***no patient handout*

Polyarteritis nodosa - Skin

Synopsis

Polyarteritis nodosa (PAN) refers to a necrotizing vasculitis of small- and medium-size arteries. The exact etiology is unknown, but it likely involves immune complex deposition, autoantibodies, inflammatory mediators, and adhesion molecules. Any organ may be affected, but PAN most commonly involves the skin, peripheral nerves, kidneys, joints and GI tract. Symptoms may include malaise, fever (in 50%), weakness, myalgias, arthralgias, abdominal pain, cutaneous ulcers, livedo reticularis, testicular pain, and weight loss. Renal involvement is common, manifested by proteinuria, hypertension, and urinary sediment abnormalities. Cardiac involvement presenting with myocardial infarction has been described. Peripheral neuropathy can result in motor and sensory deficits and may be a presenting symptom. Other complications include stroke, gangrene, renal failure, bowel perforation, GI bleeding, retinal detachment, and death. Corticosteroids and immunosuppressive drugs are the cornerstones of treatment.

Polyarteritis nodosa has been associated with infection with hepatitis B (30% of patients are positive for the B antigen), hepatitis C, HIV, CMV, parvovirus B19, HTLV, and streptococci. There appears to be an association with inflammatory bowel disease. An isolated cutaneous form also exists (benign cutaneous polyarteritis); it is more common in children. However, polyarteritis nodosa usually affects individuals in mid to late adulthood. It is slightly more common in men, and there is no apparent racial predilection.

Codes

ICD10CM:
M30.0 – Polyarteritis nodosa

SNOMEDCT:
155441006 – Polyarteritis nodosa

Look For

The lower extremities are typically involved with painful cutaneous and subcutaneous nodules. Lesions can ulcerate, bullae can form, and, rarely, there can be purpura or gangrene. Livedo reticularis is a common associated finding, as are nail-fold infarcts.

Subcutaneous nodules are 5-10 mm in diameter, are often found in groups, and are located along the blood vessels.

Diagnostic Pearls

The signs and symptoms of polyarteritis nodosa may be preceded by chronic respiratory infection (eg, bronchiectasis).

The American College of Rheumatology criteria for the classification of PAN includes 3 out of

10 of the following:

- Unintentional weight loss exceeding 4 kg since the onset of illness
- Testicular pain not attributable to other causes
- Livedo reticularis
- Presence of HB surface antigen or antibody
- Development of hypertension
- Presence of a BUN greater than 40 mg/dL or creatinine greater than 1.5 mg/dL that cannot be explained by dehydration or obstruction
- Diffuse myalgias or muscular weakness
- Development of one or more neuropathies
- Biopsy of a small- or medium-size artery with PMNs in the artery wall
- Arteriogram showing aneurysms or occlusions of visceral arteries not explained by other causes

Differential Diagnosis & Pitfalls

- **Pyoderma gangrenosum**
- **Antiphospholipid antibody syndrome**
- Necrotizing **vasculitis**
- **Cryoglobulinemia**
- **Cryofibrinogenemia**
- **Cutaneous anthrax**
- **Necrotizing fasciitis**
- **Acute meningococcemia**
- **Calciphylaxis**
- **Disseminated intravascular coagulation (DIC)**
- **Microscopic polyangiitis**

- **Henoch-Schönlein purpura**
- **Lupus erythematosus**
- **Eosinophilic granulomatosis with polyangiitis**
- **Thrombotic thrombocytopenic purpura (TTP)**
- **Granulomatosis with polyangiitis**
- **Sarcoidosis**
- **Sporotrichosis**
- **Erythema nodosum**
- **Erythema induratum**
- **Lymphomatoid granulomatosis**
- **Mucormycosis**
- **Cocaine levamisole toxicity**

Best Tests

Skin biopsy will reveal vasculitis of medium- and small-size vessels.

Histopathology Findings:

- Epidermis normal, necrotic or ulcerated
- Leukocytoclastic vasculitis
- Medium-sized arteries involved in deep dermis or subcutaneous tissue
- Granulomatous inflammation may be present in older lesions
- Lobular fat necrosis adjacent to involved vessels

Signs of nonspecific inflammation may be present: ESR and CRP are usually elevated, and decreased serum albumin, anemia, leukocytosis, and thrombocytosis may be evident.

Perform an evaluation of renal status with BUN, Cr, and urinalysis.

Obtain hepatitis B and C antibody titers.

Positive p-ANCA titers are often found but are not specific for PAN. The following laboratory

studies are also often positive and non-specific: ANA, rheumatoid factor, cryoglobulins, and antiphospholipid antibodies.

Other procedures and tests may be performed based on the clinical scenario, including but not limited to arteriography, chest X-ray, electrocardiogram, and nerve conduction tests or electromyography.

Management Pearls

In addition to treating the primary disease, excellent supportive care for the various involved organ systems is necessary. In the proper clinical context, evaluation for inflammatory bowel disease may be warranted.

Provide local wound care to any skin ulcerations. Surgical consultation may be needed for the debridement of necrotic tissue or in the context of an acute abdomen. The use of graduated compression stockings may be helpful.

Additional consultations that may be warranted include nephrology, cardiology, neurology, or rheumatology.

Therapy

The following 5 prognostic indicators may help guide treatment. Patients without these factors may be treated with corticosteroids alone, whereas patients in whom one or more factors are present often warrant additional and more aggressive therapies:

- Cardiomyopathy
- Gastrointestinal manifestations
- Central nervous system involvement
- Renal insufficiency (creatinine greater than 1.6 mg/dL)
- Proteinuria greater than 1 gram/day

Older patients need lower doses of systemic drugs.

Systemic corticosteroids (prednisone 1 mg/kg/day). Patients will often need at least 6 months of systemic corticosteroids before a long taper (3-6 months) can be started. For severe systemic disease, begin with pulse doses of methylprednisolone (15-30 mg/kg IV daily administered over 60 minutes for 1-3 days).

Immunosuppressives, including cyclophosphamide (1-2 mg/kg p.o. daily) are indicated for patients with poor prognostic factors and/or whom have not responded appropriately to more conservative regimens. Cyclophosphamide and corticosteroid therapy is often combined. Azathioprine (1-2.5 mg/kg p.o. daily) has also been used.

IVIG, infliximab, pentoxifylline, and tamoxifen have demonstrated success in isolated case reports, as has removal of the tonsils (thus eliminating a source of chronic streptococcal disease).

Patients with concomitant hepatitis B infection should receive antiviral drugs (interferon alpha-2b or vidarabine) in addition to corticosteroids. Plasma exchange may also be used.

Drug Reaction Data

Below is a list of drugs with literature evidence indicating an adverse association with this diagnosis. The list is continually updated through ongoing research and new medication approvals. Click on Citations to sort by number of citations or click on Medication to sort the medications alphabetically.

Medication	Citations
Antimalarials	1
Chelating agents	1
cocaine	1
Diuretic	1
heroin	1
methamphetamine	1
metolazone	1
minocycline	5
Opioid analgesic	1
penicillamine	1

Medication	Citations
sulfadiazine	1
sulfadoxine + pyrimethamine	1
sulfonamide	1
tetracycline antibiotic class	5