Systemic vasculitides: an overview

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Abstract

Systemic vasculitides comprise a collection of disorders characterized by the presence of fibrinoid necrosis and inflammation of blood vessels. This article provides an overview for small, medium and large vessel vasculitides.

Keywords ANCA; anti-neutrophil cytoplasm antibodies; blood vessel disorders; systemic vasculitis

Spectrum of vasculitis

There is no classification of vasculitis that is accepted without dispute.[1] One reason for this is the lack of an aetiological factor in most types of vasculitis.

- Vasculitic disorders can be divided into primary and secondary, distinguishing vasculitides in which the vasculitic process is the main focus of tissue injury (e.g. giant cell arteritis, microscopic polyangiitis) from those deemed to be associated with another underlying disease (e.g. systemic lupus erythematosus, rheumatoid arthritis, malignancy).
- Another division is between vasculitides associated with the presence of anti-neutrophil cytoplasmic antibodies (ANCA) and those in which ANCA are seldom detected. The three ANCA-associated forms of vasculitis are granulomatosis with polyangiitis (GPA; previously known as Wegener's granulomatosis), microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA; previously known as Churg–Strauss syndrome).
- Closer to a system of classification is subdivision of the primary systemic vasculitides according to the predominant size and type of the vessel affected and/or whether there are associated granulomata (Table 1).

Despite the term 'systemic', vasculitis can be localized to a single organ and does not invariably become systemic. This is illustrated by so-called 'idiopathic rapidly progressive glomerulonephritis', which is now recognized as a form of microscopic polyangiitis limited to the kidney. A limited form of GPA affecting the head and neck also occurs; this is usually granulomatous rather than vasculitic initially, but can develop into a systemic vasculitic disease.

Definitions

The primary systemic vasculitides are the most difficult to define because of the lack of known aetiological factors in most cases and the overlap of clinical features between syndromes. Nevertheless, several syndromes have been recognized. In 1994, an international consensus conference attempted to define the main syndromes to facilitate international understanding and awareness, and because of advances in understanding in 2012 the definitions were updated.[2]

Relationship to age

Vasculitis can occur at any age, but the clinical syndromes with which it is associated show age-specific differences:

- Kawasaki's disease is seen only in children
- Henoch–Schönlein purpura occurs mainly in children, but can present in adults
- MPA and GPA are generally present in adults with a peak incidence in the 60–70-year age range
- giant cell arteritis is predominantly a disease of people older than 50 years.

Importance of diagnostic precision

Distinguishing subsets of vasculitis is justified because the aetiological factors or pathogenic mechanisms are likely to differ, the requirements for therapy differ, and prognosis varies between different syndromes. Precision is also necessary for therapeutic, epidemiological and national or international studies.

Vasculitides are medical emergencies. Organ survival can be threatened if a diagnosis is not made quickly and accurately, enabling implementation of appropriate therapy. Blindness can occur in an elderly patient in whom giant cell arteritis is missed, cardiac infarction can occur in a child with Kawasaki's disease, and renal failure and life-threatening lung haemorrhage can develop in an adult with MPA or GPA. If in doubt about a diagnosis, consult an appropriate specialist.

New approaches to therapy

In recent years, understanding of how best to apply established therapies has increased, and some new therapeutic agents have been introduced.

In the ANCA-associated vasculitides, cyclophosphamide and corticosteroids have been the main treatments for 30 years. The majority of treatment trials have focused on ANCA-associated vasculitis, grouping patients with GPA and MPA together. Results of trials have helped optimize and reduce the use of cyclophosphamide and evaluate other immunosuppressive agents.[3] The CYCAZAREM trial has indicated that shorter courses of cyclophosphamide followed by azathioprine are as effective as 12 months of cyclophosphamide, so cyclophosphamide can now be safely switched to azathioprine after 3–6 months.[4] The CYCLOPS trial demonstrated that intravenous cyclophosphamide is as good as oral cyclophosphamide for remission induction with less cumulative exposure.[5] The MEPEX trial has shown that plasma exchange improves the likelihood of recovery of renal function, compared to pulses of methylprednisolone, when used in conjunction with cyclophosphamide and prednisolone in patients presenting with severe renal disease (defined as a serum creatinine >500 μmol/L)[6] and the role of plasma exchange is now being further evaluated in the ongoing PEXIVAS trial (NCT00987389).

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Definitions for the vasculitides adopted by the 2012 International Chapel Hill Consensus Conference on the Nomenclature of Vasculitis

Large vessel vasculitis (LVV)		
• Giant cell arteritis (GCA)	Granulomatous arteritis of the aorta and its major branches, with a predilection for carotid, vertebral and temporal arteries	Usually occurs >50 years of age Often associated with polymyalgia rheumatica
• Takayasu's arteritis (TAK)	Granulomatous arteritis of the aorta and its major branches	Usually occurs <50 years of age
Medium-sized vessel vasculitis (MVV)		
• Polyarteritis nodosa (PAN)	Necrotizing inflammation of medium-sized or small arteries without glomerulonephritis or vasculitis in arterioles, capillaries or venules	Not associated with ANCAs
• Kawasaki's disease (KD)	Arteritis involving predominantly medium-sized and small arteries. Associated with the mucocutaneous lymph node syndrome	Coronary arteries often involved Aorta and veins may be involved Usually occurs in children
Small vessel vasculitis (SVV)		
• ANCA-associated vasculitis (AAV)	Necrotizing vasculitis with few or no immune deposits predominantly affecting small vessels. Usually associated with proteinase 3 (PR3) ANCA or myeloperoxidase (MPO) ANCA; a few patients are ANCA negative	
• Granulomatosis with polyangiitis (Wegener's) (GPA)	Necrotizing granulomatous inflammation usually involving the upper and lower respiratory tract and necrotizing vasculitis affecting small- to medium-sized vessels (capillaries, venules, arterioles, arteries)	Necrotizing glomerulonephritis common
• Eosinophil granulomatosis with polyangiitis (Churg—Strauss) (EGPA)	Eosinophil-rich and necrotizing granulomatous inflammation involving the respiratory tract, and necrotizing vasculitis affecting small- to medium-sized vessels, associated with asthma and blood eosinophilia	ANCA is more frequent when glomerulonephritis is present
• Microscopic polyangiitis (MPA)	Necrotizing vasculitis with few or no immune deposits affecting small vessels (capillaries, venules, arterioles)	Necrotizing arteritis involving small and medium-sized arteries may be present Necrotizing glomerulonephritis very common Pulmonary capillaritis often occurs
• Immune complex vasculitis	Vasculitis with moderate to marked wall deposits of immunoglobulin and/or complement components predominantly affecting small vessels (capillaries, venules, arterioles and small arteries)	Glomerulonephritis is frequent
• Anti-glomerular basement membrane (anti-GBM) disease	Vasculitis affecting glomerular or pulmonary capillaries or both, with GBM deposition of anti-GBM autoantibodies	Lung involvement causes pulmonary haemorrhage, and renal involvement causes glomerulonephritis with necrosis and crescents
• IgA vasculitis (Henoch—Schönlein) (IgAV)	Vasculitis with IgA1-dominant immune deposits, affecting small vessels (capillaries, venules, arterioles)	Typically involves skin, gut and joints Glomerulonephritis indistinguishable from IgA nephropathy may occur
• Cryoglobulinaemic vasculitis (CV)	Vasculitis with cryoglobulin immune deposits affecting small vessels (capillaries, venules, arterioles) and associated with serum cryoglobulins	Skin and glomeruli and peripheral nerves are often involved

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