Systemic vasculitides: an overview

Dana Kidder

Paula Dospinescu

Maria Karabayas

Neil Basu

Abstract

The systemic vasculitides are a group of uncommon but serious multisystem autoimmune disorders characterized by blood vessel inflammation. Timely diagnosis and intervention are crucial in preserving organ function and reducing mortality and morbidity. Immunosuppressive agents are the cornerstone of treatment and have revolutionized outcomes. Nevertheless, disease relapse is common, and individuals with vasculitides accumulate significant risks of infection, cardiovascular disease and malignancy over time compared with the general population, and invariably report poor quality of life. Toxicity from therapeutic agents – especially glucocorticoids – contributes to these complications.

Keywords Antineutrophil cytoplasmic antibody; cryoglobulins; giant cell arteritis; granulomatosis with polyangiitis; microscopic polyangiitis; MRCP; polyarteritis nodosa

Epidemiology

In general, systemic vasculitides are uncommon disorders, their incidence varying according to type of vasculitis, age and geographical location. For example, giant cell arteritis (GCA) – the most common vasculitis – has a reported incidence of up to 20 per 100,000 population, while antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) has a typical approximate rate of 20 per million population. Although overall incidences of AAV are often similar across disparate geographies, interesting variations in AAV subtypes are reported. In Japan, for example, the annual incidence of microscopic polyangiitis is higher than in the UK (18.2 versus 6.5 per million adults), while granulomatosis with polyangiitis is more common in the UK (14.3 versus 2.1 per million adults). Other forms of vasculitis tend to manifest geographical clustering within the same age group; for

Dana Kidder *PhD MRCP is a Consultant Nephrologist and NHS Research Scotland (NRS) Career Research Fellow, at the Aberdeen Royal Infirmary, UK. Competing interests: none declared.*

Paula Dospinescu *MRCP is a Consultant Rheumatologist with an interest in vasculitis at the Aberdeen Royal Infirmary, UK. Competing interests: none declared.*

Maria Karabayas *MB ChB is a Core Medical Trainee at the Aberdeen Royal Infirmary, UK. Competing interests: none declared.*

Neil Basu *PhD MRCP is a Senior Clinical Lecturer in Rheumatology at the University of Aberdeen, UK. Competing interests: none declared.*

Key points

- This group of heterogeneous disorders is best categorized according to the size of the blood vessels involved
- The pathological hallmark is immune-mediated injury to blood vessels
- Consideration of more common disease mimics is essential during the diagnostic work-up
- Treatment invariably involves immunosuppression
- With appropriate management, these should be considered chronic disorders

Nomenclature of systemic vasculitides (CHCC 2012)

Large vessel vasculitis
- Takayasu arteritis
- Giant cell arteritis

Medium vessel vasculitis
- Polyarteritis nodosa
- Kawasaki disease

Small vessel vasculitis
- Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis
  - Microscopic polyangiitis
  - Granulomatosis with polyangiitis (Wegener's granulomatosis)
  - Eosinophilic granulomatosis with polyangiitis (Churg–Strauss syndrome)
- Immune complex small vessel vasculitis
  - Antiglomerular basement membrane (anti-GBM) disease
  - Cryoglobulinaemic vasculitis
  - IgA vasculitis (Henoch–Schönlein purpura)
  - Hypocomplementaemic urticarial vasculitis (anti-C1q vasculitis)

Variable vessel vasculitis
- Behçet's disease
- Cogan's syndrome

Single-organ vasculitis
- Cutaneous leucocytoclastic angiitis
- Cutaneous arteritis
- Primary central nervous system vasculitis
- Isolated aortitis
- Others

Vasculitis associated with systemic disease
- Lupus vasculitis
- Rheumatoid vasculitis
- Sarcoid vasculitis
- Others

Vasculitis associated with probable aetiology
- Hepatitis C virus-associated cryoglobulinaemic vasculitis
- Hepatitis B virus-associated vasculitis
- Syphilis-associated aortitis
- Drug-associated immune complex vasculitis
- Drug-associated ANCA-associated vasculitis
- Cancer-associated vasculitis
- Others

Table 1

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example, IgA vasculitis (Henoch–Schönlein purpura) is the most common childhood vasculitis in the West, while Kawasaki disease is the most common childhood vasculitis in Asia.[1]

