

# To find glomerulonephritis you have to look for it

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Anti-neutrophil cytoplasmic antibodies (ANCA) associated small vessel vasculitis is a systemic auto-immune disease with widespread and highly variable clinical manifestations. Renal involvement, usually in the form of necrotising crescentic glomerulonephritis (pure necrotising renal vasculitis without glomerulonephritis is very rare), is frequently one of the manifestations of the disease and is encountered in the majority of patients at diagnosis.<sup>1</sup> The severity of renal involvement has both therapeutic and prognostic consequences. Most management guidelines determine the intensity of immunosuppressive therapy on the severity of vital organ dysfunction, which in many patients is defined by the level of renal failure.<sup>1,2</sup> In addition, the level of renal failure at diagnosis and especially the failure to regain renal function during induction therapy is associated with a worse outcome and high mortality.<sup>3,4</sup> So assessment of the presence and severity of renal involvement in ANCA-associated vasculitis is mandatory and an essential part of patient care and the selection of appropriate treatment.

The diagnosis of ANCA-associated vasculitis has been made more straightforward by the discovery of the high sensitivity and specificity of autoantibodies directed against proteinase-3 and myeloperoxidase.<sup>5,6</sup> Reliable assays to detect these antibodies are available. Also awareness of these diseases has probably increased over the last decades. It is conceivable that the diagnosis of ANCA-associated vasculitis is made more timely and that the proportion of patients with severe organ dysfunction including severe renal failure is declining and patients are diagnosed in an earlier and more limited phase of the disease. This view is illustrated by the finding of Houben et al. described in this issue of the journal that in 109 patients diagnosed with ANCA-associated vasculitis the median serum creatinine at diagnosis was low despite renal involvement in 61% of the patients at diagnosis.<sup>7</sup>

Most patients with ANCA-associated vasculitis will not present with visual or other overt signs of renal

involvement: macroscopic haematuria is usually absent as one of the presenting symptoms and proteinuria is frequently mild, not leading to the clinical signs of nephrotic syndrome. This is also nicely illustrated by the paper by Houben as only 21 of the patients from their cohort were diagnosed by the renal department. This means that patients present with combinations of other signs and symptoms and are referred to other disciplines. Renal involvement, therefore, has to be actively investigated once the diagnosis of ANCA-associated vasculitis is suspected. This means that in every patient in whom the diagnosis of ANCA-associated vasculitis is seriously considered, assessment of renal function (serum creatinine, estimated glomerular filtration rate (eGFR), 24-hour urine creatinine clearance) and urinalysis (erythrocyturia and if present urinary microscopy for glomerular erythrocyturia and/or erythrocyte casts, proteinuria) should be performed.<sup>1,2</sup> As Houben et al. describe, it is worrying that renal involvement is not actively investigated in a proportion of patients with suspected or confirmed ANCA-associated vasculitis, not even in the weeks and months following the diagnosis. The 19 of 109 patients (22% in patients not diagnosed in the renal department) with ANCA-associated vasculitis not screened for renal involvement in their study had a lower serum creatinine (median 70  $\mu\text{mol/l}$ , IQR 56-89  $\mu\text{mol/l}$ ) at diagnosis, which may have led to the misconception that a serum creatinine in the 'normal' range effectively excludes the presence of renal involvement. In addition, we have to repeat the message that a so called 'normal' serum creatinine is not the equivalent of normal renal function. Especially in an older population (mean age at diagnosis 62  $\pm$  14 years in the cohort described by Houben) and in persons with a systemic inflammatory illness lasting for some time and leading to muscle wasting, serum creatinine levels can be deceptively low despite significant renal impairment.

As renal involvement is usually seen as a sign of more severe disease in ANCA-associated vasculitis, the failure to

recognise renal involvement early may lead to insufficient treatment of patients, which is suggested by the fact that cyclophosphamide induction therapy was given to only 37% of those not screened for renal involvement. Also the fact that, despite a lower serum creatinine at diagnosis, at three years of follow-up renal function as estimated by eGFR was clearly lower in patients who did not receive cyclophosphamide induction compared with those who did may point in that direction. Finally, it should be highlighted that even in the minority of patients with documented absence of renal involvement at diagnosis, during follow-up renal involvement may develop. In a recent series from our centre this was the case in 21%, while at least half of all relapses in patients with renal involvement at diagnosis show renewed renal activity.<sup>4</sup> This means that screening for renal involvement is not only mandatory in the diagnostic phase, but also is an essential part of assessment for disease activity during follow-up. This is essential to all of us who diagnose and treat patients with these diseases. To paraphrase one of the rules from ‘The House of God’ by Samuel Shem: you won’t find renal small vessel vasculitis if you don’t do a urinary sediment.

## REFERENCES

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