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 immunosuppresants (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

PEARL: Neurologic changes affect 75% of PAN pts and include paresthesias and motor neuropathies resulting in foot drop!

  - Cardiac (e.g. cardiac arrythmias & infarction)
  - GI: NVD, bowel infarction → hemorrhage
  - Renal: renal failure & HTN

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 neuropathies.
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**"
    - **C**onjunctivitis
    - **R**ash (Polymorphus exanthem)
    - **A**denopathy (Cervical lymphadenopathy)
    - **S**trawberry Tongue
    - **H**and & Feet desquamation
    - **Burn**ing Fever (>39^{o}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 vascul*opathies* 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!