Disclosure

• We have no financial interests or relationships to disclose.
CUTANEOUS SMALL-VESSEL VASCULITIS

A. Hypersensitivity Vasculitis/Leukocytoclastic Vasculitis
B. Henoch-Schonlein Purpura
C. Acute Hemorrhagic Edema of Infancy
D. Urticarial Vasculitis
E. Cryoglobulinemic Vasculitis
F. Erythema Elevatum Diutinum
HYPERSENSITIVITY VASCULITIS / CUTANEOUS LEUKOCYTOCLASTIC VASCULITIS (LCV)

- All ages & sexes, MC in adults
- **Etiology**: immune complex deposition
- **Presentation**: palpable purpura, erythematous papules, urticarial lesions involving **dependent areas**
  - Koebner phenomenon
  - Fever, weight loss, myalgias with flares
- **Pathology**:
  - H&E: LCV, karyorrhexis, extravasated RBC
  - DIF: C3, IgM, IgA and/or IgG granular deposits in vessels
HYPERSENSITIVITY VASCULITIS / CUTANEOUS LEUKOCYTOCLASTIC VASCULITIS (LCV)

• Secondary LCV
  • Idiopathic (50%)
  • Infection (15-20%)
  • Inflammatory Disorders (15-20%)
  • Drug Exposure (10-15%)
  • Neoplasms (2-5%)
  • Genetic Disorders (Rare)

• Treatment:
  – Acute
    • Often resolves without treatment
    • Avoid trigger
    • Supportive care
  – Chronic (>4 wks)
    • Colchicine, dapsone, corticosteroids
HENOCH-SCHONLEIN PURPURA
IGA VASCULITIS

- MC children
- **Etiology:** bacterial & viral infections
- **Presentation:** palpable purpura, arthralgias, abdominal pain, renal disease
- **Pathology:**
  - H&E: LCV
  - DIF: IgA vasculitis
- **Treatment:** systemic corticosteroids, immunosuppressants, ACE-I
- **Prognosis:** monitor for chronic renal insufficiency

ACUTE HEMORRHAGIC EDEMA OF CHILDHOOD

- Children < 2 yrs
- **Etiology**: likely infectious
- **Presentation**: cockade, annular, purpuric plaques involving the face, ears, distal extremities
  - No systemic findings
- **Pathology**: 
  - H&E: LCV
  - DIF: IgA vasculitis
- **DDx**: Child abuse, urticaria, urticarial vasculitis, erythema multiforme
- **Treatment**: Resolves spontaneously in 1-3 weeks

URTICARIAL VASCULITIS

- Adults, peak 50s, F>M
- **Etiology**: unknown
- **Variants**:
  - Normocomplementemic
  - Hypocomplementemic
- **Associations**:
  - CTD (Sjögren’s, SLE)
  - Serum sickness
  - Cryoglobulinemia
  - Infections (HBV, HCV, EBV, Lyme)
  - Medications
  - Hematologic & solid malignancies: colon & renal cell cancer
URTICARIAL VASCULITIS

- **Presentation:**
  - Erythematous annular or targetoid wheals resemble urticaria → progress to purpura with residual hyperpigmentation
  - Favor trunk or proximal extremities
  - >24 hours
  - Recurrent lesions
  - Painful or burning
  - Systemic findings: angioedema, arthralgias, abdominal or chest pain, fever, dyspnea, uveitis, glomerulonephritis & Raynaud's

**URTICARIAL VASCULITIS**

3 clinical features distinguish skin lesions of urticarial vasculitis from true urticaria:

1. Lesions are often **painful**, rather than pruritic.
2. Lesions >24 hrs and are **fixed**, rather than migrating.
3. Post-inflammatory purpura or hyperpigmentation.

**URTICARIAL VASCULITIS**

- **Diagnosis**: skin biopsy
  - H&E: < 48 hours in onset
  - DIF: < 24 hours in onset
- **Pathology**:
  - H&E: LCV + neutrophilic infiltrate
  - Hypo DIF: C3 granular pattern in BV & BM
- **Treatment**:
  - 1st line: antihistamines, NSAIDs
  - Alt: colchicine, hydroxychloroquine, dapsone
  - Systemic tx: steroids, azathioprine, mycophenolate mofetil, rituximab
- **Prognosis**:
  - Chronic and benign ~ 3 years
CRYOGLOBULINEMIC VASCULITIS

• Vasculitis is ONLY seen with **types II and III**
  – Type I can present with vasculopathy
• Small & medium-sized vessels, but preferentially involves **small vessels**
• Association with **HCV & HBV infections**

