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
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)
  - Medications (e.g. beta lactam antibiotics, bactrim, thiazides, and oral contraceptives)
  - Autoimmune CTD (e.g. lupus, RA or Sjogren’s)
  - NSAIDs
  - Infections (e.g. group A strep, hepatitis and HIV, and candida) or IBD
  - Cancer (<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

**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

Urticaria 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.

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