Vasculitides
Vasculitic syndromes

- Inflammation of blood vessels
- Types
  1. Large to medium-sized vessels: GCA, Takayasu’s arteritis
  2. Medium to small-sized vessels:
  3. Small-sized vessels: Microscopic polyangiitis, HSP, Idiopathic cutaneous vasculitis
Etiopathogenesis:

Environmental Factors

Genetic Predisposition

Persistent Abnormal Immune Response

Auto-Abs (ANCA)

Complement activation

DTH & CMI
Why specified locations for vasculitis?

- Ability of RES to clear circulating immune complexes
- Physio-chemical properties of immune complexes
- Dynamics (turbulence, hydrostatic pressure) of regional blood flow
- Pre-existing integrity of vessel endothelium
Clinical approach to patient

When to suspect??

1. Palpable Purpura
2. Microscopic hematuria/ Ac. Nephritic Synd
3. Chr. Inflammatory sinusitis
4. Pulmonary infiltrates
5. Mononeuritis multiplex
6. Unexplained ischemic events
7. Multisystem presentations
Clinical approach to patient

- Clinical Mimickers (to be ruled out first)
  I. Infectious diseases:
     1. SABE
     2. Disseminated Gonococcal infection
     3. Syphilis
     4. Lyme disease
     5. RMSF
     6. Whipple’s disease
  II. Coagulopathies: APLA, TTP
Approach to patient

- Clinical Mimickers (to be ruled out first)

III. Infiltrative & other disorders:
1. Sarcoidosis
2. Amyloidosis
3. Goodpasture’s synd.

IV. Malignancies & Drugs
1. Lymphoma
2. Atrial myxoma
3. Cocaine, Amphetamine
4. Ergot alkaloids, Methylsurgide
Vasculitic disorders: Classification

I. Pr. Vasculitis synd. →

1. Wegener’s Granulomatosis

2. Churg-Strass Synd.

3. PAN

4. GCA

5. Takayasu’s arteritis

6. HSP

7. EMC

8. Behcet’s disease, Kawasaki ds, Cogan’s synd.

9. Pr. CNS vasculitis

10. Idiopathic cutaneous vasculitis
Vasculitic disorders: Classification

II. Sec. Vasculitis Synd.
1. Infections
2. Malignancies
3. Drug induced
4. CTDs
5. Serum sickness
Wegener's Granulomatosis

- Granulomatous vasculitis of Upper n Lower Resp Tracts + Glomerulonephritis
- M:F = 1:1
- Median age of onset = 40 years
- Histopath: Granulomatous, necrotizing vasculitis of small arteries n veins
  - Upper resp tract→ necrotizing granulomas
  - Lungs→ nodulo-cavitary lesions
  - Kidneys→ Pauci-immune glomerulonephritis but no granulomas
Wegener's Granulomatosis

- Clinical manifestations:
  1. Resp tract → Rhinosinusitis, Otitis media, Subglottic stenosis
  2. Lungs → nodulo-cavitary disease, reticular infiltrates, hemoptysis, pleuritis
  3. Kidneys → Glomerulonephritis...proteinuria, hematuria, RBC casts
  4. Eyes → Conjunctivits, Keratitis, Scleritis, Uveitis, Retinitis
Wegener's Granulomatosis

- **Clinical manifestations:**
  5. Skin → Purpura, Ulcers, Subcutaneous nodules
  6. Others (Systemic) → Fever, Arthritis, Weight loss, Peripheral neuropathy, Mononeuritis multiplex
Wegener's Granulomatosis

Diagnosis:
- By histopath of tissue biopsy...Necrotizing Granulomatous Vasculitis
- Pulmonary tissue has highest diagnostic yield
- Upper Resp tract Bx show only necrotising granulomas but no vasculitis
- Renal Bx shows only Glomerulonephritis (Pauci-immune) and no granulomas
- C-ANCA only adjunctive evidence to tissue
Wegener’s Granulomatosis

Differential diagnoses:

- Goodpasture’s disease
- Sarcoidosis
- Lung malignancies
- Mucocutaneous leishmaniasis
- Midline destructive disease → Midline granuloma and upper airway neoplasm

- erosion through skin of the face commonly occurs and vasculitis is not seen on histopath
Wegener’s Granulomatosis

**Treatment:**

- **Oral Cyclophosphamide 2mg/Kg OD....continued till 1 year post complete remission and thereafter gradually withdrawn**
  
  +

- **Oral Glucocorticoids....for initial 6 mths**

  - 50% relapse after initial complete remission
  - No cyclophosph for isolated sinus ds/muco-cutaneous ds ...f/u for target organ damage such as lungs, kidney or eyes
Wegener's Granulomatosis

