Vasculitis: Classification + Workup

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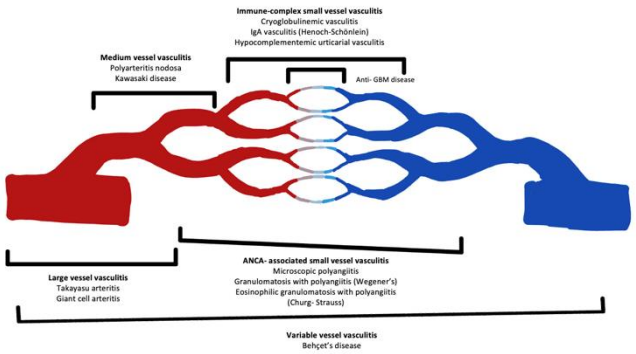

Vasculitis → heterogeneous group of pathologies characterized by inflammation of vessels.

- Clinical / pathological features are variable; depend on the site + type of blood vessels affected.
- Can be 1° or 2° to another underlying disease.
- Defined by presence of leukocytes in the vessel wall and reactive damage to the mural structures → bleeding in wall→ tissue ischemia and necrosis.
- Etiology: unclear, however likely due to immune complexes, autoantibodies, antigenic agents
- Often classified by vessel: **large**, **medium,** and **small**
    - **Large vessel**: Takayasu, Giant Cell Arteritis (GCA)
    - **Medium vessel:** Polyarteritis Nodosa (PAN), Kawasaki
    - **Small vessel** (ANCA- associated): Microscopic Polyangiitis (MPA), Granulomatosis with Polyangiitis (GPA, *formerly Wegner's)*, Eosinophilic granulomatosis with Polyangiitis (EPGA*, formerly Churg-Strauss*)
    - **Small vessel** (immune complex mediated): cryoglobulinemic, IgA (Henoch-Scholein), hypocomplementemic urticarial vasculitis, PAN can also affect small vessels
    - Others to be aware of:
        - Kawasaki- small/medium/ large vessels- seen in children, usually affects coronary arteries
        - Thromboangiitis obliterans – small/medium vessel, formerly Buerger's disease, seen in young smoker's
        - Vasculitis 2/2 autoimmune (RA, SLE, Systemic sclerosis, Sjögren's, syndrome; inflammatory myopathies, relapsing polychondritis, IBD, primary biliary cirrhosis)
        - Behcet's disease- any size vessels in arterial and venous circulation, mean age 25-35, recurrent oral and/or genital ulceration, eye lesions, skin lesions, +pathergy test)
        - Primary angiitis of the CNS (PACNS) – small/medium-vessels, affects the brain parenchyma, spinal cord, and leptomeninges.
- Secondary vasculitis due to medications: antimicrobial agents (minocycline, sulfadiazine), antithyroid agents (propylthiouracil, methimazole, carbimazole) hydralazine, TNF-inhibitors and more rarely: vaccines, antiepileptic agents, antiarrhythmic agents, diuretics, anticoagulants; antineoplastic agents, hematopoietic growth factors, NSAIDs, psychotropic drugs, sympathomimetic agents, allopurinol, interferon alfa, levamisole (associated with cocaine).
- **Associations** to be aware of:
    - Bechet disease → more common among inhabitants of countries that border the ancient Silk Route, higher severity in men
    - Cryoglobulinemic vasculitis → > 90% associated with chronic hepatitis C infection.
    - Takayasu disease → is more prevalent in South Asian countries, females
    - GCA → above age 50, more in elderly women
    - GCA → associated with polymyalgia rheumatica.
    - PAN → Hepatitis B, also Hepatis C hairy cell leukemia.
    - Silica dust → pauci-immune vasculitis
    - Cocaine and levamisole induced vasculitis
- History & Physical – **when to consider vasculitis:**
    - Systemic or constitutional symptoms + with evidence of single / multiorgan dysfunction.
    - History (+) fevers, unexplained weight loss, nasal crusting, epistaxis, upper airway disease, ocular inflammation, acute foot drop or wrist drop, limb claudication, unexplained hemoptysis, hematuria, and hx of hepatitis.