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Molecular composition</th>
<th>Associations</th>
<th>Pathophysiology</th>
<th>Clinical manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Monoclonal IgM &gt; IgG *</td>
<td>Plasma cell dyscrasias, lymphoproliferative disorders</td>
<td>Vascular occlusion</td>
<td>Raynaud’s phenomenon, retiform purpura, gangrene, acrocyanosis</td>
</tr>
<tr>
<td>II*</td>
<td>Monoclonal IgM &gt; IgG * against polyclonal IgG</td>
<td>HCV, HIV, autoimmune connective tissue diseases, lymphoproliferative disorders</td>
<td>Vasculitis</td>
<td>Palpable purpura, arthralgias, peripheral neuropathy, glomerulonephritis</td>
</tr>
<tr>
<td>III*</td>
<td>Polyclonal IgM &gt; IgG against polyclonal IgG</td>
<td>-</td>
<td>-</td>
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</tr>
</tbody>
</table>

\*Refers to as "mixed" cryoglobulins because either monoclonal or polyclonal immunoglobulins bind to polyclonal immunoglobulins.

\*Typically have rheumatoid factor activity (i.e., are directed against the Fc portion of IgG).

\*Rarely IgA.

Table 24.6 Classification of cryoglobulins. HCV, hepatitis C virus; HIV, human immunodeficiency virus.
CRYOglobulinemic Vasculitis

- Palpable purpura MC
- Other findings: erythematous papules, ecchymoses, nodules, urticaria, livedo reticularis, necrosis, ulcerations, bullae
- Extracutaneous findings:
  - Arthralgias/ arthritis (70%)
  - Peripheral sensory neuropathy (40%)
  - GI symptoms or hepatitis (30%)
  - Membranoproliferative glomerulonephritis (25%)

CRYOGLOBULINEMIC VASCULITIS

- **Laboratory Evaluation:**
  - *Often falsely negative,* need to **test multiple times**
  - Blood samples should be kept at 37C (98.6F) while being transported to lab
- **70% are RF (+); 20% are ANA (+)**
- **Low C4 levels** - do not correlate with disease activity
- **Treatment:** **treat underlying disease!**
  - Hep C (+): new antivirals (i.e Harvoni), Ribavirin, Interferon
  - Plasma exchange or cyclophosphamide with corticosteroids may be needed for severe renal or neurological involvement
  - Rituximab
ERYTHEMA ELEVATUM DIUTINUM

• Symmetric red-violet to red-brown papules & plaques
• Persistent lesions that develop on extensor surfaces/small joints
  – Trunk generally spared
  – A/w infections, hematologic, rheumatologic diseases
• Limited to skin
• Pathology: LCV with fibrinoid necrosis
• Treatment: typically responds promptly to Dapsone or sulfapyridine

MIXED (MEDIUM & SMALL) VESSEL VASCULITIS

A. Connective Tissue Disease Associated (usually rheumatoid vasculitis)
B. Septic Vasculitis
C. ANCA-Associated
   1. Microscopic Polyangiitis
   2. Granulomatosis with Polyangiitis
   3. Allergic Granulomatosis (Churg-Strauss)
POLYARTERITIS NODOSA

• Classic PAN (25% cases have skin findings): palpable purpura, livedo reticularis, retiform purpura, “punched-out” ulcers

• Cutaneous PAN (10%): painful subcutaneous nodules & ulcerations over the lower extremities, particularly near malleoli

• Extracutaneous manifestations:
  – Fever
  – Arthralgias
  – Myalgias
  – Paresthesias
  – Abdominal pain
  – Orchitis
  – Renovascular hypertension
POLYARTERITIS NODOSA

- Cutaneous variant has chronic, more benign course
  - Often a/w strep infection in children
- HBV, HCV, infections, inflammatory diseases, malignancies (hairy cell leukemia) & medications
- **Pathology:** Segmental necrotizing vasculitis in subcutaneous tissue
- **Treatment**
  - Classic PAN – systemic corticosteroids (1 mg/kg/day of prednisone)
  - Cutaneous PAN – topical or intralesional steroids, may need systemic steroids if progressive or extensive

**RHEUMATOID VASCULITIS**

- Rare, late complication in patients with longstanding, erosive, deforming RA
- High morbidity and mortality
- **Risk Factors:**
  - **Smoking**, HLA-DRB1/similar epitopes, uncontrolled RA, **high +RF titer** and anti-CCP, PVD
- **Presentation:**
  - Purpura, cutaneous ulcers (upper or lower ext), rheumatoid nodules, digital infarcts, nail fold infarcts
  - Extracutaneous: **severe erosive arthritis**, ocular, cardiovascular, pulmonary, renal, GI, & CNS findings
- **Treatment:**
  - No established guidelines to help guide therapy, high-dose glucocorticoids + cyclophosphamide has shown promising results

