29- Vasculitis II

ANCA-Associated Vasculitis

Background:
- Annual incidence of 20 cases/million in North America & Europe
- ANCA: anti-neutrophilic cytoplasmic ab (IgG)
  - C-ANCA: cytoplasmic ANCA target proteinase 3
  - P-ANCA: perinuclear ANCA target myeloperoxidase
1. Granulomatosis w/ polyangiitis (Wegener’s granulomatosis)
2. Microscopic polyangiitis
3. Eosinophilic granulomatosis w/ polyangiitis (Churg-Strauss)

Granulomatosis w/ polyangiitis (GPA)

Clinical Presentation:
- Triad of upper respiratory, lower respiratory, and renal changes
  - Upper respiratory are often initial presentation
    - Severe sinusitis
    - Oral ulcerations
    - “Strawberry gums”
  - Lower respiratory changes seen in 70% of patients
    - Cough
    - SOB
    - Hemoptysis
  - Renal disease present in 85% of patients
    - Severe glomerulonephritis w/ hematuria (80% mortality in first year w/out tx)
    - Skin Changes: Palpable purpura, pyoderma-gangrenosum-like ulcers, or sub-Q nodules
    - Peripheral neuropathy & stroke-like sx
    - Systemic fevers, anorexia, & arthralgias

Histology:
- Leukocytoclastic vasculitis along w/ necrotizing palisading granulomas

Labs: + C-ANA & elevated sed rate

Treatment:
- Cyclophosphamide, prednisone, & other immunosuppressants (e.g. methotrexate & rituximab)

Microscopic Polyangiitis

Clinical Presentation:
- Most common cause of pulmonary-renal syndrome
  - Lower Respiratory (25%)
  - Glomerulonephritis (80-90%)

PEARL: Simply put, MPA is like GPA (with lower respiratory and renal changes) but without the upper resp changes + granulomas
- Skin Changes: palpable purpura, petechia, & livedo reticularis
- Peripheral neuropathy: mononeuritis multiplex

Labs:
- P-ANCA

Eosinophilic granulomatosis w/polyangiitis

Clinical Presentation:
- Presents in 3 stages
  1. Adult-onset asthma, allergic rhinitis, nasal polyps
  2. Eosinophilia, pneumonia, GI issues
  3. Systemic vasculitis w/ palpable purpura, worsening asthma & allergic rhinitis, and mononeuritis multiplex & cardiac issues (e.g. cardiomyopathy)

PEARL: EGPA does NOT have renal changes, which differentiates it from GPA & MPA

Labs:
- + P-ANCA, ↑IgE, ↑WBC

Treatment:
- Systemic corticosteroid, cyclophosphamide
Polyarteritis Nodosa (PAN)

Clinical Presentation:
- Palpable purpura on the lower legs, painful sub-Q nodules, lacy livedo reticularis
- Constitutional sx: fevers, malaise, arthralgias
- Organ involvement:
  - Nerves
  - Cardiac (e.g. cardiac arrythmias & infarction)
  - GI: NVD, bowel infarction → hemorrhage
  - Renal: renal failure & HTN

PEARL: Neurologic changes affect 75% of PAN pts and include paresthesias and motor neuropathies resulting in foot drop!
- GU: male testicular pain
- Spares the lungs

PEARL: Why do PAN pts not get glomerulonephritis? PAN affects medium-sized vessels that perfuse the kidneys, NOT the small vessels w/in the glomeruli = HTN NOT glomerulonephritis
- GU: male testicular pain
- Spares the lungs

