NOTES
VASCULITIS

GENERALLY, WHAT IS IT?

PATHOLOGY & CAUSES

- Inflammation of blood vessels
- *Vasculitides categorized by blood vessel size:* small, medium, large

CAUSES

Damaged endothelium

- Damaged endothelium → exposed collagen, tissue → increased blood coagulation → weakened, damaged blood vessel walls → aneurysms → vessel wall heals, stiffens as fibrin deposits

Autoimmune disease

- *Direct method:* body mistakes endothelial layer of blood vessel for foreign pathogen → attacks
  - *Molecular mimicry:* immune system white blood cells (WBCs) mistake normal antigens of endothelial cells for foreign invaders (e.g. bacteria)
  - Medium, large-vessel vasculitides
- *Indirect method:* immune system attacks healthy cells near vascular endothelium → damages endothelial cells
  - Small-vessel vasculitides (exception: Henoch-Schönlein purpura)

SIGNS & SYMPTOMS

- *Inflammatory response symptoms:* fever, weight loss, malaise, fatigue
- Ischemia
  - Blood cells clump to exposed collagen inside blood vessels → blood clots → restricted blood flow
  - Fibrin deposits in vessel wall → wall thickens, bulges into vessel → stenosis → restricted blood flow

DIAGNOSIS

LAB RESULTS

- C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), complete blood count (CBC), various autoantibodies
- Biopsy vessel segment

TREATMENT

MEDICATIONS

Reduce inflammatory response

- Corticosteroids/immunosuppressive drugs

VASCULITIDES OVERVIEW

	AFFECTED VESSELS	LOCATION	SIGNS & SYMPTOMS
GIANT CELL ARTERITIS	Large	Temporal branch of carotid artery	Headache, visual disturbances, jaw pains
TAKAYASU ARTERITIS		Arteries from aortic arch (branch points)	Weak pulse, neurological symptoms
KAWASAKI DISEASE	Medium	Coronary arteries serving heart	4 of 5 CRASH symptoms, prolonged high fever
POLYARTERITIS NODOSA		Commonly affects skin, can affect almost any organ	"String of beads" appearance on angiogram, end organ ischemic damage
BUERGER'S DISEASE		Blood clots in small arteries of fingers, toes	Ulcers, dead tissues in extremities
GRANULOMATOSIS WITH POLYANGIITIS	Small	Nasopharynx, lungs, kidneys	Chronic pain, saddle nose deformity, breathing difficulties, ulcers with bloody coughing, decreased urine production, increased blood pressure
MICROSCOPIC POLYANGIITIS		Vessels of kidneys, lungs	Kidney inflammation, weight loss, skin lesions, fever, nerve damage
CHURG-STRAUSS SYDNROME		Vessels of kidneys, lungs	Sinusitis, lung damage, kidney damage
HENOCH-SCHONLEIN PURPURA		Vessels of kidneys, lungs	Symptoms depend on where IgA attacks small blood vessels
BEHCET'S SYNDROME	All vessels	All vessels	Recurrent oral ulcers, genital ulcers, skin papules, decreased vision, headaches, fever, disorientation, stroke, Swollen joints affecting knees, wrists, ankles

BEHCET'S DISEASE

osms.it/behcets-disease

PATHOLOGY & CAUSES

- Autoimmune multisystem vasculitis affecting any sized vessel, arterial/venous

RISK FACTORS

- Individuals who are 20–30 years old, of Middle Eastern/Asian descent, biologically male

COMPLICATIONS

- Blindness from untreated uveitis (inflammation in eyes)

SIGNS & SYMPTOMS

- Recurrent, painful, sterile oral/genital ulcers (pathergy)
- Skin papules indistinguishable from acne
- Uveitis, optic neuritis, conjunctivitis iritis
- Neurologic involvement (meningoencephalitis, intracranial HTN, stroke, headache)
- Arthritis (knees, ankles)
- Fever, weight loss

DIAGNOSIS

OTHER DIAGNOSTICS

Clinical presentation

- Recurrent oral ulcers (three in one year) + two of following
- Recurrent genital ulcers
- Eye lesions, uveitis
- Skin lesions
- Positive pathergy test
- ≥ 2mm papule 24–48 hours after oblique insertion 5mm into skin with 20-gauge needle, often performed on forearm