Follow-up:
1. Monitor for TLC to be > 3000 cells/µL
2. Steroid S/E → Infections, Osteoporosis, Cushing’s synd
3. Cyclophosphamide toxicity → Hem. Cystitis, Ca bladder, Gonadal failure
Churg-Strass Syndrome

- aka Allergic Angitis and Granulomatosis
- Involved vessels...medium to small sized arteries, capillaries, venules n veins
- Characteristic Histopath.....Granulomatous reaction with eosinophilic infiltrates.... (hence the name...allergic angitis n granuloma)
- Major sites involved...Lungs (predom), Kidney, Skin n PNS
Churg-Strass Syndrome

Clinical manifestations:
1. Resp Syst $\rightarrow$ Allergic rhino-sinusitis, Bronchial Asthma with Pulm infiltrates
2. Kidney $\rightarrow$ lesser involved as compared to wegener's ds
3. Skin $\rightarrow$ Purpura, Cutaneous or Subcutaneous nodules
4. PNS $\rightarrow$ Mononeuritis multiplex
Churg-Strass Syndrome

Lab investigations:
1. ESR
2. α2 microglobulins
3. P-ANCA
4. DLC (Eosinophilia)
5. CXR
6. PFT
7. Tissue Biopsy
Churg-Strass Syndrome

- **Diagnosis:**
  Bronchial Asthma + Eosinophilia
  +
  Clinical features consistent with vasculitis

- **Treatment:**
  - Systemic steroids (long-term for Asthma)
  - Cyclophos....if Fulminant ds or Steroid failure
Polyarteritis Nodosa (PAN)

- Necrotizing vasculitis (No Granuloma) of medium sized arteries & veins (No Venules)

- Involved sites: Renal and Visceral arteries (Pulmonary vessels spared)

- Characteristic pathology: aneurysmal dilatations (up to 1 cm) along involved arteries
Polyarteritis Nodosa (PAN)

■ Clinical manifestations:
  1. Renal → CKD, HTN
  2. GIT → GI bleed, Bowel perf/ulceration/infarction, Pancreatic or hepatic infarction
  3. CNS → TIA, CVA, GTCS
  4. PNS → Peripheral neuropathy, Mononeuritis multiplex
  5. Skin → Purpura, Nodules, Infarcts
Polyarteritis Nodosa (PAN)

Diagnosis:
1. No diagnostic serologic tests
2. Histopath...s/o vasculitis (Bx from involved tissue/organ)
3. Angiography...if tissue diagnosis not feasible aneurysmal dilatations n stenotic segments in Renal, Hepatic n other visceral vasculature
4. HBsAg + in 30%
Polyarteritis Nodosa (PAN)

- Prognosis n Treatment:
  - Prognosis extremely poor
    ...5 yr survival rates around 10-20%
  - Death usually from GI complications
    ...Bowel infarction n perforation
  - Steroids/Steroids + Cyclophos
    ....as per disease severity & organ involved
  - IFN + Steroids for HBsAg +
Microscopic Polyangiitis

- Necrotizing vasculitis (but no granulomas) of small vessels (arterioles, capillaries and venules)
- Predominant manifestation as Glomerulonephritis
- However, Pulm capillaritis also common (as opposed to PAN); Also c-ANCA +
- Reno-Pulmonary synd.....similar to Wegener’s ds but upper airway involv not found
- T/t as for Wegener’s granulomatosis
GCA/Temporal/Cranial Arteritis

- Vasculitis of large- to medium-sized arteries
- Characteristic involv of one or more branches of Carotid artery..esp Temporal art

- Epidemio: Female preponderance
  > 50 years of age
  asso with Polymyalgia rheumatica
GCA/Temporal/Cranial Arteritis

- Clinical manifestations:
  - Fevre
  - Headache
  - Anemia
  - ESR ……..in a 50+ female patient
  - Scalp pain/tenderness, jaw claudication, Ischemic Optic Neuropathy (ION), MI, CVA
  - Asso. c/o Polymyalgia (neck, shoulders, lower back, hips, & thighs) rheumatica
GCA/Temporal/Cranial Arteritis

- Diagnosis: clinical suspicion confirmed by diagnostic biopsy from temporal artery (3-5 cm long segment with serial sections). Negative histopathology doesn’t rule out the diagnosis.

- Treatment: highly responsive to systemic steroids (X 2-3 years);
  - However, delay in treatment can cause permanent visual loss.
Takayasu’s Arteritis

- aka Pulseless ds/ Aorto-arteritis/ Aortic Arch Synd

- Large- to medium-sized arteritis..esp Arch of Aorta n its branches
Takayasu’s Arteritis

Clinical manifestations:

- Systemic
- Regional

1. Subclavian: Arm claudication, Raynaud’s
2. Common Carotid: TIA, CVA, Visual defects
3. Renal: CKD, HTN
4. Pulm: Atypical chest pain
5. Coronary: MI, USA
Takayasu’s Arteritis

- Diagnosis: suspected in young women with weak or absent peripheral pulses, discrepancies in BP and presence of arterial bruit.

