Systemic Vasculitis

Arizona Osteopathic Medical Association
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Objectives

- Definition
- Vascular anatomy/injury
- Diseases
- Therapy
- General points
Case #1

Mr. M.

- 52 y/o WM seen in the ICU
- 6 months of “not feeling well”
- Several episodes of ear infections
- Recurrent sinus infections and nosebleeds
- Joint aches, muscle pains, fatigue
- Anorexia, 15 lb weight loss
- Began coughing up blood and short of breath
- Treated as outpatient for pneumonia
- Came to ER, in kidney failure and needed immediate dialysis
Case #2

Ms. C.

- 48 y/o WF, busy executive, working 120+ hours week without difficulty
- Sudden ankle swelling, shortness of breath in airport, with near syncope
- Admitted for suspected pulmonary embolism
- Absent blood pressure, pulse in one arm
- Angiogram showed near complete blockage of one carotid artery and subclavian artery
What is vasculitis?

- Group of chronic inflammatory diseases
- Unknown etiology
- Immune-mediated injury targeted at vessel
- Dialogue between the vessel and the immune system
- Can target any organ or tissue
- Multisystem disease
- Manifests differently in any one individual
**Intima**: nutrition and oxygenation, cell entry, effector molecule production

**Media**: vasomotor function, macrophage differentiation, growth factor production

**Adventitia**: adhesion molecule and cytokines, migration of T cells and macrophages
The end result...

Alteration of lumen, vessel integrity, procoagulant state leads to compromised flow, resulting in tissue ischemia.
Features by size

<table>
<thead>
<tr>
<th>Small</th>
<th>Medium</th>
<th>Large</th>
</tr>
</thead>
<tbody>
<tr>
<td>Purpura</td>
<td>Cutaneous nodules</td>
<td>Extremity claudication</td>
</tr>
<tr>
<td>Vesicles/bullae</td>
<td>Ulcers</td>
<td>Asymmetric blood pressures</td>
</tr>
<tr>
<td>Urticaria</td>
<td>Livedo reticularis</td>
<td>Absent pulses</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>Digital gangrene</td>
<td>Bruits</td>
</tr>
<tr>
<td>Alveolar hemorrhage</td>
<td>Mononeuritis multiplex</td>
<td>Aortic aneurysm</td>
</tr>
<tr>
<td>Cutaneous necrosis</td>
<td>Microaneurysms</td>
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<td>Scleritis/episcleritis</td>
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Constitutional symptoms: fever, weight loss, malaise, arthralgias/arthritis (common to vasculitides of all vessel sizes).

Saleh et al, Best Pract Clin Rheum, 2005
Small Vessel Vasculitis

Wegener’s granulomatosis
(Granulomatosis with polyangiitis)
Microscopic polyangiitis
Wegener’s granulomatosis

- Inflammation of small blood vessels and tissues of upper and lower respiratory tract
- 1/30,000 in US
- Caucasian
- No gender preference
- Adult
- Relapsing disease in the majority of patients
Wegener’s granulomatosis

Triad of:

- Vasculitis of the upper and/or lower respiratory tract
- Glomerulonephritis
- Necrotizing, granulomatous inflammation
Constitutional manifestations

- Fever
- Chills
- Night sweats
- Anorexia
- Weight loss
ENT manifestations

- Otitis media
- Hearing loss
- Chronic sinusitis
- Septal perforation
- Nosebleeds
- Nasal and oral ulcers
- Cartilaginous inflammation and loss
Pulmonary manifestations

- Airway inflammation
- Infiltrates
- Nodules
- Alveolar hemorrhage
- Cavitary lesions common
Renal manifestations

- Proteinuria
- Hematuria
- Active urinary sediment: red, white blood cell casts
- Acute renal failure
- Glomerulonephritis
Common laboratory findings

- Acute phase picture: “cytoses”
- Anemia (multiple etiologies)
- Acute phase reactants (C-reactive protein, erythrocyte sedimentation rate)
- Rheumatoid factor + in about 50%
- Proteinuria, hematuria, cast formation
ANCA

- Antineutrophil cytoplasmic antibodies
- IgG
- Directed against Ag in the cytoplasm of neutrophil granulocytes
- Numerous types
ANCA

P-ANCA
- Perinuclear staining pattern
- Nucleus with negatively charged DNA
- Antigens targeted by P-ANCA are cationic
- Myeloperoxidase primary target

C-ANCA
- Cytoplasmic staining pattern
- Binding to antigen targets throughout cytoplasm
- Proteinase-3 most common target
If ANCA+, is it vasculitis?

- PPV of C-ANCA: 45-50%
- Other conditions associated with ANCA:
  - Asbestosis (20%)
  - Pulmonary TB (30%)
  - Pneumonia
  - Sporotrichosis, Cryptosporidiosis
  - Other autoimmune (SLE, SS, Sjogren’s)
The Zen of ANCA

- Helpful in confirming a diagnosis
- Does not rule out infection
- Does not eliminate need for tissue biopsy
- Prediction of flares?
- Measure in remission
- If flare in question, can recheck
Summary: WG

- Triad: granulomatous inflammation, respiratory tract involvement, glomerulonephritis
- Chronic sinusitis/otitis
- Orbital pseudotumor
- Saddle-nose deformity, tracheal stenosis
- C-ANCA/PR-3 most common
Microscopic polyangiitis

- “microscopic periarteritis”
- Characterized by lack of immunoglobulin deposits on biopsy
- Similar to WG and CSS
- Glomerulonephritis
- Alveolar hemorrhage
- Any ANCA in 85%, most commonly P-ANCA
MPA

- 90% with renal disease
- Mortality greatest with pulmonary-renal syndrome
- Increased mortality if treated with steroids only (5X)
- 36% with relapsing disease
Summary

