

# Introduction

# Introduction

section 21 Disorders of the kidney and urinary tract 4988 21.10.2 The kidney in systemic vasculitis

David Jayne ESSENTIALS Systemic vasculitis can occur as a primary autoimmune disorder, or as a secondary manifestation of another disease process (related to infection, malignancy, chronic inflammatory disorder, or drugs). Primary systemic vasculitis is classified according to the predominant size of the blood vessel involved and the presence of circulating antineutrophil cytoplasm autoantibodies (ANCA). Incidence and prevalence rates are between 15 and 20 per million and 200 to 400 per million population, respectively. Vasculitic syndromes frequently involve the kidney, causing tissue infarction, loss of function, and rapid progression to endstage renal disease within weeks or months. They account for 5% of cases of endstage renal failure. ANCA-associated vasculitis (AAV) is the most common cause of renal vasculitis and has been the focus for most research. Management aims for an early diagnosis, recovery of renal function, and prevention of renal relapse. Small-vessel vasculitides—renal disease is common. There are two subgroups: AAV, which comprises three syndromes: granulomatosis with polyangiitis (GPA, formerly Wegener's granulomatosis), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with angiitis (EGPA, formerly Churg–Strauss syndrome). The second subgroup is immune complex vasculitis and comprises IgA vasculitis (formerly Henoch–Schönlein purpura), antglomerular basement membrane disease, and cryoglobulinaemia: these are ANCA negative and characterized by immune complex deposition. Medium- and larger-vessel vasculitides—renal disease is uncommon in the medium-vessel disorders polyarteritis nodosa (ANCA negative) and Kawasaki's disease, and rare in the large-vessel disorders, giant cell arteritis and Takayasu's arteritis. Aetiology and pathogenesis—there is a complex genetic contribution to AAV, and rare drug-induced forms. Neutrophil dysregulation is associated with ANCA and alternative complement pathway activation. Pathology—the typical renal lesion of small-vessel vasculitis is a neutrophil-dominant glomerular capillaritis leading to segmental necrotizing glomerulonephritis with epithelioid crescent formation. Glomerular immune deposits are scanty or absent in AAV ('pauci-immune'). Clinical presentation—the diagnosis of vasculitis is often delayed for many months because initial symptoms such as fever, night sweats, polymyalgia, and weight loss are nonspecific. Patients with vasculitis present with (1) persistent symptoms of constitutional disturbance; (2) nonrenal vasculitic manifestations, the nature of which may indicate a specific diagnosis, for example, upper respiratory tract symptoms or signs (GPA), 'maturity-onset' asthma (EGPA), or mononeuritis multiplex (MPA); or (3) features of renal insufficiency. AAV is the most common cause of rapidly progressive glomerulonephritis—crescentic glomerulonephritis with renal failure—and should be considered in any unexplained case of acute renal impairment, especially when nonvisible haematuria with proteinuria is present and the kidneys are of normal size on ultrasound examination. Patients with renal-limited vasculitis present with more advanced renal

failure than those with extrarenal disease because they are asymptomatic until symptoms of renal insufficiency develop. Diagnosis—this depends on the recognition of patterns of clinical features, supported by serology, histology, and imaging, and the exclusion of secondary causes. ANCA positivity, confirmed by a positive proteinase 3 ANCA (PR3-ANCA) or myeloperoxidase ANCA (MPO-ANCA), has a predictive value of over 95% for the diagnosis of AAV with renal involvement in a patient with suspected nephritis. The diagnosis of polyarteritis nodosa is usually made by demonstration of aneurysms of medium-sized muscular arteries on angiography, or when biopsy of affected tissue reveals fibrinoid necrosis of involved vessels, accompanied by a marked inflammatory response. Other investigations determine the extent and severity of systemic disease. Management—combination therapy with cyclophosphamide or rituximab and high-dose oral prednisolone leads to control of active disease in 80 to 90% of patients, but is complicated by toxicity, particularly cytopenias and infection. Azathioprine, methotrexate, or mycophenolate mofetil in combination with low-dose prednisolone or rituximab are used to maintain remission after 3 to 6 months, and mycophenolate mofetil may also be considered for the induction of remission in MPO-ANCA-associated renal disease. High-dose intravenous methylprednisolone is widely used as initial therapy for renal vasculitis, and plasma exchange improves the chances of renal recovery in patients with severe renal impairment. Careful follow-up of patients in experienced centres with regular monitoring of blood counts, biochemical indices, inflammatory markers (erythrocyte sedimentation rate and C-reactive protein), and ANCA permits the prevention and early detection of drug-related toxicity and infection, and the early diagnosis and treatment of disease relapse. Collaborative research networks have facilitated randomized controlled trials and the development of evidence-based treatment guidelines. Disease relapse—this is seen in 50% of patients by 5 years and is more common in PR3-ANCA-positive patients, in the presence of persisting ANCA positivity, and after withdrawal of immunosuppressive drugs. Rituximab is the first choice for relapsing or refractory disease: patients then require long-term therapy as subsequent relapses are likely. Prognosis—patient survival in AAV with renal involvement is 83 and 73% at 1 and 5 years, respectively, with a high serum creatinine at diagnosis, older age, and extensive extrarenal vasculitis indicating a poorer prognosis. Fifty per cent of those presenting with a serum creatinine greater than 500  $\mu\text{mol/litre}$  will be alive and off dialysis at 1 year of follow-up.

**Introduction** Renal involvement is common in primary systemic vasculitis affecting small blood vessels and is subdivided into those associated with antineutrophil cytoplasm autoantibodies (ANCA) (Table 21.10.2.1) (ANCA-associated vasculitis (AAV): comprising granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA)) and those without ANCA but with immune complex deposition on

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