Vasculitis
(1+2)

Ali Al Khader, M.D.
Faculty of Medicine
Al-Balqa’ Applied University
Email: ali.alkhader@bau.edu.jo
Overview

= inflammation of vessel wall

• Symptoms and signs depend on the tissue of which the vessels are affected

• Often with systemic symptoms...fever, myalgia, arthralgia, malaise...etc.

• Most affect small vessels (arterioles, capillaries & venules)

• Considerable clinical & pathological overlap between types of vasculitis

• Infectious or noninfectious

• Physical and chemical injury may also cause vasculitis
<table>
<thead>
<tr>
<th>Immune complex associated</th>
<th>Antineutrophil cytoplasmic antibodies</th>
<th>Anti-endothelial cell antibodies</th>
<th>Autoreactive T cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>- e.g., vasculitis in SLE - these Ag-Ab complexes also activate complement in vessel wall - 2 important examples: 1- Drug hypersensitivity vasculitis ... penicillin for example: acts as a hapten (= “does’nt induce immune response alone but it binds to a self normal “carrier” protein to become immunogenic) ... other drugs are immunogenic by themselves (e.g., streptokinase) ... mainly skin manifestations 2- Vasculitis due to immune response to certain infections... example: 30% of polyarteritis nodosa cases are due to immune complexes of HBsAg &amp; anti-HBsAg</td>
<td>See next slide</td>
<td>Like Kawasaki disease</td>
<td>Also have role</td>
</tr>
</tbody>
</table>
Antineutrophil cytoplasmic antibodies

- Antibodies against neutrophil cytoplasmic antigens...detected in blood

- These Abs are directed against neutrophil primary granules, monocyte lysosomes, and endothelial cells

- Their titers in blood are important in diagnosis, clinical severity and recurrence

- **2 types are most important:**
  1. *Antiproteinase-3 (PR3-ANCA)*
     - = c-ANCA
     - PR3 is of azurophilic granule constituents
     - PR3 may resemble certain microbial peptides...so certain infections may induce c-ANCA formation
     - *Wegener granulomatosis*
  2. *Anti-myeloperoxidase (MPO-ANCA)*
     - = p-ANCA
     - may be induced by certain drugs, like propylthiouracil
     - *Microscopic polyangiitis & Churg-Strauss syndrome*
Mechanisms of ANCA vasculitis

- Drugs or cross-reactive microbial antigens

- Infection/endotoxins/inflammation

- Increased PR3 & MPO expression on neutrophil surface

- TNF

ANCA formation

will bind

ANCAs activate neutrophils and neutrophils will attack the endothelium
ANCAs, cont’d

• These vasculitides are called: pauciimmune because Ab-Ag complexes & complements are not typically detected in vascular lesions

• Other types of ANCAs can be seen in certain nonvasculitic inflammatory disorders...inflammatory bowel disease, sclerosing cholangitis and rheumatoid arthritis...etc.
Giant Cell (Temporal) Arteritis

• **Chronic granulomatous inflammation**

• **Small to large arteries**

• **Especially: temporal arteries**

• **Others: vertebral, ophthalmic, aorta (giant cell aortitis)**

*Mechanisms: mainly T cells...also: cytokines (TNF) & antiendothelial cells antibodies*

*Good response to steroids...anti-TNF may be also used*

*Rare before the age of 50 years*

*Dx. depends on biopsy but: patchy involvement of temporal artery...so: negative biopsy doesn’t exclude the disease*

*Symptoms may be vague and constitutional (fever, fatigue, weight loss)...
or facial pain or headache...
...most intense along the course of the superficial temporal artery, which is painful to palpation...
...Ocular symptoms...ophthalmic artery involvement...abruptly appear in about 50% of patients; these range from diplopia to complete vision loss*

Visit [https://medicalpoint.org/temporal-arteritis/](https://medicalpoint.org/temporal-arteritis/) for references
Giant Cell (Temporal) Arteritis, biopsy

• Changes are patchy along the length of affected vessels, and these include:

  - nodular intimal thickening (and occasional thromboses)...distal ischemia

  - granulomatous inflammation...mainly inner media and inner elastic membrane
   ...lymphocytes + macrophages + MNGCs

  - fragmentation of internal elastic lamina

  - healing: Fibrosis of media and adventitia + intimal thickening

  - lesions at different stages of development are seen in the same artery

25% of the cases...nonspecific mixed inflammation without granulomas/giant cells
Takayasu arteritis

- Not only in Japan
- Granulomatous inflammation
- Medium to large arteries
- Characterized by: ocular disturbances + weak upper limb pulses (also faint carotid pulses) ...so called: pulseless disease
- Transmural scarring + thickening of aorta (arch and major branches) ↓ severe narrowing
- May resemble giant cell arteritis (clinically and histologically)
Takayasu arteritis, cont’d

- Involvement may reach aortic root...dilation and aortic valve insufficiency

- Pulmonary a. involved in 50% of the cases...can cause pulm. HTN

- Distal aorta involvement can be involved...leg claudication

- Renal a. (can cause HTN) and coronary a. can also be affected

- Clinically:
  - initially: nonspecific (systemic signs and symptoms)
  - then: as we said before
Polyarteritis nodosa (PAN)

- Small to medium muscular arteries...mainly renal & visceral vessels
- Pulmonary circulation is spared
- Not associated with ANCA
- 1/3 of the cases...hepatitis B...immune complexes of HBsAg and its Ab deposit in the vessel wall
- Involvement: segmental & transmural...often with thrombosis
  ...usually not the whole circumference
  ...prefers branching points
  ...in descending order: kidney, heart, liver & GI
PAN, cont’d

