28- Vasculitis I

Purpura

Background:

- Purpura = visible hemorrhage into the skin or mucosa
- 6 types:
  - ***Petechiae*** - nonblanchable, pinpoint red macules ≤ 4 mm, think platelets
  - ***Macular Purpura*** - nonpalpable and 5-9mm in size, think coagulation
  - ***Macular Ecchymosis*** - aka a bruise, nonpalpable and is ≥1cm, think coagulation
  - ***Palpable Purpura*** - can range in size from a few mm's to many cm's, suggests vasculitis and inflammation because inflammation brings edema with it that swells the skin
  - ***Non-inflammatory*** or ***Inflammatory Retiform Purpura*** - purpura with an angulated or branching pattern, BAD SIGN!!

Pathogenesis:

- 3 big categories based on location of blood vessel pathology
  - **problems with the vessel walls themselves** such as inflammation in vasculitis, or other alterations due to diabetes, amyloid deposition, or calcium deposition, as in calciphylaxis
  - **intravascular pathology** such as coagulation or platelet abnormalities, along with embolic conditions
  - **problems outside the blood vessel wall** such as connective tissue issues like scurvy or actinic purpura
    - In both scurvy and actinic purpura, you have problems with collagen in the dermis cushioning the vessels, therefore minimal trauma leads to easy bruising

Vasculitis

- Vasculitis is caused by inflammation of the blood vessel wall
  - ***Palpable purpura*** on dependent areas (e.g. lower legs)
    - ***Inflammation*** of vessels bring edema with it → palpable
- Vasculopathies refer to blood vessel damage with ***minimal or no inflammation*** of the vessel walls
  - typically causes **macular or nonpalpable purpura**
- Typically a ***type 3 hypersensitivity***
  - Antibodies to an antigen → immune complexes form → deposit in vessel walls → complement cascade activated → inflammation of blood vessel walls
- 4 groups based on vessel size:
  - **Small vessel only**
    - Arterioles, capillaries, and postcapillary venules in the upper and mid dermis
    - palpable purpura, petechiae, urticarial papules
    - *Cutaneous* small vessel vasculitis (CSVV), Henoch-Schonlein purpura (HSP), urticarial vasculitis, acute hemorrhagic edema of infancy, erythema elevatum diutinum (EED), and granuloma faciale
  - **small plus medium vessel**
    - medium vessels include *larger but still small* arteries and veins in the deep dermis or sub-Q
    - purpura, petechiae, urticarial papules, livedo reticularis, ulcers, sub-cutaneous nodules, and even retiform purpura
    - More visceral involvement than small vessel only (e.g. kidneys, liver, heart, and mesentery)
    - group 1: mixed cryoglobulinemia types 2 and 3
    - group 2: ANCA-associated vasculitides
      - granulomatosis with polyangiitis (GPA or

Wegener's granulomatosis)
        - microscopic polyangiitis
        - *eosinophilic* granulomatosis with polyangiitis (EGPA or Churg-Strauss syndrome)
    - **medium vessel only**
        - **Examples:** polyarteritis nodosa (PAN) and Kawasaki disease
    - **large vessel**
        - larger-named arteries like the aorta
        - temporal arteritis (giant cell arteritis) and Takayasu's arteritis

Cutaneous Small Vessel Vasculitis (CSVV)

Background:

- leukocytoclastic vasculitis (LCV) that is *mostly* confined to the skin
- **Pathogenesis:** an antigen trigger is bound by antibodies and forms big immune complexes that deposit into post-capillary venules → these lodged immune complexes then activate complement, which activates the immune system → causes inflammation that damages the vessels and allows red cells to leak out → petechiae and palpable purpura in dependent areas
- **Triggers: MANIC** (same as urticarial vasculitis, EED, and Sweet's syndrome)
    - **M**edications (e.g. beta lactam antibiotics, bactrim, thiazides, and oral contraceptives)
    - **A**utoimmune CTD (e.g. lupus, RA or Sjogren's)
    - **N**SAIDs
    - **I**nfections (e.g. group A strep, hepatitis and HIV, and candida) or **I**BD
    - **C**ancer (<5% of cases, e.g. leukemias and solid organ cancers)

Clinical Presentation:

- **Petechiae and palpable purpura on lower legs** that present **~ 1-2 weeks after a trigger (~ 6 months for autoimmune diseases or cancer)**
- May become bullous or pustular
- May be more severe under areas of pressure like the sock line
- May be itchy or painful
- May have systemic symptoms (e.g. fevers and arthralgia)
- Typically resolve over several weeks

Histology:

- **LCV:**
- **Vessels in the superficial dermis with fibrin deposition and expansion of the vessel walls**
- **RBC extravasation**
- **Perivascular infiltrate containing neutrophils and karyorrhexis (nuclear debris)**

PEARL: When it comes to terminology for CSVV, some people refer to it as "Leukocytoclastic vasculitis", but keep in mind that LCV is actually a histology finding and can also be seen in other systemic vasculitic disorders such as GPA.

