Systemic Vasculitis

- Vasculitic diseases are a group of rare autoimmune diseases characterized by blood vessel inflammation (vasculitis) which can lead to ischemia, necrosis or hemorrhage with subsequent end-organ damage
- Secondary vasculitis is more common than primary (idiopathic), secondary causes include
    - Infections : TB / HIV / HBV / Syphilis
    - Drug induced : heroin / cocaine / amphetamines / Allopurinol / hydralazine / propylthiouracil
    - Malignancies : multiple myeloma
    - Autoimmune diseases : sarcoidosis / SLE
- Temporal Arteritis is the most common form of vasculitis
- Classification of Vasculitic diseases is based on the size of the involved blood vessels
    - Large-vessel vasculitis
    - Medium-vessel vasculitis
    - Small-vessel vasculitis
        - ANCA associated
        - Non-ANCA associated
- General constitutional symptoms seen in ALL cases of Vasculitis : fever / weight loss / arthralgia / myalgia / night sweats / fatigue / high ESR and CRP
- Urinalysis is the most important investigation as prognosis is determined by the extent of renal involvement
- The appearance of active urinary sedement or a rise in serum creatinine in a vasculitic patient is an indication for prompt aggressive treatment
- In treatment
    - Medium to small vessel respond to steroids + immunosuppressives
    - Large vessel respond to high dose steroids
    - Small vessel respond to low dose steroids

ANCA-Associated Small Vessel Vasculitis

- Include : GEM
    - Granulomatosis with polyangiitis GPA
    - Eosinophilic Granulomatosis with polyangiitis EGPA
    - Microscopic polyangiitis MPA
- ANCA : Antineutrophil Cytoplasmic Antibodies, 2 types :
    - cANCA : against proteinase 3 : found in GPA
    - pANCA : against myeloperoxidase : found in MPA & EGPA
- This type of vasculitis has a late age onset and is found more in women
- Wegner Granulomatosis (GPA)
    - It typically affects the lungs, ENT and kidneys
    - Symptoms depend on the affected organ

        - Lungs : dyspnea / hemoptysis / cough / pulmonary fibrosis, hemorrhage or nodules
        - ENT (first presentation) : chronic recurrent rhinitis or sinusitis / epistaxis / nasal septal perforation / chronic otitis media / saddle nose deformity / Strawberry gingivitis
        - Skin : purpura or papules
        - Renal : RPGN
        - Eye : episcleritis / conjunctivitis / proptosis
        - Cardiac : Pericarditis / involvement of the coronaries
    - Diagnosis
        - Microscopic hematuria, proteinuria or urine sediments in renal involvement
        - Pulmonary CT or Xray
        - Biopsy
    - Treatment
        - Glucocorticoids PLUS a glucocorticoid-sparing agent like methotrexate
        - Plasmapheresis
- Churg Strauss Syndrome (EGPA)
    - Usually involves the respiratory tract mimicking severe asthma
    - Cardiac involvement is the main cause of death
    - 3 phases
        - Prodromal phase : Severe allergic asthma attacks that may last up to four years, manifesting as atopic features like rhinitis and sinusitis
        - Eosinophilic phase : eosinophilic infiltration of the lungs, the heart and the GI tract
        - Vasculitic phase : skin nodules / palpable purpura / Mononeuritis multiplex usually with foot drop / RPGN
    - Diagnostics
        - CBC will reveal eosinophilia
        - High IgE
        - Pulmonary CT
        - Echocardiography
        - Biopsy
    - Treatment : glucocorticoids PLUS cyclophosphamide
- Microscopic Polyangitis MPA
    - The only form of vasculitis without granulomatous inflammation
    - It is mainly a renal disease (RPGN) with pulmonary manifestations (hemoptysis and pulmonary hemorrhage)
    - The nasopharynx is usually not affected (no sinusitis or rhinitis)
    - Other symptoms
        - Palpable purpura
        - GI : abdominal pain or GI bleeding
        - Mononeuritis multiplex

    - The absence of granulomas on histopathology plus pANCA positivity helps differentiate MPA from GPA, as they have very similar clinical features
    - Treatment : glucocorticoids PLUS cyclophosphamide
- In GPA, the lung infiltrates are fixed while in EGPA they are not fixed
- Renal & lung involvement are negative prognostic factors in GPA and MPA
- Treatment of ANCA associated vasculitis
    - Induction : IV steroids + IV cyclophosphamide or rituximab
    - Maintenance : Oral steroids or methotrexate or azathioprine