TREATMENT

MEDICATIONS

- Skin creams, mouth rinses, eye drops
- *Corticosteroids*: (e.g. prednisone) control inflammation
- *Medications:* (e.g. azathioprine, cyclosporine, or cyclophosphamide) suppress immune system
- *Medications:* (e.g. interferon alfa-2b) alter immune system response

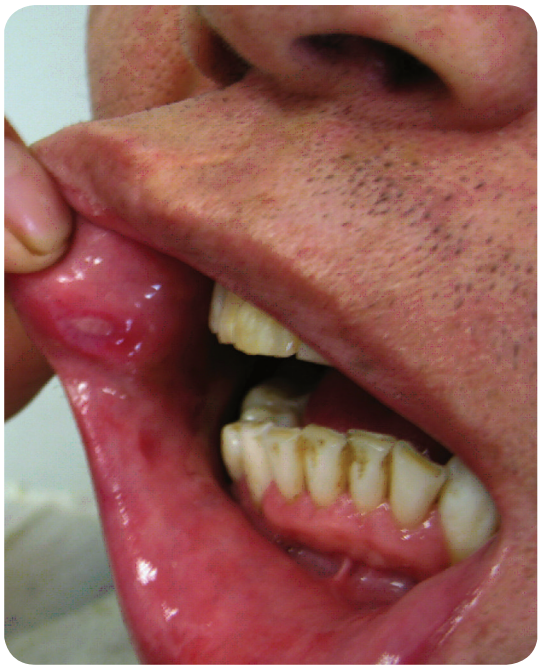

Figure 25.1 Mucosal ulcer in an individual with Behcet's disease.

BUERGER'S DISEASE

osms.it/buergers

PATHOLOGY & CAUSES

- Nonatherosclerotic, segmental, inflammatory disease affecting small-, medium-sized veins, arteries of extremities → inflammatory occlusive thrombus → distal extremity ischemia, digit ulcers/gangrene → autoamputation
- AKA thromboangiitis obliterans
- Associated with use of tobacco products

RISK FACTORS

- Individuals < 45 years old, who are biologically male, use tobacco
- Chronic anaerobic periodontal infection (⅔ of people with Buerger disease)

SIGNS & SYMPTOMS

- Ulceration of digits
- *Ischemic claudication:* cold, painful, cyanotic distal extremities
- Subcutaneous nodules, superficial thrombophlebitis
- Paresthesias of extremities
- Raynaud phenomenon

DIAGNOSIS

DIAGNOSTIC IMAGING

Angiogram

- Lack of atherosclerosis
- *Collateralization, segments of diseased vessel interspersed:* smoking → atherosclerosis + Buerger disease simultaneously

LAB RESULTS

Biopsy

- Definitive; rarely (healing a concern)
- Histopathologically, acute-phase lesions show highly cellular, inflammatory thrombus with minimal inflammation of blood vessel

TREATMENT

- Immediate smoking cessation

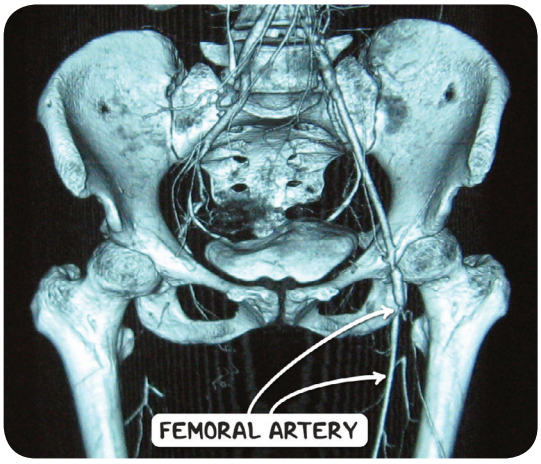

Figure 25.2 A volume rendered CT angiogram demonstrating obliteration of the right femoral artery secondary to thromboangiitis obliterans. There is also stenosis of the femoral artery on the left.