Nomenclature of systemic vasculitides

The 2012 International Chapel Hill Consensus Conference on the Nomenclature of Systemic Vasculitides (CHCC 2012) proposed names and definitions for most common types of systemic vasculitides. Fundamentally, this framework categorized this complex group of disorders according to the size of the predominantly affected vessels: large, medium and small (Table 1).[2] Although principally aimed at primary vasculitis (unknown aetiology), the proposal recognized that vasculitis can also exist secondarily to other systemic diseases, such as systemic lupus erythematosus and rheumatoid arthritis, and that some understanding of aetiology exists for a few forms of vasculitis, for example hepatitis C-associated cryglobulinaemic vasculitis.

Pathology

Complex interactions between genetic and environmental factors probably lead to immune perturbations and the development of vasculitis. The key pathological feature of all vasculitides is *immune-mediated injury of the vessel wall*. The pattern of injury, however, varies between types of vasculitis.

In **GCA**, affected large-sized vessels – such as the aorta and cranial arteries – show intimal thickening, patchy infiltration of the media with lymphocytes, macrophages and multinucleated giant cells, media necrosis and disruption of the internal elastic lamina. Resultant occlusion leads to end-organ damage such as blindness.

In **polyarteritis nodosa**, medium-sized vessels – such as the mesenteric arteries – show necrotizing inflammatory lesions with destruction of the internal and external elastic laminae, fibrinoid necrosis and formation of aneurysms. Rupture and haemorrhage of these aneurysms result in organ ischaemia, for example bowel infarction. Immune complex-mediated injury is observed in a subset of patients where hepatitis B is aetiologically implicated.[3]

In **AAV**, affecting small vessels such as capillaries, venules or arterioles, there is evidence of necrotizing vasculitis with few or no immune deposits. Significant organ dysfunction often develops rapidly. Autoantibodies (ANCA) against enzymes contained in the granules of neutrophils and monocytes play a central role. These ANCAs can be directed against either myeloperoxidase (MPO) or proteinase 3 (PR3).[4]

Clinical profile and key investigations in systemic vasculitides

Vasculitis	History (common features)	Examination	Laboratory tests	Imaging	Biopsy
Large vessel vasculitis	Constitutional symptoms, headache, jaw claudication, visual changes, limb claudication	Scalp tenderness, absent or asymmetrical pulses, bruit	Elevated ESR/CRP	PET-CT: abnormal FDG uptake (Figure 1) MRA, USS: focal arterial stenosis, aneurysm, inflammation	Temporal artery: inflammation of the arterial wall with disruption of the internal elastic lamina and infiltration with multinucleated giant cells
Medium vessel vasculitis	Constitutional symptoms, abdominal pain, sensory symptoms and focal weakness	Cutaneous ulcers, mononeuritis multiplex, e.g. foot or wrist drop	↓ C4 Cryocrit Hepatitis B and C	Conventional angiography (Figure 1), MRA, CTA Aneurysms, beading and smooth tapering stenotic lesions	Skin or sural nerve biopsy: necrotizing inflammatory lesions destroying internal and external elastic lamina with fibrinoid necrosis
Small vessel vasculitis	Constitutional symptoms, haematuria, nasal discharge, epistaxis, rash, sinus pain, wheeze, haemoptysis, sensory symptoms and focal weakness	Palpable purpura, mononeuritis multiplex, chest rales	Urinalysis: positive for blood, protein and cell casts Eosinophilia CRP ↑ ANCA Blood urea Serum creatinine ↑, immunoglobulins (↑ IgA in IgA vasculitis)	Chest X-ray High-resolution CT of the chest (Figure 1)	Kidney: Without immune deposits, i.e. pauci-immune necrotizing glomerulonephritis with crescents (Figure 2) in AAV With immune deposits, e.g. small vessel vasculitis in IgA vasculitis

ANCA, antineutrophil cytoplasmic antibody; C4, complement component 4; CRP, C-reactive protein; CT, computed tomography; CTA, CT angiogram; CT-PET, CT-positron emission tomography; ESR, erythrocyte sedimentation rate; FDG, fluorodeoxyglucose; IgA, immunoglobulin A; MRA, magnetic resonance angiogram; USS, ultrasound scan.

Table 2

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