SMALL VESSEL VASCULITIS 🧬

Small vessel vasculitis affects capillaries, arterioles, and venules and is divided into two pathogenetically distinct groups:

- ANCA-associated vasculitis
- Immune complex-associated vasculitis

  Only the more common entities are discussed here.

Microscopic Polyangiitis (MPA) 🩺

Definition:

- Necrotizing vasculitis involving capillaries, small arterioles, and venules.
- Also called hypersensitivity vasculitis or leukocytoclastic vasculitis.

- Unlike PAN, all lesions are of the same age in a given patient.

Organs commonly involved:

- Skin, mucous membranes, lungs, brain, heart, GI tract, kidneys, muscles.
- Necrotizing glomerulonephritis (≈90%) and pulmonary capillaritis are especially common ⚠️.

Pathogenesis

- Strongly associated with MPO-ANCA.
- Neutrophil recruitment and activation → endothelial injury → necrotizing vasculitis.
- Immune complexes are absent (pauci-immune).
- Triggers (in some cases):
  - Drugs (e.g., hydralazine)
  - Microbes (e.g., *Staphylococcus aureus*) 🦠

Morphology 🔬

- Segmental fibrinoid necrosis of the media with focal transmural necrotizing lesions.
- No granulomatous inflammation.
- Spares medium- and large-sized arteries → macroscopic infarcts uncommon.
- In postcapillary venules: neutrophils with nuclear fragmentation (karyorrhexis) → leukocytoclastic vasculitis.
- Most lesions are pauci-immune, although early skin lesions may show Ig and complement.

Clinical Features

- Typically affects older adults, but can occur in children.
- Manifestations depend on the vascular bed involved:
    - Hemoptysis (pulmonary capillaritis)
    - Hematuria & proteinuria (glomerulonephritis)

    - Abdominal pain or bleeding
    - Myalgia, muscle weakness
    - Palpable purpura on skin 🟣
- Treatment: immunosuppression + removal of triggering agent → durable remission in most patients, except those with severe renal or CNS disease.

Granulomatosis with Polyangiitis (GPA) 🫁

Definition (formerly Wegener granulomatosis): ANCA-positive necrotizing vasculitis characterized by a classic triad:

- Necrotizing granulomas of the upper respiratory tract (ear, nose, sinuses, throat) ± lower respiratory tract (lungs)
- Necrotizing or granulomatous vasculitis of small- to medium-sized vessels (capillaries, venules, arterioles, arteries), especially in lungs and upper airways

- Focal necrotizing, often crescentic, glomerulonephritis

"Limited" GPA may involve only the respiratory tract, whereas widespread disease can affect eyes, skin, heart, and other organs, clinically resembling PAN plus respiratory involvement ⚠️.

Pathogenesis

GPA is thought to begin as a cell-mediated hypersensitivity reaction to inhaled infectious or environmental antigens.

PR3-ANCA is present in ~95% of cases and is central to tissue injury.

Flow sequence:

Inhaled antigen exposure → T-cell activation → PR3-ANCA formation → neutrophil activation → endothelial injury → necrotizing granulomatous vasculitis 🔁

PR3-ANCA titers correlate with disease activity:

- Effective therapy → titers fall
- Relapse → titers rise 📈

Morphology 🔬

- Upper respiratory tract: granulomatous sinusitis; ulcerated lesions of nose, palate, or pharynx
- Lungs: diffuse infiltrates → granulomatous nodules → central cavitation; vessel destruction may cause hemorrhage and hemoptysis
- Vasculature: multifocal necrotizing granulomatous vasculitis with surrounding fibroblastic proliferation
- Kidneys:
    - Mild disease → focal, segmental necrotizing glomerulonephritis
    - Severe disease → diffuse necrosis with epithelial crescent formation (crescentic GN)

Chronic lesions may progress to fibrosis and organization 🧠.