- PE (+) sensory or motor neuropathy, palpable purpura, nasal septal perforation, saddle nose deformity (GPA), absent/diminished/ tender pulses, bruit, and blood pressure discrepancies, palpable purpura, livedo reticularis, digital gangrene, scalp tenderness/jaw claudication (GCA).
- Clinical abnormalities (alone or in combination) suggestive: pulmonary infiltrates + microscopic hematuria, chronic inflammatory sinusitis, mononeuritis multiplex, unexplained ischemic events, and glomerulonephritis w/ evidence of multisystem disease.

- DDx: Vasculitis has several **mimics**:
  - Important to rule out infection before starting immunosuppressants – ex: infective endocarditis, histoplasmosis, and gonococcal infection.
  - Coagulopathies can present with similar symptoms – ex: antiphospholipid syndrome, TTP/HUS, drugs (symptomatic, amphetamines, ergots), neoplasms (atrial myoma or lymphoma), emboli (septic, cholesterol), vascular malformations (fibromuscular dysplasia, Moya Moya)
- **Lab evaluation**:
  - CBC → may show neutrophilia, anemia, and thrombocytosis.
  - BMP and UA w/ urinary sediment → may see renal involvement in GPA, EGPA, PAN (glomerular sparing)
  - ESR, CRP (elevated acute phase reactants in most vasculitis)
  - LFTs, viral hepatitis panel, RF (elevated in PAN/cryo), complements (low in cryoglobulinemic) serum cryoglobulins, immunoelectrophoresis (monoclonal gammopathies can occur in Hepatitis C related vasculitis)
  - ANCA – can be detected by IIF (p-ANCA or c-ANCA) or ELISA (Specific antibodies anti-Pr3 and MPO)
    - Anti-proteinase 3 (anti-Pr3) is the antibody associated with the C-ANCA pattern
    - Anti-myeloperoxidase (anti-MPO) is the antibody associated with the P-ANCA pattern
    - ANCA-a Associated disorders:
      - c-ANCA/PR3: most common in GPA, also seen with MPA/EPGA, RPGN
      - p-ANCA/MPO: MPA > EPGA, also seen in drugs (hydralazine, propylthiouracil, d-pencillamine, minocycline)
      - p-ANCA to other antigens: in SLE, RA, myositis, HIV, IBD
      - If both (+) anti-MPO and anti-pr3 - consider Levamisole (cocaine induced vasculitis)
- **Imaging**
  - CXR or CT → indicated in patients with respiratory symptoms.
  - CT Sinuses if suspect GPA
  - Vascular imaging (MRI, MR angiograms, CT angiograms, vascular ultrasound, PET) may be used to detect large artery lesions, can be helpful if biopsy is negative/no accessible biopsy site
- Biopsy of the involved tissue → often essential for the diagnosis
  - GCA should be confirmed by biopsy (or imaging for large vessel vasculitis) when possible. Biopsy findings remain abnormal for up to 4 weeks after initiation of glucocorticoids, so always treat with high-dose prednisone and do not delay biopsy. If biopsy is negative, it does not completely exclude due to skip lesions, so treat if high clinical suspicion.
  - Skin biopsy of purpuric lesions = high diagnostic yield
  - Renal biopsies in patients with glomerulonephritis = high diagnostic yield
- Vascular Histology:

	Giant Cell Arteritis	**Granulomatosis With Polyangiitis (GPA)**	**Microscopic Polyangiitis (MPA)**	**Eosinophilic Granulomatosis With Polyangiitis (EGPA)**	**IgA Vasculitis**	**Hypersensitivity Vasculitis**
Vascular Histology	Granulomatous inflammation of large- and medium-sized arteries, with infiltration of CD4-positive lymphocytes, macrophages, and multinucleated giant cells	-Pauci-immune necrotizing granulomatous vasculitis	Pauci-immune non-granulomatous necrotizing vasculitis	Pauci-immune necrotizing granulomatous vasculitis with eosinophilic infiltration of vessel walls and tissues; extravascular granulomas.	Skin biopsy - leukocytoclastic vasculitis w/ heavy deposits of IgA and complement.	Skin biopsy - leukocytoclastic vasculitis without heavy IgA deposits.

Sources: https://www.ncbi.nlm.nih.gov/books/NBK545186/, MKSAP-19, graphic is original inspired from here