MICROSCOPIC POLYANGIITIS

• **Presentation**: purpuric papules, macules, *retiform purpura*, cutaneous ulceration, livedo, rarely urticaria
  – Systemic: fever, weight loss, myalgias, arthralgias, **segmental necrotizing and crescentic glomerulonephritis**, with **pulmonary involvement**, pulmonary capillaritis, vasculitis neuropathy, eye disease

• **Pathology**: necrotizing LCV

• **Laboratory findings**: ANCA + (70%), p-ANCA > c-ANCA

• **Treatment**: systemic corticosteroids
  – Localized: TMP/SMX + corticosteroids
  – Generalized: MTX + CS
  – Organ involvement: cyclophosphamide then MMF, MTX, or azathioprine, IVIG and anti-TNF (refractory)
GRANULOMATOSIS WITH POLYANGIITIS

- Rare, potentially life-threatening PR3-ANCA associated necrotizing vasculitis of small to medium-sized vessels and extravascular necrotizing granulomatous inflammation
- F>M; peak age 45-65 years
- Triad
  - 1) Necrotizing granulomatous inflammation of upper & lower respiratory tracts
  - 2) Glomerulonephritis
  - 3) Necrotizing small to medium-vessel vasculitis
- Presentation:
  - Palpable purpura followed by oral ulcers/friable gums “strawberry gums”
  - Painful SQ nodules resemble pyoderma gangrenosum
  - Upper or lower respiratory tract involvement
  - Glomerulonephritis
  - Other: musculoskeletal, ocular, neurological, GI, and cardiac
  - Saddle-nose deformity due to mucosal necrotizing granulomas

GRANULOMATOSIS WITH POLYANGIITIS

- Labs:
  - (+) c-ANCA in 80-90%, generalized disease, 60% in localized
  - RF, ESR, CRP, anemia, leukocytosis, anti-MPO Ab in 10%, proteinuria, RBC casts

- Pathology:
  - LCV-like changes, palisading granulomas, granulomatous vasculitis surrounding foci of basophilic necrobiosis

- Treatment:
  - Corticosteroids + cyclophosphamide = 75% remission
  - Corticosteroids + rituximab may be equally effective
**CHURG-STRAUSS SYNDROME**

- **Presentation**: palpable purpura, subcutaneous nodules of extremities and scalp, firm non-tender purpuric papules of fingertips, urticaria
- **3 phases:**
  1. **Initial**: allergic rhinitis, nasal polyps, asthma (35 yo)
  2. **Secondary** (2-12 years later): fever, eosinophilia, with pneumonia and gastroenteritis
  3. **Tertiary**: diffuse angiitis of the liver, spleen, kidneys, intestines, and pancreas, *mononeuritis multiplex* common
- **Medication triggers**: vaccination, desensitization, leukotriene inhibitors, azithromycin, nasal fluticasone, rapid d/c corticosteroids
- **Death from CHF d/t granulomatous inflammation of myocardium**
CHURG-STRAUSS SYNDROME

- **Laboratory findings**: peripheral eosinophilia, *p*-ANCA (anti-myeloperoxidase ab) positive, c-ANA (anti-PR3) sometimes positive
- **Pathology**: small and medium LCV, Wells syndrome with flame figures, palisaded granulomas lacking giant cells with central eosinophils
- **Treatment**: corticosteroids, cyclophosphamide with corticosteroids if neuro, renal, myocardial, or gastrointestinal involvement
  - MTX or other steroid-sparing agents can be used to maintain remission
BEHCET’S DISEASE

- **HLA-B51**

- **Diagnostic Criteria:**
  - Oral ulcers 3 times in 12 month period plus 2 of below
    - Recurrent genital ulcers
    - Positive pathergy test
    - Uveitis, retinal vasculitis
    - Skin findings: Ulcerations, acneiform, papulopustular, EN-like

- **Clinical Features:**
  - Painful
  - CNS lesions (MS-like)
  - Thrombophlebitis
  - Thrombosis of SVC
  - Asymmetric, non-erosive polyarthritis

- **Histology:**
  - Vasculitis may involve small and medium vessels
  - Predominantly neutrophilic infiltrate

- **Treatment:**
  - Colchicine, dapsone, thalidomide, TNF-inhibitors
Thank You