Henoch-Schonlein Purpura (HSP)

Background:

- IgA vasculitis which is THE most common form of vasculitis in children
- **Triggers**:
    - Infections (e.g. tinea)
    - Medications (e.g. HCTZ)
    - Foods (e.g. blue cheese)
    - Autoimmune conditions
    - Cancer

Clinical Presentation:

- Development of the following **tetrad 1-2 weeks** after a **URI** or **strep infection:**
    1. **Palpable purpura** on the **legs** and **butt**
    2. **Arthralgias** of **knees** and **ankles**
    3. **GI issues** (e.g. **abdominal pain** and **diarrhea** with or without **melena**
    4. **Renal changes: hematuria,** possible **nephritis,** and **renal failure** in around **1% of cases**
- **Adults** usually have a ***more aggressive*** and ***chronic* HSP course**
    - Associated with **solid organ and blood cancers**
    - **3 Risk factors for renal involvement in adults:**
        1. **Fevers**

2. **↑ ESR**
3. **Purpura** located **ABOVE** the **waist ("closer to kidneys")**

Histology:

- **LCV (see above)**
- **+ DIF** with **IgA** in **blood vessel walls**

Treatment/Management:

- **Supportive** treatment with or without **prednisone** or **dapsone**
- **Monitor** patients with **serial UA's *and* stool guaiac** if they have **GI symptoms**

Urticarial Vasculitis

- **Urticaria clinically, LCV histopathologically**
- 4 unique differences than regular urticaria:
  - Individual lesions ***last longer*** than 24 hours (vs. <24 hours)
  - ***More pain*** and ***burning*** than itching
  - ***Purpura***
  - ***Systemic Symptoms***
- Divided into **normocomplementemic** and **HYPOcomplementemic**
  - ~3/4 of cases have ***normal*** complement levels and are ***skin-limited***
  - ~1/4 of cases are ***HYPOcomplementemic***
    - associated with ***systemic changes*** (e.g. arthralgias; pulmonary, GI, renal, and ocular changes; decreased CH50, C3, and C4 levels; and anti-C1q antibodies)

PEARL: A patient with urticarial vasculitis, IgM gammopathy, and fevers, bone pain, and arthralgias has ***Schnitzler's syndrome.***

Cryoglobulinemias

- **Cryoglobulins** are immunoglobulins that precipitate in the cold
- 3 types:
  - **Type 1 Cryoglobulinemia**
    - caused by **monoclonal IgM > monoclonal IgG** → sludging and occlusion of blood vessels → vasculopathy NOT vasculitis → ***no LCV*** on path
    - associated with lymphoproliferative disorders
    - Presents with **livedo reticularis**, **Raynaud's phenomenon**, **acrocyanosis**, and **purpura**
  - **Type 2 and Type 3 Mixed Cryoglobulinemia**
    - Type 2 exhibits ***monoclonal*** **IgM** or **IgG** with **polyclonal IgG** and Type 3 has ***polyclonal*** **IgM** with **polyclonal IgG ("poly/poly")**
    - Immune complexes activate complement and cause LCV with **palpable purpura** and **systemic changes**
    - Higher association with **Hep C**
    - **Lab Tests:**
      - **↑ cryoglobulins** (sample *must* be maintained near 98.6°F until it is spun down, otherwise you get a false-negative result)
      - **↓ C4 complement levels** due to consumption
      - **+ rheumatoid factor** (70-90%)
      - **+ hepatitis B or C** test

PEARL: Rheumatoid factor by definition is the presence of an antibody that is binding to the Fc portion of IgG. Remember that the Fc portion is the bottom of the antibody's Y shape. Since types 2 and 3 mixed cryoglobulinemias have polyclonal IgG, it makes sense that you end up with antibodies binding to IgG and thus a positive rheumatoid factor.