- Initially: transmural mixed inflammation...often with fibrinoid necrosis
- Older lesion...fibrous thickening
- Different stages can be seen in different foci
- Mainly young adults
- Mostly episodic with long symptom-free intervals
- Renal a. involvement is often predominant...HTN
- When GI vessels involved...abdominal pain & bloody stools
- Peripheral nerves...neuritis (mainly in motor nerves)
- Fatal if untreated...esp. due to renal a. involvement
- Immunosuppression is effective
Kawasaki disease

• Not only in Japan

• Acute

• Febrile

• Usually self-limited

• Infancy & childhood...80% are younger than 4 years

• Large to medium sized arteries

• The most important: involvement of coronary a.
  ...may be complicated by aneurysms...rupture or thrombosis...MI and sudden death

• Pathogenesis: genetic susceptibility and triggered by certain viral infections
  ...T cell response that induces cytokines and B cells (antibodies)
Kawasaki disease, cont’d

- Transmural inflammation similar to PAN...but less fibrinoid necrosis here

- Resolve spontaneously or by treatment...but aneurysmal change is a problem

- As other types of vasculitis: healing may cause intimal thickening & narrowing

  - oral erythema and blistering
  - edema of the hands and feet
  - erythema of the palms and soles
  - desquamative rash
  - cervical lymph node enlargement (hence its other name, mucocutaneous lymph node syndrome)
  - the CVS sequelae are seen in 20%...from mild to death
  - IVIG and aspirin are good
Microscopic polyangiitis

• Capillaries, small arterioles & venules

• = hypersensitivity vasculitis or leukocytoclastic Vasculitis

• Unlike PAN...all lesions are of same age

• Skin (purpura), mucous membranes, lung, GI (abd. pain or bloody stools), CNS...etc.

• necrotizing glomerulonephritis (seen in 90% of patients)...common...hematuria/proteinuria

• pulmonary capillaritis...common...hemoptysis

• Can be seen in certain immune disorders, e.g., Henoch-Schonlein purpura
Microscopic polyangiitis, cont’d

- Can be induced by drugs (e.g., penicillin), infections or tumor antigens...etc.

- Most cases...associated with MPO-ANCA (p-ANCA)

- Segmental fibrinoid necrosis of the media with focal transmural necrotizing lesions...resemble PAN

- Granulomatous inflammation is absent

- Unlike PAN: sparing of medium-sized and larger arteries
  ...so macroscopic infarcts are uncommon
Microscopic polyangiitis, cont’d

• Most lesions are pauciimmune

• Treated by immunosuppression & removal of offending agents
Wegener granulomatosis

• Also: a necrotizing vasculitis

• More in middle aged males

• Triad: -Granulomas & ulcerative lesions...of the lung &/or upper respiratory tract
  -Vasculitis...small to medium vessels...esp. lungs and upper resp. tract
  -Glomerulonephritis

• Limited or widespread (if involves eye, skin, heart...etc.)

• Clinically, widespread disease resembles PAN + lung involvement

• PR3-ANCA is present in 95% of the cases
Wegener granulomatosis, cont’d

• Necrotizing granulomatous vasculitis with a surrounding fibroblastic proliferation

• Multiple granulomata can coalesce to produce radiographically visible nodules with central cavitation

• If untreated: mortality reaches 80% after 1 year

• Risk of relapse & renal failure

Classic presentations:
- bilateral pneumonitis with nodules and cavitary lesions (95%), chronic sinusitis (90%), mucosal ulcerations of the nasopharynx (75%), and renal disease (80%)
Churg-Strauss syndrome

= allergic granulomatosis and angiitis

• Rare

• Small vessels

• Associated with:
  - asthma
  - allergic rhinitis
  - lung infiltrates
  - blood eosinophilia
  - extravascular necrotizing granulomas
  - striking infiltration of vessels and perivascular tissues by eosinophils
Churg-Strauss syndrome, cont’d

• Cutaneous involvement (with palpable purpura)
• Gastrointestinal bleeding
• Renal disease
• Cardiac involvement in 60%...cardiomyopathy due to eosinophils

• MPO-ANCAs in a minority of cases

• Differs from polyarteritis nodosa or microscopic polyangiitis by the presence of *granulomas* and *eosinophils*.
Thromboangiitis Obliterans (Buerger Disease)

• Severe complications with gangrene of extremities

• Small and medium sized arteries...esp. tibial and radial

• Focal acute and chronic inflammation with thrombosis

• Usually before 35 years

• Increased prevalence in certain ethnic groups (Israeli, Indian subcontinent, Japanese)

Visit https://en.wikipedia.org/wiki/Cigarette for references
Thromboangiitis Obliterans (Buerger Disease)

- Sharply segmental acute and chronic transmural vasculitis of medium sized and small arteries...mainly those of extremities

- Early stages: -mixed inflammation & thrombosis
  -small microabscess
  -occasionally: granulomas

- Inflammation often extends into contiguous veins and nerves (a feature that is rare in other forms of vasculitis)

- Fibrosis
Thromboangiitis Obliterans (Buerger Disease), clinical notes

...Early:
• cold-induced Raynaud phenomenon
• instep foot pain induced by exercise (*instep claudication*)
• superficial nodular phlebitis (venous inflammation)
• severe pain due to nerve involvement

...then: chronic ulcers and gangrene

*Smoking abstinence...beneficial only early
Thank You