CHURG–STRAUSS SYNDROME

osms.it/churg-strauss-syndrome

PATHOLOGY & CAUSES

- Small, medium vessel granulomatous vasculitis involving many organ systems (cardiac, gastrointestinal, respiratory, skin, renal, neurologic) in individuals with allergy-related respiratory conditions (esp. asthma)
- AKA eosinophilic granulomatosis with polyangiitis (EGPA), allergic granulomatosis
- P-ANCA reacting with neutrophilic myeloperoxidase
- Etiology unknown

RISK FACTORS

- Age 30–50; asthma/nasal issues

SIGNS & SYMPTOMS

- Allergies
  - Asthma, chronic rhinosinusitis, usually precedes vasculitic phase by 8–10 years
- Neurological
  - Peripheral neuropathy (usually mononeuritis multiplex)
  - Subarachnoid, cerebral hemorrhage, cerebral infarction, cranial nerve palsies
- Skin
  - Palpable purpura, subcutaneous nodules
- Cardiac
  - Damage → heart failure, arrhythmias
  - Accounts ½ deaths
- Other organ systems (renal, gastrointestinal) → symptoms similar to medium-vessel vasculitides

DIAGNOSIS

DIAGNOSTIC IMAGING

Chest X-ray

- Transient, patchy, symmetrical opacities, often in hilar/peripheral distribution
- Pulmonary hemorrhage
- Bilateral nodular disease without cavitation

High-resolution CT scan

- Peribronchial, septal thickening
- Widely scattered indistinct opacities

Pulmonary function test

- Obstructive pattern consistent with asthma

Bronchoalveolar lavage

- High % of eosinophils

LAB RESULTS

- Eosinophilia > 1500/microL, > 10% on differential leukocyte count
- P-ANCA/MPO-ANCA antibodies
- Acute phase reactants: ↑ ESR, CRP

Lung/skin biopsy

- Definitive

TREATMENT

- Prognosis poor (five year survival, 25% without treatment; 50% with treatment)

MEDICATIONS

- Corticosteroids, immunosuppressive drugs

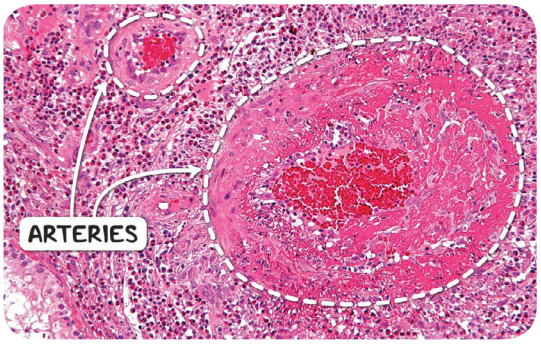

Figure 25.3 Histological appearance of vasculitis in Churg-Strauss syndrome. The background is composed almost entirely of eosinophils.

GIANT CELL ARTERITIS

osms.it/giant-cell-arteritis

PATHOLOGY & CAUSES

- Chronic vasculitis of large-, medium-sized vessels
- AKA temporal arteritis
- Cranial branches of arteries originating from aortic arch
  - Temporal branch of carotid artery
- Aorta, carotids also affected
- Most common systemic vasculitis

CAUSES

- *Unknown:* possibly genetic, environmental, autoimmune-related

RISK FACTORS

- Almost always in individuals ≥ 50
- More common in individuals who are biologically female
- Strong association with polymyalgia rheumatica (40–50% of GCA individuals)

COMPLICATIONS

- Irreversible blindness (if untreated)

SIGNS & SYMPTOMS

- *New-onset headache (most common):* temporal branch of carotid artery
- Jaw claudication (pain when chewing)
- *Transient unilateral vision loss (amaurosis fugax):* ophthalmic artery
- Carotid bruits, decreased pulses in arms, aortic regurgitation
- Tender, palpable nodules, absent temporal pulse
- Increased risk of aortic dissection, aortic aneurysm

MNEMONIC: TEMPORAL

Characteristics of Temporal (Giant cell) arteritis

Temporal artery tenderness
ESR >100
Multinucleated giant cells
Pain
Onset >50 years old
polymyalgia **R**heumatica association
Amaurosis fugax
Lost vision

DIAGNOSIS

LAB RESULTS

- Extremely elevated ESR (> 100mm/hr), ↑ IL-6 associated with active disease

Temporal artery biopsy

- Tightly packed monocytes/macrophages, as if one giant cell, in internal elastic lamina; segmental pattern; 90% sensitivity

TREATMENT

- Corticosteroids

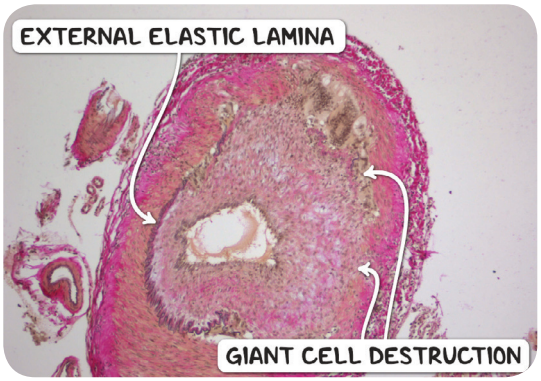

Figure 25.4 A histology photomicrograph demonstrating giant cell arteritis. The external elastic lamina to the right has been completely destroyed by granulomatous inflammation.