Non-ANCA-Associated Small Vessel Vasculitis

- Henoch Schonlein Purpura HSP aka IgA Vasculitis
    - Occurs in young children aged 4-6 years and is more common in males
    - It is the most common form of vasculitis in children
    - Up to 90% of cases are preceded by an upper respiratory infection mainly by group A streptococcus usually 1-3 weeks prior to presentation
    - Other causes : IgA nephropathy / drugs like ACEi / vaccines / genetic predisposition
    - Symptoms
        - Skin (present in 100% of cases) : Symmetrically distributed erythematous papules or urticarial lesions that coalesce into palpable purpura most commonly on the legs and buttocks
        - Arthralgia and arthritis
        - GI : Colicky abdominal pain / Melena / Vomiting / Intussusception
        - Kidneys : IgA neuropathy / Hematuria & proteinuria / focal or diffuse proliferative glomerulonephritis
    - Mnemonic is PAPAH : purpura / abdominal pain / arthritis / hematuria
    - Diagnosis
        - High Serum IgA
        - Skin biopsy will show leukocytoclsdtic vasculitis and IgA & C3 complex deposits
        - Abdominal ultrasound for Intussusception
        - Urine analysis
        - Stool blood test for GI bleeding
    - It is a self limiting disease and only requires supportive care (Systemic glucocorticoids are usually given)
- Cryoglobulinaemia
    - Cryoglobulins are immunoglobulins (IgG / IgM / IgA) that precipitate at temperatures < 37 and redissolve on rewarming
    - These IGs get deposited in blood vessels causing inflammation
    - The most common etiology is viral infections specifically Hepatitis C (80-90% of cases). Other causes include SLE and other rheumatic diseases
    - Clinical presentation

        - Most patients are asymptomatic
        - Skin (in 100% of cases) : palpable purpura
        - Vasomotor : Raynaud phenomenon / acrocyanosis
        - Polyneuropathy
        - Hepatosplenomegaly
        - Membranoproliferative glomerulonephritis
    - Diagnosis
        - Elevated Cryoglobulins and Rheumatoid Factor RF
        - Low C4
        - Hep C serology
        - Renal or skin Biopsy
    - Treatment
        - Immunosuppressants : IF-alpha / ribavirin / rituximab
        - Plasmapheresis for severe cases to remove cryoglobulins
        - Antivirals for hepatitis C
- Hypersensitivity vasculitis
    - Immune complex mediated vasculitis involving cutaneous small vessels WITHOUT other organs (or very mild involvement)
    - Can be primary (idiopathic) or secondary to drugs, infections, or rheumatic diseases
    - Patients may report flare triggers such as prolonged sitting or standing, alcohol consumption, or URTIs
    - Clinical presentation : Painful, symmetric nonblanching palpable purpura on the lower limbs
    - Other skin manifestations like subcutaneous nodules, urticaria, ulcers or vesicles may be present
    - Diagnosis : skin biopsy
    - Treatment
        - Treat the underlying etiology or stop the drug
        - Immunosuppressants

Medium Vessel Vasculitis (muscular arteries)

- Polyarteritis Nodusa PAN
    - Aneurysms and stenosis lesions at muscular arteries at their branching points and mainly involve the renal arteries
    - It most commonly involves the skin, peripheral nerves, muscles, joints, GI tract and kidneys (the lungs are NOT involved)
    - It is more common in males
    - Most cases are idiopathic but it is associated with viral infections like HBV or HIV
    - Symptoms are based on the involved organ
        - Renal (60% of cases) : renal failure & hypertension
        - Coronary arteries : heart failure & MI

