artery aneurysms or stenoses result in hypertension or renal dysfunction, rather than glomerulonephritis as in MPA. Neurologic involvement may manifest as mononeuritis multiplex. Orchitis may be seen, manifesting as acute testicular pain. Anemia, elevated erythrocyte sedimentation rate or C-reactive protein or both, and hypertension (if renal artery involvement is present) are common. As in all vasculitides, constitutional symptoms may also be present.

The diagnosis of PAN is made based on angiographic or biopsy findings in the appropriate clinical setting. ANCA typically are absent in PAN. A work-up for infection, including tests for hepatitis B and C and HIV, is warranted, given their known associations with PAN. The differential diagnosis includes MPA and mixed cryoglobulinemic vasculitis. The latter vasculitis shares many clinical features with PAN, including peripheral neuropathy, arthralgias, myalgias, purpura, and association with hepatitis C.

Kawasaki Disease

The clinical presentation of Kawasaki disease includes fever lasting longer than 5 days, conjunctival injection, oropharyngeal changes (strawberry tongue, mucous membrane desquamation), peripheral extremity changes (cutaneous desquamation), polymorphous rash, and cervical lymphadenopathy. Arthralgias, abdominal pain, hepatitis, aseptic meningitis, and uveitis have also been reported. Coronary artery aneurysms, one of the most serious complications of this vasculitis, appear within the first 4 weeks after onset of disease and are often detectable with echocardiography. Although areas of ectasia and small aneurysms may regress, larger aneurysms often persist and can result in coronary ischemia at any time after development, even into adulthood. Kawasaki disease is a triphasic disease, consisting of an acute febrile period lasting up to 14 days, a subacute phase of 2 to 4 weeks, and a convalescent phase that can last months to years. In the acute phase, the fever is persistent and high (>38.5° C) and is minimally responsive to antipyretics.

The differential diagnosis is wide and includes viral infections, toxin-mediated illnesses (e.g., toxic shock syndrome, scarlet fever), systemic juvenile idiopathic arthritis, hypersensitivity reactions, and drug reactions (e.g., Stevens-Johnson syndrome).

Large Vessel Vasculitis

Giant Cell Arteritis or Temporal Arteritis

At presentation, patients with GCA most commonly have new continuous headache, jaw claudication, visual disturbances (e.g., amaurosis fugax, diplopia), fatigue, and arthralgias. They are usually older than 50 years of age, have tender or thickened temporal arteries, and have an elevated erythrocyte sedimentation rate (>50 mm/hour by the Westergren method). Disease onset may be insidious or acute. Blindness due to anterior ischemic optic neuropathy occurs in 10% to 15% of patients with GCA and can occur at disease onset. Given the association between GCA and PMR, patients with PMR should be educated regarding signs and symptoms of GCA, and patients with GCA should be monitored for symptoms of PMR.

The diagnosis of GCA is often made by a biopsy of the superficial temporal artery. It is important to obtain a sufficient length of tissue (2 to 3 cm) because the vasculitis can have "skip lesions."

Takayasu's Arteritis

The typical clinical manifestations of TAK include a systolic blood pressure difference of greater than 10 mm Hg between the arms, decreased brachial or radial artery pulses, bruits auscultated over the subclavian arteries or aorta, claudication of extremities, neck or jaw pain, headache, dizziness, hypertension, constitutional symptoms, arthralgias, and myalgias.

The diagnosis of TAK is often based on vascular imaging studies that demonstrate long, tapering stenotic lesions or aneurysmal lesions in the aorta and primary branches. The differential diagnosis includes syphilis, spondyloarthropathies, rheumatoid arthritis, inflammatory bowel disease, and connective tissue disorders. Vascular imaging studies including computed tomographic angiography and magnetic resonance angiography are typically performed for both diagnosis and disease surveillance.

TREATMENT AND PROGNOSIS

Small Vessel Vasculitis

ANCA-Associated Vasculitides

Glucocorticoids, often with other agents, are uniformly used to induce and maintain remission in AAV. They are typically initiated at a prednisone equivalent dose of 1 mg/kg/day with or without pulse methylprednisolone (1 g IV daily × 3 days), followed by a gradual taper over approximately 6 to 12 months. In addition, the standard. In addition, the standard of care in both GPA and MPA has traditionally been cyclophosphamide, either oral or intravenous, for 3 to 6 months. This has been reported to yield remission rates varying from 30% to 93% in GPA and from 75% to 89% in MPA.

Rituximab, an anti-CD20 chimeric monoclonal antibody that depletes B cells, was shown to be noninferior to cyclophosphamide in remission induction for AAV in several randomized controlled trials (RITUXVAS and RAVE trials).

Plasmapheresis, or plasma exchange therapy, is often used in combination with remission induction therapy in patients with life-threatening disease such as alveolar hemorrhage, or rapidly progressive glomerulonephritis (pulmonary-renal syndrome). The MEPEX study was a randomized controlled trial comparing plasmapheresis with high-dose methylprednisolone for severe renal vasculitis. Plasmapheresis was shown to be superior to methylprednisolone in reducing the number of patients remaining dependent on dialysis.

For limited (early) GPA, such as disease confined to the upper respiratory tract, methotrexate may be used for remission induction, rather than cyclophosphamide; this conclusion was supported by level I evidence in the NORAM trial. Trimethoprim-sulfamethoxazole was shown in two randomized controlled trials to be helpful in preventing relapses after remission induction in GPA.

Remission maintenance therapies in AAV (level I evidence) include methotrexate, azathioprine, or mycophenolate mofetil. Because there are known risks of bladder cancer, hemorrhagic cystitis, and bone marrow suppression with cumulative use of