GRANULOMATOSIS WITH POLYANGIITIS

osms.it/granulomatosis-with-polyangiitis

PATHOLOGY & CAUSES

- Small-vessel vasculitis involving nasopharynx, lungs, kidneys
- AKA Wegener's granulomatosis
- Granulomatous disease of respiratory tract → systemic necrotizing vasculitis
- B-cells release cytoplasmic antineutrophil cytoplasmic antibodies (c-ANCA) → binds to proteinase 3 (neutrophil granule) in neutrophils → neutrophils release free radicals → free radicals damage neighboring endothelial cells → vasculitis
- Triad
  - Focal, necrotizing vasculitis
  - Necrotizing granulomas in upper airway, lungs
  - Necrotizing glomerulonephritis (renal vasculitis)

RISK FACTORS

- Middle aged individuals who are biologically male

MNEMONIC: 3Cs

"C" drawn from upper respiratory tract to lungs, kidneys (all involved)

C-anca

Corticosteroids/ cyclophosphamide (treatment)

SIGNS & SYMPTOMS

- *Chronic pain:* oral ulcers, bloody nasal mucus, chronic sinusitis, saddle nose (nose caves in/curls)
- Hemoptysis, dyspnea, cough, pleuritic chest pain (inflammation of lung vessels)
- Decreased urine production, hypertension, hematuria, red cell casts, proteinuria (glomerular inflammation)

DIAGNOSIS

DIAGNOSTIC IMAGING

Abnormal chest X-ray

- Nodules, fixed infiltrates, cavities, bronchial stenosis

LAB RESULTS

- c-ANCA in 90%, thrombocytopenia
- Abnormal urinary sediment; microscopic hematuria (with/without red cell casts)

Open lung biopsy

- Confirm diagnosis; granulomatous inflammation of artery/perivascular area

OTHER DIAGNOSTICS

Nasal/oral inflammation

- Oral ulcers; painful/painless
- Purulent bloody nasal discharge
- Chronic sinusitis, saddle nose/destructive sinonasal disease

TREATMENT

- Relapse common if c-ANCA still present

MEDICATIONS

- Corticosteroids, cyclophosphamide/rituximab

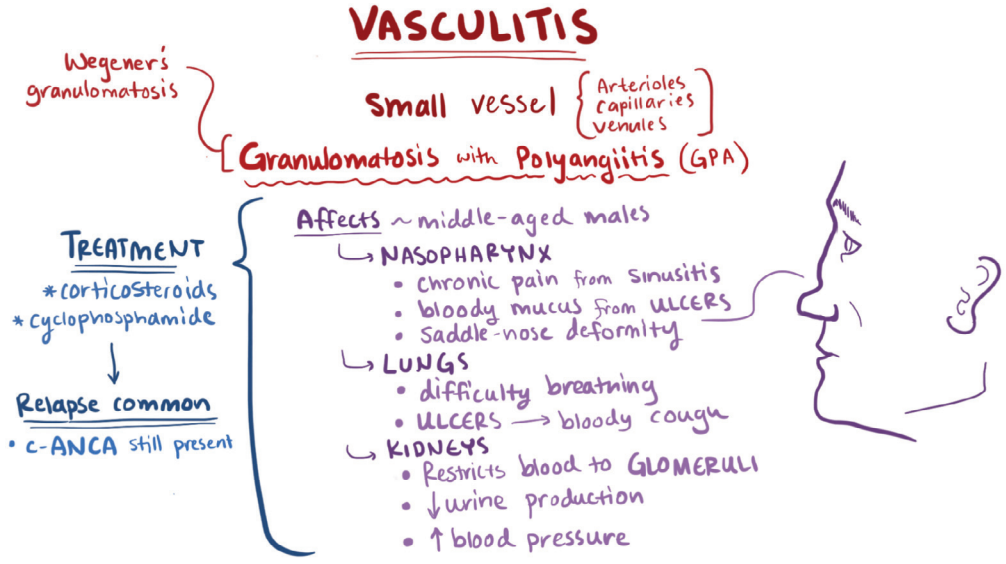

Figure 25.5 Illustration demonstrating the effects of granulomatosis with polyangiitis.