PEARL: Associations include Hep B, Hep C, HIV, CMV, strep, IBD

Diagnosis:
- Criteria: 3 of 10 = Diagnosis
  1. Weight loss of 4kg or more
  2. Livedo reticularis
  3. Testicular pain/tenderness
  4. Myalgias or leg weakness or tenderness
  5. One or more neuropahties.
  6. Hypertension with diastolic blood pressure >90
  7. Elevated BUN >40 or creatinine >1.5 that can’t be explained by dehydration or obstruction.
  8. Positive hepatitis B antigen or antibodies.
  9. Arteriogram demonstrating aneurysms or occlusion of visceral arteries without another explanation.
  10. Biopsy showing small or medium-sized vessel with inflammation (including PMN’s)
- Other work-up: Hep B+C ab titers, BMP, UA, BCB, ESR, CRp, C&P-ANCAs, ASO titers
- Renal Angiogram: Look for aneurysms or renal artery stenosis

Histology:
- Leukocytoclastic vasculitis w/in medium-sized arteries in the deep dermis or sub-Q +/- lobular panniculitis next to the involved vessels

Treatment
- Immunosuppresants (e.g. systemic corticosteroids for 6 months) + methotrexate or cyclophosphamide
- Consult nephro & cardio

Kawasaki Disease
- Children <5 years old
- Asian ancestry
- Coronary artery aneurysms develop several weeks after sx onset in 25% of untreated pts

Clinical Presentation:
- Fever (5 days duration) + 4/5 criteria
  - Think “CRASH & BURN”
    - Conjunctivitis
    - Rash (Polymorphus exanthen)
    - Adenopathy (Cervical lymphadenopathy)
    - Strawberry Tongue
    - Hand & Feet desquamation
    - Burning Fever (>39°Celsius) for 5+ days
- Other sx: uveitis, arthralgias, gastroenteritis, irritability, urethritis

Labs:
- Think “WATCH”
  - ↑ WBC, Anemia, Thrombocytosis/Thrombocytopenia, ↑CRP, Hypoalbuminemia
- Rapid Strep, Blood cultures, UA, ASO titers
- Stat ECHO

Treatment:
- IVIG @ 2g/kg over 12 hrs as a single dose
- Aspirin @ 80-100 mg/kg daily
- +/- corticosteroids, cyclophosphamide or cyclosporine
Temporal Arteritis (Giant Cell Arteritis)
- Onset: >50 y/o (~70’s)
- Develop granulomatous vasculitis of the temporal artery

Clinical Presentation:
- Tenderness along temporal artery, loss of pulses, headache, jaw claudication
- Skin Changes: erythema, cyanosis, purpura, or tender nodules
- Systemic Changes: fevers, associated polymyalgia rheumatica, visual changes

Labs:
- ESR, CRP, temporal artery biopsy

Treatment:
- Aspirin & systemic steroids

Takayasu’s Arteritis
- Onset: <40 y/o
- Granulomatous vasculitis affecting the aorta or its main branches

Clinical Presentation:
- ↓ radial pulses and a difference in blood pressure >10 mmHg between each arm
- Constitutional sx: fevers, night sweats, and weight loss, claudication of the extremities
- Skin changes: erythematous papules, purpura, erythema nodosum, and Raynaud’s phenomenon

Labs:
- Elevated ESR

Treatment:
- Systemic Corticosteroids

Septic Vasculitis
- Systemic infection that damages the vessels by either 1) invading the vessels directly or 2) causing immune-mediated damage
- Causes: Subacute bacterial endocarditis, Staphylococcal or Pseudomonas septicemia, Neisserial gonococcemia and meningococcemia, Vibrio vulnificus, rickettsialpox and Rocky Mountain Spotted fever

Clinical Presentation:
- Presentation of septic vasculitis can vary widely, from hemorrhagic pustules of staph septicemia to large ulcerating bullae caused by pseudomonas in cases of ecthyma gangrenosum

Histology:
- Small vessel vasculitis with neutrophils and thrombi

PEARL: Septic Vasculitis histology differs from the vasculopathies in that vasculopathies like DIC and TTP have minimal or no inflammatory infiltrate to go with their thrombi on path, while septic vasculitis does have inflammation with thrombi!