        - Nervous : peripheral neuropathy / mononeuritis multiplex / strokes / seizures
        - Skin : Raynaud / livedo reticularis / digital ischemia
        - GI : pancreatic and hepatic interaction / bowel infarction / cholecystitis / Melena
    - Diagnosis
        - Negative ANCA
        - A biopsy or visceral angiography is required to confirm the diagnosis
        - In cases of renal involvement : look for proteinuria, hematuria and abnormal KFTs
    - Treatment : Immunosuppressants PLUS glucocorticoids
- Kawasaki Disease
    - It mainly affect boys younger than 5
    - It is the common cause of acquired coronary artery disease in children
    - Diagnosis requires fever for at least 5 days PLUS one of the following
        - ≥ 4 other specific symptoms
        - < 4 specific symptoms but there is involvement of the coronary arteries
    - Specific symptoms include
        - Erythema and edema of both hands and feet including the palms and soles in the first week
        - Possible desquamation of fingertips and toes after 2–3 weeks
        - Polymorphous rash originating on the trunk
        - Painless bilateral injected conjunctivitis without exudate
        - Cervical lymphadenopathy (mostly unilateral)
        - Oropharyngeal mucositis
            - Erythema and swelling of the tongue (strawberry tongue)
            - Cracked red lips
    - Mnemonic : CRASH (Conjunctivitis, Rash, Adenopathy, Strawberry tongue, Hand-foot changes) and BURN (≥ 5 days of fever)
    - Other non specific symptoms : diarrhea, fatigue, abdominal pain, arthritis, hoarseness or dyspnea
    - Diagnostics
        - High ESR and CRP
        - Echocardiography
    - Treatment
        - IV immunoglobulins
        - High-dose oral aspirin
        - IV glucocorticoids
    - Main complication is coronary artery aneurysm

Large Vessel Vasculitis

- Giant Cell Arteritis (Temporal Arteritis)

    - It is the most common form in adults with late onset
    - It is more in women
    - It is highly associated with Polymyalgia Rheumatica PMR which is muscle aches in the neck, shoulders and hips especially in the morning
    - No antibodies are involved
    - Symptoms
        - Headache : temporal, pulsatile and throbbing
        - Hardened or tendered temporal artery
        - Jaw claudication
        - Tingling tongue
        - Unilateral blindness or diplopia
        - Amaurosis Fugax
    - GCA can involve other arteries like branches of the aorta causing symptoms like Angina, Limb claudication, Arterial bruits or asymmetrical pulses or blood pressure readings
    - Diagnosis
        - Temporal artery biopsy is the gold standard but skip lesions are common
        - Duplex ultrasound can be used
    - Treatment : High dose IV or oral glucocorticoids depending on clinical presentation
    - Complications
        - Permanent vision loss
        - Cerebral ischemia
        - Aortic aneurysm
- Takayasu Arteritis TAK (pulseless disease)
    - It is a granulomatous inflammation of the aorta and its major branches (mainly affect the aortic arch) leading to stenosis
    - More in women and young adults (15-45)
    - No antibodies are involved
    - Symptoms
        - Decreased bilateral brachial and radial pulses (pulseless)
        - Syncope and Angina pectoris
        - Bilateral carotid bruits
        - Carotidynia
        - Impaired vision
        - Limbs claudication
        - Raynaud phenomenon
        - Hypertension
        - Urticaria and erythema nodosum
    - The disease has 3 phases
        - Systemic phase : general symptoms
        - vascular phase : asymmetrical peripheral pulses / claudication of arms and legs / visual disturbances

        - burnt out pulseless phase
    - Diagnosis
        - The preferred initial study is MR angiography (MRA)
        - Echocardiography
        - Biopsy is not required
    - Treatment
        - High dose oral prednisolone PLUS a steroid sparing agent like Azathioprine or methotrexate
        - Surgery : bypass or grafts

Behcet Disease

- Common along the silk route (the Middle East) more in males
- It is an autoimmune disease with HLA-B51 association
- Diagnosis requires the presence of Recurrent non-scarring painful oral ulceration PLUS at least 2 of the following
    - Recurrent scarring genital ulceration (mostly affecting the vulva and scrotum)
    - Ocular lesions : bilateral anterior uveitis (iridocyclitis or chorioretinitis)
    - Skin lesions : folliculitis / Erythema nodosum / Dermatographism / acniform eruptions
    - Pathergy test : development of erythematous sterile pustules 48 hours after a skin prick
- Other manifestations
    - Arthritis : asymmetric monoarthritis or oligoarthritis
    - GI : abdominal pain / anorexia / NVD / lower GI bleeding
    - Vascular manifestations
        - Arterial aneurysms and thrombosis
        - Thrombosis of large main veins
        - Superficial thrombophlebitis
    - Neural symptoms : ataxia / hearing loss / Optic neuritis / headache / Peripheral neuropathy / meningitis
- No confirmatory blood or histological diagnostic tests
- Autoantibodies like ANA, ANCA and rheumatoid factor are usually absent
- Treatment
    - Colchicine for oral ulcers and arthritis
    - Topical glucocorticoids : limited efficacy for oral and genital ulcers
    - Glucocorticoid-sparing agents like MTX
    - TNF inhibitors