HENOCH–SCHÖNLEIN PURPURA

osms.it/henoch-schonlein-purpura

PATHOLOGY & CAUSES

- Small vessel vasculitis secondary to IgA immune complex deposition.
- *Elevated IgA in blood targets self-endothelial cells:* molecular mimicry
- Most common systemic vasculitis of childhood
- Frequently follows upper respiratory infection
- Associated with Berger disease (IgA nephropathy)
- Unknown cause; immune-mediated vasculitis triggered by infections/immunizations
- Self-limited disease
- Tetrad
  - Palpable purpura, without coagulopathy/thrombocytopenia; mainly lower extremities
  - Arthritis/arthralgias
  - Renal disease
  - Abdominal pain

SIGNS & SYMPTOMS

- Palpable purpura of buttocks, legs (skin discolouration, as if blood collected under skin surface); abdominal pain; arthritis/arthralgias; hematuria, decreased kidney function (associated with IgA nephropathy)

DIAGNOSIS

LAB RESULTS

Biopsy

- Definitive, not necessary

TREATMENT

- Self-resolving, may reoccur

MEDICATIONS

- Steroids, only if severe

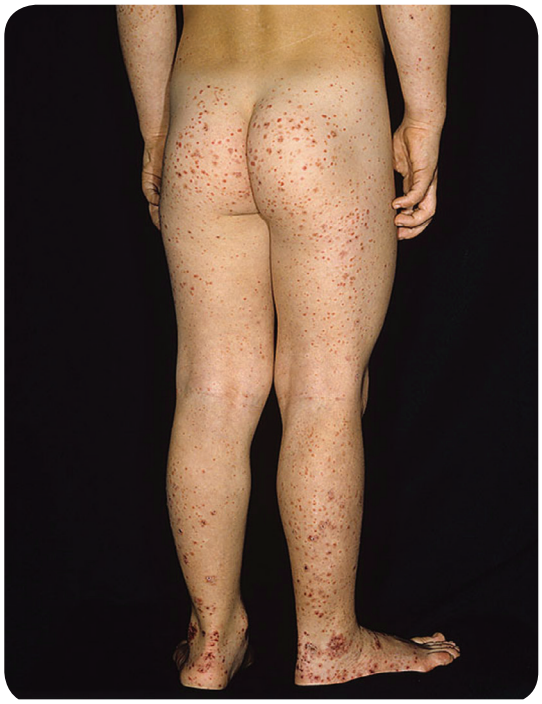

Figure 25.6 The clinical appearance of Henoch-Schönlein purpura.

KAWASAKI DISEASE

osms.it/kawasaki-disease

PATHOLOGY & CAUSES

- *Coronary arteries:* inflammation → aneurysms
- AKA mucocutaneous lymph node syndrome
- Most common type of vasculitis in children
- Usually self-limited

RISK FACTORS

- Infants, children < five years old, Asian descent, biologically male

COMPLICATIONS

- Coronary artery aneurysm
- Decreased myocardial contractility → heart failure
- Myocardial infarction (MI)
- Arrhythmias
- Peripheral artery occlusion

SIGNS & SYMPTOMS

MNEMONIC: CRASH & BURN

Signs & Symptoms

Conjunctivitis: bilateral, nonexudative

Polymorphous **R**ash: desquamating

Cervical lymph**A**denopathy

Strawberry tongue: cracked red lips, oral mucositis

Hand-foot erythema/desquamation: edema, erythema

Fever: **"burn"**

DIAGNOSIS

DIAGNOSTIC IMAGING

Chest X-ray

- Cardiomegaly

Echocardiography

- Coronary artery aneurysms, pericardial effusions, decreased contractility

LAB RESULTS

- ↑ CRP, ESR, platelet count (reactive thrombocytosis)

