononeuritis multiplex/neuropathy

**DIAGNOSIS OF PRS:**

- Biopsy (gold standard) or serologies + symptoms (not-optimal but may be necessary)

**WORKUP & DIAGNOSIS**

- **Labs:**
  - ANCA Associated Vasculitis (AAV)
    - MP A → usually p-ANCA
    - GPA → usually c-ANCA
    - EGPA → ANCA in 40-50%
    - Anti-GBM:
      - ANCA (MPO)
        - P-ANCA (MPO) 65% 15% 45% 20%
      - C-ANCA (PR3)
        - 15% 85% 5% 10%
      - X-ANCA (elastase, cathepsin, lysozyme, others)
        - Perinuclear pattern (but not MPO)
        - Seen with medications
          - Levamisole/cocaine, hydralazine
      - ANCA also seen in many diseases:
        - SLE, RA, PS, PBC, AIH, IBD (UC > CD)

**RENAL FINDINGS:**

- U/A: microscopic or gross hematuria, RBC casts, low grade proteinuria
- Path: rapidly progressive (crescentic) glomerulonephritis (fibrinoid necrosis, hypercellular glomeruli, & cellular crescents)
- IF staining patterns in crescentic GN:
  - Linear IgG staining on basement membranes seen in anti-GBM dx
  - Complement deposits in clusters; seen in SLE, post-strep GN,
  - Absence of IF staining; seen in AAV (MPA, GPA, and EGPA)

**OTHER FINDINGS:**

- Skin lesions: palpable purpura, petechiae, ulcerations, & occasionally nodules. Nasal or sinus mucosa often involved in EGPA. Biopsy of skin or nasal mucosa can reveal vasculitis, such as leukocytoclastic vasculitis of skin.

**APPROACH:**

- Initial tx focused on remission-induction
- Later tx focused on maintenance.

**PULMONARY-FINDINGS:**

- **AAV or Goodpasture’s cause pulmonary capillaritis** leading to diffuse alveolar hemorrhage (DAH)
- Diffuse ground glass or consolidative opacities with sparing or the lung periphery is typically seen on chest CT.
- BAL reveals increasing blood return in serial lavages and >20% hemosiderin laden macrophages (diagnostic of DAH)

**Surgical lung biopsy** (not always required) may reveal:

- **Granulomatous** (e.g., sarcoidosis)
- **Granulomatous** (e.g., granulomatosis with polyangiitis)
- **Granulomatous** (e.g., Wegener's granulomatosis)

- **Drug induced** (e.g., hydralazine, methimazole)
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**APPROACH:**

- Initial tx focused on remission-induction
- Later tx focused on maintenance.

**SECONDARY FINDINGS:**

- **Skin:** palpable purpura, petechiae, ulcerations, & occasionally nodules. Nasal or sinus mucosa often involved in EGPA. Biopsy of skin or nasal mucosa can reveal vasculitis, such as leukocytoclastic vasculitis of skin.

**APPROACH:**

- Initial tx focused on remission-induction
- Later tx focused on maintenance.

**FURTHER FINDINGS:**

- **Rituximab** and/or cyclophosphamide
- **Pulse dose steroids**