Clinical Features

- Typical patient: middle-aged man, though all ages and women may be affected
- Common manifestations:
  - Bilateral pneumonitis with nodules/cavities (≈95%)
  - Chronic sinusitis (≈90%)
  - Nasopharyngeal mucosal ulceration (≈75%)
  - Renal disease (≈80%) → hematuria, proteinuria, or rapidly progressive renal failure
  - Rash, myalgias, arthritis, neuritis, fever
- Untreated disease: ≈80% mortality at 1 year
- Treatment: steroids + cyclophosphamide, TNF inhibitors, or rituximab → marked survival improvement, but relapses are common ⚕️

Eosinophilic Granulomatosis with Polyangiitis (EGPA / Churg-Strauss Syndrome)

Definition:

Rare (~1 in 1 million) small-vessel necrotizing vasculitis associated with:

- Asthma & allergic rhinitis
- Lung infiltrates
- Peripheral eosinophilia
- Extravascular necrotizing granulomas
- Eosinophil-rich inflammation of vessels and perivascular tissues

Pathogenesis

Likely due to hyperresponsiveness to allergic stimuli.

- MPO-ANCA present in ~50% of cases → classified as ANCA-associated vasculitis

- ANCA-positive patients more commonly develop glomerulonephritis

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Key Pathologic Features

- Small-vessel necrotizing vasculitis
- Prominent eosinophils + granulomas (distinguishes EGPA from PAN and microscopic polyangiitis)
- Renal involvement usually as focal and segmental glomerulosclerosis

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Clinical Features

- Cutaneous palpable purpura
- Gastrointestinal bleeding
- Renal disease
- Cardiac involvement in ~60% due to eosinophilic myocardial infiltration → cardiomyopathy, major cause of death ❤️

Thromboangiitis Obliterans (Buerger Disease) 🚬

Definition

Thromboangiitis obliterans is a segmental, thrombosing inflammatory disease affecting small- and medium-sized arteries, mainly of the extremities (tibial and radial arteries).

Veins and nerves may also be involved, which is a distinguishing feature.

Etiopathogenesis

Strongly associated with heavy tobacco smoking, usually beginning before 35 years of age.

Pathogenetic sequence:
Tobacco exposure → Endothelial cell dysfunction
→ ↓ Endothelium-dependent vasodilation + ↑

prothrombotic mediators → Endothelial injury → Immune-mediated vascular inflammation → Segmental thrombosis and vessel occlusion

Additional contributing factors:

- Direct endothelial toxicity from tobacco components
- Hypersensitivity to tobacco extracts
- Genetic predisposition (association with certain HLA haplotypes)

Morphology

Early stage changes:
Acute and chronic inflammation of vessel wall → Luminal thrombosis → Mixed inflammatory infiltrate → Formation of small microabscesses → Occasional granulomatous inflammation

Progression:
Inflammation spreads outward → Involvement of adjacent veins and nerves → Organization of thrombus

→ Recanalization (partial) → Progressive fibrosis encasing artery, vein, and nerve

(Key point: Extension into veins and nerves is uncommon in other vasculitides.)

Clinical Features

- Early manifestations:

Cold exposure → Raynaud phenomenon

Exercise → Instep claudication (foot pain on walking)

Venous involvement → Superficial nodular phlebitis

- Advanced disease:

Persistent vascular insufficiency → Severe rest pain (often due to nerve involvement) → Chronic ischemic ulcers → Gangrene

- Effect of smoking cessation:

Early disease → May prevent progression

Established disease → Vascular lesions usually do not regress despite abstinence

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Infectious Vasculitis 🦠

Etiology

Caused by direct invasion of vessel walls by infectious organisms.

- Common pathogens:

- Bacteria
- Fungi (especially *Aspergillus* and *Mucor* species)

- Routes of infection:

Local spread from adjacent infection → Pneumonia / abscess → Direct arterial invasion

OR

Hematogenous spread → Bacteremia → Septic emboli from infective endocarditis

Pathologic Consequences

Infection of vessel wall → Weakening of arterial wall → Mycotic aneurysm formation

OR

Inflammation of vessel → Thrombosis → Ischemia → Infarction

Example (CNS):

Bacterial meningitis → Arterial inflammation → Thrombosis → Infarction → Spread of infection into brain parenchyma

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-> The End <-