OTHER DIAGNOSTICS

- Four of five CRASH symptoms, high fever lasting five days

ECG

- Arrhythmias, abnormal Q waves, prolonged PR, QT intervals

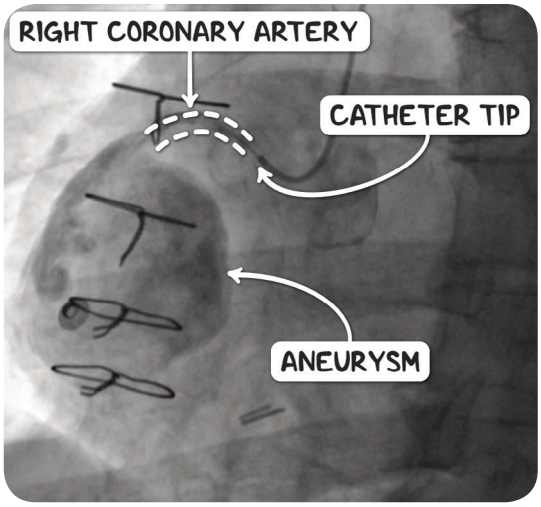

Figure 25.7 A coronary angiogram demonstrating a massive right coronary artery aneurysm.

TREATMENT

MEDICATIONS

- Intravenous immunoglobulin (IVIG)
- Aspirin

MICROSCOPIC POLYANGIITIS

osms.it/microscopic-polyangiitis

PATHOLOGY & CAUSES

- *Necrotizing vasculitis:* kidney, lung vessels
- No granulomas present
- Associated with perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA)/MPO-ANCA
- Pauci-immune glomerulonephritis (minimal immunofluorescent staining for IgG)
- Older adults

SIGNS & SYMPTOMS

- Similar to granulomatosis with polyangiitis, without nasopharyngeal involvement
- Fever, weight loss, fatigue, myalgia, arthralgias
- Cough, dyspnea, hemoptysis, pleuritic chest pain
- Decreased urine output, hematuria, red cell casts, proteinuria
- *Skin lesions (especially lower extremities):* purpura → focal necrosis → ulceration

DIAGNOSIS

LAB RESULTS

- p-ANCA/MPO-ANCA levels; elevated ESR, CRP, anemia, increased creatinine
- Protein, red blood cells (RBCs)

TREATMENT

- Relapse common

MEDICATIONS

- Corticosteroids, cyclophosphamide

POLYARTERITIS NODOSA

osms.it/polyarteritis-nodosa

PATHOLOGY & CAUSES

- Immune system forms antibody antigen complex (sometimes associated with hepatitis B) → deposits in vessel wall → immune reaction → invasion of polymorphonuclear leukocytes → segmental, transmural inflammation of muscular arteries → necrosis of three artery layers (tunica intima, media, adventitia) → fibrosis as walls heal (fibrinoid necrosis) → fibrosed vessel wall weakens, prone to aneurysms → fibrotic aneurysms (hard bulges) develop
- Different stages of inflammation in different vessels

RISK FACTORS

- Individuals > 40 years old, biologically male
- Active hepatitis B (HBV)/hepatitis C (HCV) infection
- HIV
- Prescription/illicit drug exposure, amphetamines

SIGNS & SYMPTOMS

- *Systemic:* fever, fatigue, weight loss, arthralgia
- End organ ischemic damage
- *Renal arteries:* HTN
- *Mesenteric artery:* mesenteric ischemia, severe abdominal pain, gastrointestinal bleeding
- *Mononeuropathy multiplex:* motor, sensory deficits occur in > one nerve throughout body
- *Skin arteries:* skin lesions (e.g. ulcers, erythematous nodules resembling erythema nodosum, purpura, livedo reticularis)

DIAGNOSIS

DIAGNOSTIC IMAGING

Mesenteric angiogram

- "String of beads" pattern along artery, spasms

LAB RESULTS

- HBV, HCV serologies, Cr, muscle enzymes, urinalysis

Biopsy

OTHER DIAGNOSTICS

Physical exam

- Vascular lesions, motor weakness (due to ischemia)

TREATMENT

MEDICATIONS

- Corticosteroids
- *Cyclophosphamide:* supplement corticosteroids in moderate to severe cases