- confirmed by Arteriography showing Stenosis, Post-stenotic aneurysmal dilatation.
Takayasu’s Arteritis

- Prognosis and Treatment:
  - Course is Chronic and Relapsing
  - Medical treatment with systemic steroids
  - Invasive interventions → Bypass grafting
    - Stenting
  - For Steroid Refractory / Steroid Dependant patients… MTX
Henoch-Schölein Purpura

- aka Anaphylactoid Purpura
- Small vessel vasculitis
- Purpura + Arthralgia + GI s/s + Glomerular hematuria- Proteinuria
- 4-7 yrs of age; not a rare ds
- Diagnosis based on clinical suspicion...skin biopsy shows Leukocytoclastic vasculitis with Ig A & C3 deposits on Immunofluorescence
Henoch-Schölein Purpura

- **Treatment**
  - Usually resolves spontaneously without T/t
  - Steroids...effective only for Arthralgia and Abdominal symptoms
    ...no role in Purpura/ Renal disease
Idiopathic Cutaneous Vasculitis

- Inflammation of small-sized blood vessels of dermis...post-cap venules most prominently affected

- Cutaneous vasculitis: 70% from Pr./Sec. Vasc
  30% are idiopathic

- Skin lesions: Palpable Purpura, Subcutaneous nodules, vesicles, ulcers on dependant areas i.e. legs (ambulatory) n sacral area (recumb)
Idiopathic Cutaneous Vasculitis

- No specific diagnostic tests
- Mild ↑ ESR n leukocytosis, other lab inves to primarily rule out Pr./Sec. Vasculitis

- Treatment: symptomatic (NSAIDs n Anti-histaminics); Steroids only for refractory cases
Essential Mixed Cryoglobulinemia

- Essential → Primary
- Mixed → Mono-, Oligo-, Polyclonal Ig
- Cryoglobulinemia → Cold ppt. Ig

- Sec. cryoglobulinemia →
  1. Myelo-lymphoproliferative dr
  2. CTDs
  3. HCV infection
EMC

- **Clinical manifestations:**
  1. Cutaneous Vasculitis
  2. Peripheral Neuropathy
  3. Glomerulonephritis...Ac. Mortality rare but 15% progress to ESRD

- **Lab tests:**
  1. Cryoprecipitates
  2. RF (almost always...helpful when no cryoppt)
  3. Hypocomplementemia (90%)
  4. HCV n ESR
EMC

- Treatment:
  1. IFN + Ribavirin.....if HCV positive
  2. Steroids..................if HCV negative
Behcets Syndrome

- Recurrent oral & genital ulcers with ocular involvement
  1. Oral ulcers...sine qua non
     heal over 1-2 weeks without scarring
  2. Genital ulcers...less frequent but more spf.
     don’t affect glans penis n urethra
     scrotal scars +
  3. Ocular involv....Uveitis, Optic neuritis, Retinitis
Behcets Syndrome

Other manifestations:
- Supf n deep vein thrombosis (25%)
- Skin...Erythema nodosum, acneform eruptions
- Skin...non-spf inflm reacn to any scratches or intradermal saline injection (Pathergy test)

Diagnosis ➔ Recurrent Oral Ulcers + any 2 of
1) Genital ulcers  2) Eye lesions
3) Skin lesions    4) Pathergy test
Behcets Syndrome

- Treatment:
  - Oral/Genital ulcers $\rightarrow$ Topical Steroids
  - Venous thrombosis $\rightarrow$ Aspirin 325 mg/d
  - Uveitis/Retinitis/Optic neuritis $\rightarrow$ Steroids + AZT
Primary CNS Vasculitis

Presentation:
1. Severe headache
2. Encephalopathy/ behavioral changes
3. TIA/CVA/FND

Diagnosis: Angiography (beaded appearance) brain bx (for confirmation)

Prognosis poor (even with treatment)
Cogan Syndrome

- Co....Cornea (Interstitial keratitis)
- Ga....Great arteries (Aortitis)
- N.....Nerve (8th Cr. N.)

Def: Non-syphilitic interstitial keratitis with vestibulo-auditory deficit (B/L SNHL)

Treatment: Systemic Steroids
Kawasaki ds/ Mucocutaneous LN syndrome

- Non-suppurative cervical LAP with mucocutaneous lesions (erythema, edema, desquamation)
- Mainly in children (80% cases under 5 yrs)
- 25% have coronary artery aneurysm
- Mortality = 0.5-2.8 %; otherwise complete recovery
- T/t: IV Ig 2g/Kg Single infusion over 10 hrs
  Aspirin 100 mg/Kg X 2 wks f/b 5 mg/Kg X 2