Serology

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21.10.2 The kidney in systemic vasculitis 4993 Investigation There are no diagnostic criteria for vasculitis syndromes and diag- nosis depends on recognition of the pattern of clinical features, supported by serology, histology, and imaging, and the exclu- sion of secondary causes and mimics of vasculitis. Patients with suspected renal vasculitis require systematic review of all organ systems for the detection of other foci of vasculitis and the identi- fication of comorbidities likely to influence treatment choice and prognosis. Serology ANCA positivity (Fig. 21.10.2.3) has historically required a positive cytoplasmic ANCA (C-ANCA) or perinuclear ANCA (P-ANCA) by indirect immunofluorescence, confirmed by a positive PR3- ANCA or MPO-ANCA, but improvements in the quality and speci- ficity of PR3 and MPO-ANCA assays have reduced the value of the indirect immunofluorescence assay. The clinical utility of ANCA assays depends on the clinical context, but in suspected nephritis a positive PR3 or MPO-ANCA has a 95% specificity for vasculitis. However, 5 to 10% of patients with a pauci-immune necrotizing crescentic glomerulonephritis are ANCA negative, and ANCA will be negative in some early or limited forms of AAV, and after treat- ment. Immune-complex-mediated vasculitis syndromes, such as IgA vasculitis and large-vessel vasculitis, are ANCA negative. Complement C3 and C4 and immunoglobulin levels are normal in AAV and anti-GBM disease; rarely, they are reduced in IgA vas- culitis. A positive rheumatoid factor, paraprotein (usually IgM), and low C3 and C4 is the typical pattern in cryoglobulinaemia. A low-titre positive rheumatoid factor and atypical pattern antinuclear antibody can be seen in AAV, where they appear to be of no significance. Urine analysis The presence of haematuria, occasionally visible, is universal in renal vasculitis and is accompanied by proteinuria. In AAV and anti-GBM disease, proteinuria is non-nephrotic and averages 1 g/24 h, although an increase in proteinuria can be seen in the recovery phase due to glomerular remodelling. Phase contrast microscopy reveals dys- morphic red cells of glomerular origin, and the presence of red cell casts is almost diagnostic of a crescentic nephritis (Fig 21.10.2.4). Nephrotic-range proteinuria may be found in vasculitis associated with immune complexes, such as cryoglobulinaemia or IgA vascu- litis, but other causes of the nephrotic syndrome are more likely if this is the initial presentation, especially if the serum creatinine is normal. Histology Renal histology enables the most secure diagnosis to be made. The typical renal biopsy features in AAV are a pauci-immune necrotizing glomerulonephritis with crescent formation (Fig. 21.10.2.1). MPA is associated with more severe biopsy changes, with greater evidence of chronicity and scarring. In GPA, acute tubular changes are more frequent, scarring is less apparent, and the prognosis is better. Histological severity is classified according to the Berden system into focal, crescentic, mixed, and sclerotic subgroups, which associate with renal prognosis (Table 21.10.2.3). The presence of severe scarring does not exclude the possibility of a good renal outcome and this system is not used to guide induc- tion therapy. Extensive tubulointerstitial inflammation or damage, extraglomerular arterial disease, and MPO-ANCA are

further negative predictive factors for renal outcomes. Occasionally, a dual pathology is identified, such as anti-GBM disease or IgA nephropathy. (a) (b) Fig. 21.10.2.3 Indirect immunofluorescence assay for ANCA. (a) Typical staining pattern of cytoplasmic ANCA that is usually due to antibodies to proteinase 3. (b) Typical staining pattern of perinuclear ANCA that is usually due to antibodies to myeloperoxidase. (a) (b) Fig. 21.10.2.4 (a) Dysmorphic urinary red blood cells. (b) A red blood cell cast.

Revision #1
Created 2026-01-22 16:42:11 UTC by Omar Ayman
Updated 2026-01-22 16:42:11 UTC by Omar Ayman