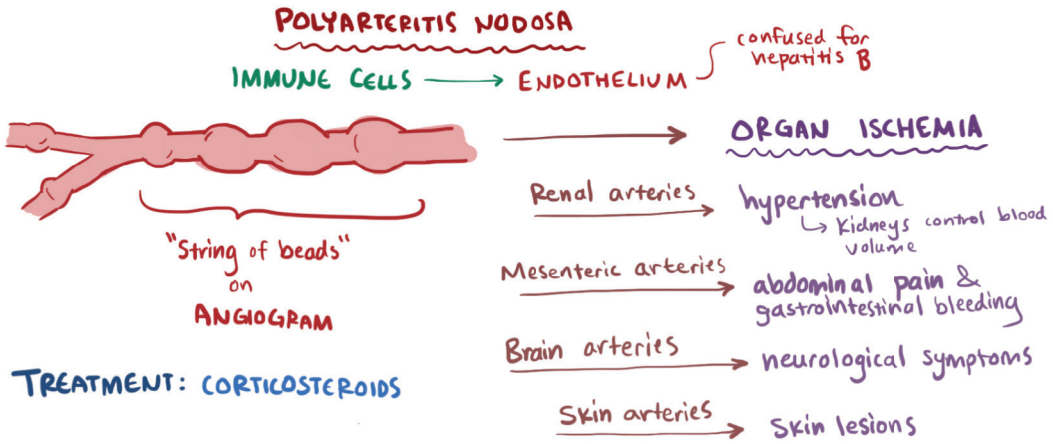

Figure 25.8 Illustration showing polyarteritis nodosa's characteristic "string of beads" pattern running along the artery.

TAKAYASU ARTERITIS

osms.it/takayasus-arteritis

PATHOLOGY & CAUSES

- Segmental, patchy granulomatous vasculitis of aortic arch, major branches
- Stenosis, thrombosis, aneurysm

CAUSES

- Unknown; possibly bacterial (e.g. spirochetes, Mycobacterium tuberculosis, streptococcal)
- Genetic

RISK FACTORS

- Individuals of Asian descent, < 40 years old, biologically female

COMPLICATIONS

- Limb ischemia; aortic aneurysm; aortic regurgitation; stroke; secondary hypertension (HTN) due to renal artery stenosis

SIGNS & SYMPTOMS

- Inflammation
  - *Aortic branches, upper extremities:* weak/absent pulse
  - *Aortic branch, head:* neurological symptoms (e.g. headaches, syncope, stroke)
  - *Coronary arteries:* angina
  - *Renal arteries:* HTN
- *Visual disturbances:* ocular vessels/retinal hemorrhage
- *Constitutional symptoms:* fever, night sweats, arthralgias, malaise, fatigue
- Ischemia in areas of stenosis

DIAGNOSIS

DIAGNOSTIC IMAGING

CT angiography (CTA), magnetic resonance angiography (MRA)

- Luminal narrowing/occlusion of major aortic branches
- Vessel wall thickening
- Aortic valve disease (e.g. regurgitation,

stenosis)
- Aneurysmal dilation/pseudoaneurysm formation

Ultrasound
- Homogeneous and circumferential thickening of arterial wall (contrast to atherosclerotic plaque: non-homogeneous, calcified, irregular walls)
- Vascular occlusion due to intimal thickening/secondary thrombus formation
- Loss of pulsatility of vessel

LAB RESULTS
- ↑ ESR

TREATMENT

MEDICATIONS
- Corticosteroids
- Treat HTN

SURGERY
- Angioplasty (when no acute inflammation); bypass grafting if severe

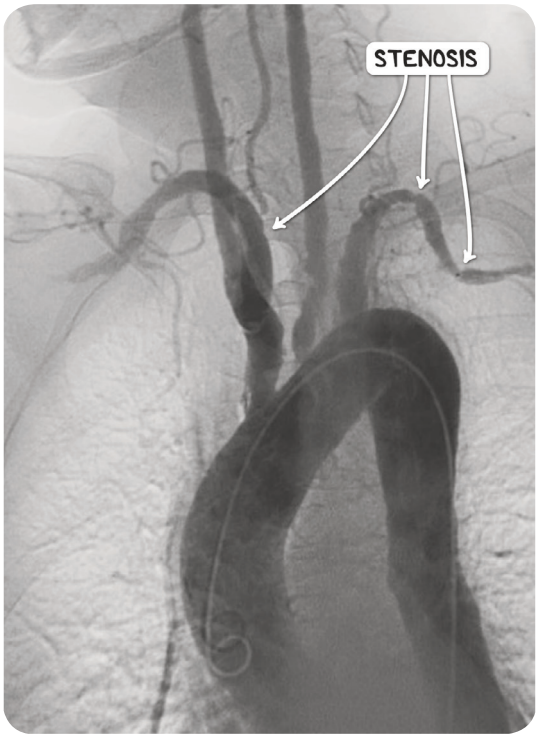

Figure 25.9 An angiogram demonstrating multiple stenosis of the aortic arch vessels, a feature of Takayasu arteritis.