- SVV similar to WG and CSS
- Does not clearly fit into either
- Pulmonary hemorrhage, GN, neuropathy
- ANCA +
Medium-Vessel Vasculitis

Polyarteritis Nodosa
Polyarteritis nodosa

- Involves muscular arteries
- Spares smallest vessels
- **Aneurysms**, stenosis, occlusions
- Segmental, branch points
- Association with viral infection
System involvement

- NO glomerulonephritis
- Spares lungs as a rule
- Otherwise, everything fair game

Common:
Skin
Visceral arteries
Nerves
Disease criteria

- Wt loss > 4kg
- Livedo reticularis
- Testicular pain
- Myalgias or weakness
- Mononeuropathy/polyneuropathy

- DBP > 90
- New elevation BUN (>40) or Cr (>1.5)
- Hepatitis B
- Characteristic arteriographic abnormalities
- Biopsy
Diagnostic studies

- Acute phase picture
- No specific serologic test
- Rare ANCA +
- Angiography (usually visceral)
- Biopsy (muscle, nerve, skin)
Summary

- Medium vessel vasculitis of muscular arteries
- Association with chronic viral infections (hepatitis B)
- Vascular stenoses and aneurysms
- Visceral arteries frequently involved
- Livedo reticularis, hypertension
- No autoantibodies
- Immunosuppression + antiviral therapy may be necessary to treat disease
Large Vessel Vasculitis

Takayasu’s arteritis
Giant cell arteritis
Takayasu’s arteritis

- Involves aorta, primary branches
- Identified in young females from Far East
- Worldwide distribution
- F: M 8:1
- Mid 20s at diagnosis
- Characterized by arterial stenotic or aneurysmal lesions
Clinical presentation

- Acute presentation
  flu-like symptoms--NONSPECIFIC, often missed
- Incidental detection
  absent pulse/BP
  vascular bruits
  premature vascular disease
- Symptoms from artery narrowing lead to investigations and diagnosis
ACR Criteria

- Age at onset < 40
- Decreased brachial artery pulse
- Extremity claudication
- BP difference >10mmHg between limbs
- Subclavian or aortic bruit
- Vascular abnormalities on imaging studies
Imaging

- MRI/A with STIR weighted images: wall edema, thickness, stenosis, aneurysm
- CTA: wall thickness, stenosis, aneurysm
- Catheter-directed angiography: stenosis, aneurysm, ability to measure pressures or perform interventions

- Patients with lesions affecting limbs need catheter-directed angiography to measure central pressures
Summary

- “Pulseless disease”
- Young females
- Present often with nonspecific inflammatory picture, or with signs/sx arterial insufficiency
- Frequently asymptomatic at presentation and relapse
- Require sequential imaging for monitoring
- Morbidity and mortality often from premature, progressive atherosclerosis and events
Temporal/giant cell arteritis

- Vasculitis involving aorta, primary branches - predilection for extracranial arteries
- Mean age at onset 70
- European decent
- Female: male 2:1
- Gradual or abrupt onset
Signs/symptoms

- Headache
- Fever
- Visual symptoms
- Temporal artery/scalp tenderness
- Jaw fatigue
- Cough
A meaningful association?

About 40% of patients with giant cell arteritis have polymyalgia rheumatica.

- Polymyalgia rheumatica is an inflammatory disorder that occurs in adults over the age of 50.
- Characterized by subacute onset of aching and stiffness in the muscles of neck, shoulder girdle, and hip girdle.
- Usually symmetric.
- Associated with morning stiffness.
Large vessel involvement

- Path specimens of aorta
- Growing awareness with more frequent, less invasive imaging techniques
- Same areas as Takayasu’s
- Aortic root involvement common, with dissection/rupture

http://radiographics.rsna.org/cgi/content-nw/full/28/1/e28/F7
Giant cell arteritis

- Cranial arteritis/temporal arteritis
- Disease of older, primarily Caucasian adults
- Headache
- Visual changes and blindness
- Stroke, aneurysm rupture
- Can involve arteries of extremities also
- Immediate treatment imperative
- Brisk response to steroid therapy
Treatment of LVV

- Glucocorticoids only therapy that consistently controls disease in LVV
- Treatment instituted immediately if suspicion of GCA (that day)
- Temporal artery biopsy should be obtained as soon as possible
- Aspirin
- No other agents effective in disease control for GCA
- Anti-TNF therapy promising in Takayasu’s
Is this vasculitis in either of my patients?
Case 1: Part 2

Mr. M hospitalized 6 weeks:
- Lung biopsy with small vessel vasculitis, pulmonary hemorrhage, ANCA +
- Dialysis and plasma exchange
- Steroids and cyclophosphamide
- Blood clots in legs-then had bleeding from heparin
- Severe C. diff colitis
- Herpes virus infection of esophagus and stomach
- Died
Case 2: Part 2

Ms. C.

- Inflammatory markers very high
- Diagnosis of Takayasu’s arteritis established
- Given high dose steroids (50 lb wt gain, depression, severe anxiety), methotrexate (hair loss)
- Steroids decreased ⇒ symptom relapse, inflammatory markers increased
- MR imaging showed wall thickening and enhancement
- Started biologic therapy
Summary

- Group of diseases characterized by immunologic attack and damage of blood vessels
- Classified by size of blood vessel involved
- Different age, sex, ethnic distributions
- Infection believed to be an important precipitant of disease
- Multi-system disease
- Constitutional symptoms frequent and nonspecific
Summary

- No test is diagnostic by itself
- Diagnosis made by history + exam + labs + biopsy/imaging
- Chronic, frequently relapse
- Many mimics-exclude infection and other possibilities
- Treatment is not benign, and can cause significant morbidity
- Prompt diagnosis and treatment can be life saving