Polyarteritis Nodosa

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Overview

- Definition
  - An uncommon but potentially lethal multisystem nongranulomatous necrotizing vasculitis of small- or medium-sized arteries, principally at branching and bifurcation points.
  - Typically ANCA negative.
  - Associated with certain viral infections (hepatitis B most common), drug abuse, hyposensitization/desensitization treatment, B cell neoplasms, and acute otitis media.
  - Ocular manifestations occur in 10–20% of patients and include necrotizing scleritis, peripheral ulcerative keratitis, uveitis, and choroidal and retinal vasculitis.
- Symptoms
  - Redness
  - Exquisite pain – periorbital or with extraocular movements
  - Photophobia
  - Blurry vision
- Laterality
  - Unilateral or bilateral
- Course
  - Progressive and fatal without treatment due to renal and cardiac complications (5-year mortality rate is 80–95% if untreated)
- Age of onset
  - 40–60 years
- Gender/race
  - M:F = 2:1.
  - No racial predilection *per se*, but polyarteritis nodosa (PAN) has the highest prevalence in Alaskan Eskimo because the population has a very high rate of hepatitis B infection

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- Systemic association
- Multisystem involvement tends to occur early
  - Renal (75%)
    Glomerulonephritis, hematuria, hypertension
    Primary cause of death
  - Cardiac (75%)
    Coronary thrombosis, pericarditis, pericardial hemorrhage, acute aortitis.
    Myocardial involvement leads to dysrhythmias and infarction.
    Second leading cause of death.
  - Cutaneous (20–50%)
    Cutaneous or subcutaneous nodules along superficial arteries around the knee, anterior lower leg, and dorsum of foot
    - Nodules can rupture resulting in cutaneous hematomas or ecchymosis.

    Infarction or gangrene involving the fingers or toes
  - Gastrointestinal
    Abdominal pain caused by intestinal or mesenteric ischemia
    Infarcts in the liver and spleen
    Other findings: peritonitis, bowel gangrene and perforation, and intra-abdominal hemorrhage
  - Neurologic
    Ischemia to peripheral nerves, causing mononeuritis multiplex
  - Genitourinary
    Epididymitis: virtually pathognomonic in appropriate clinical context
  - Musculoskeletal
    Non-deforming arthritis
    Myalgia

Exam: Ocular

External

- Orbital inflammation, sometimes causing exophthalmos/proptosis

Anterior Segment

- Conjunctival hyperemia, hemorrhage, or infarction
- Episcleritis
- Necrotizing scleritis with peripheral ulcerative keratitis (most common type of scleritis in PAN)
- Acute nongranulomatous anterior uveitis

Posterior Segment

- Choroidal and retinal vasculitis (most common)
- Exudative retinal detachment
- Vascular occlusion
- Hypertensive retinopathy

Neuro-Ophthalmic Findings

- Optic nerve vasculitis causing optic disc edema
- Vasculitis involving the central and peripheral nervous systems leading to third, fifth, sixth, or seventh cranial nerve palsies, hemianopia, nystagmus, amaurosis fugax, and/or Horner's syndrome

Exam: Systemic

- Cutaneous or subcutaneous nodules along superficial arteries of lower extremities
- Peripheral nerve paresis or paresthesia
- Abdominal tenderness
- Testicular/epididymal tenderness

Imaging

- FA
  - Delayed choroidal filling
  - Retinal arteritis
- ICG
  - Choroidal infarction

Laboratory and Radiographic Testing

- Diagnosis is made on clinical and histological grounds.
  - Biopsy of involved tissue may show hemorrhagic vasculitis and fibrinoid necrosis
  - Testicular and skin biopsy confirm diagnosis in 50–80% of patients
- Hepatitis B panel: 33% have positive surface antigen (HBsAg).
- Other labs are nonspecific and simply reflect the systemic nature of PAN.
  - Elevated ESR/CRP and neutrophil count
  - Hypocomplementemia
  - Elevated BUN and serum creatinine

  - Urinalysis: RBC, red cell casts, or protein
  - p-ANCA is NOT typically associated with PAN, but a subset of PAN called microscopic polyangiitis (involving even smaller vessels) IS associated with p-ANCA
- Abdominal and renal angiography.
  - Saccular arterial aneurysms in renal, hepatic, and gastrointestinal vasculature

Differential Diagnosis

- Systemic vasculitides
  - Granulomatosis with polyangiitis
  - Eosinophilic granulomatosis with polyangiitis (Churg-Strauss)
  - Microscopic polyangiitis
- Rheumatoid arthritis
- Adamantiades-Behcet's disease
- Systemic lupus erythematosus
- Dermatomyositis
- Progressive systemic sclerosis
- Idiopathic retinal vasculitis, aneurysms, and neuroretinitis (IRVAN)
- Syphilis
- Mooren's ulcer (no scleritis)

Treatment

- Prednisone 1 mg/kg/day + cyclophosphamide 1–2 mg/kg/day.
- Biologics in refractory cases, including adalimumab, infliximab, rituximab, tocilizumab, and tofacitinib.
- Treatment of HBV may produce remission.

Referral/Co-management

- Rheumatology
- Nephrology
- Urology
- Cardiology
- Neurology
- Gastroenterology