

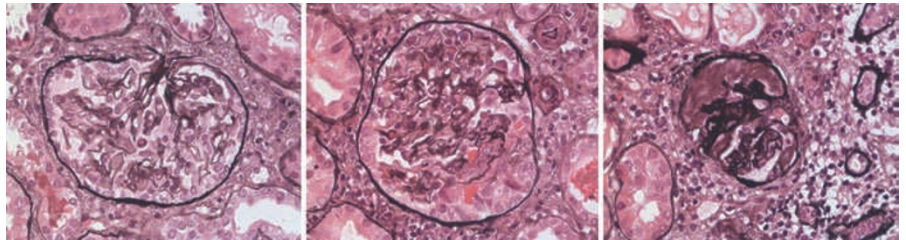
## GLOMERULAR DISEASE

## ANCA-associated glomerulonephritis: a new histopathological classification

**K**idney biopsy samples from patients with clinically manifest antineutrophil cytoplasmic antibody (ANCA)-associated glomerulonephritis demonstrate a great variety of lesions but no consensus exists for their pathological classification. Renal pathologists from an international working group now report a histopathological classification system for ANCA-associated glomerulonephritis, which they believe will be useful for assessing the prognosis of patients affected by this disease. “For the treating physician it is very important to know what specific findings in the renal biopsy sample mean in terms of patient prognosis. Our proposed classification scheme will improve the prognostication of patients at the time of diagnosis and facilitate uniform reporting between centers worldwide”, explains lead author, Annelies Berden.

Renal biopsy is the current gold standard for establishing a diagnosis of ANCA-associated glomerulonephritis. Several clinicopathologic studies have demonstrated relationships between specific lesions encountered on renal biopsy examination and patient or renal outcome; however, no histopathological classification of ANCA-associated glomerulonephritis existed. The need for a classification system to distinguish levels of disease severity led Berden to initiate the current study in collaboration with an international consortium of clinicians and pathologists from eight countries. “Our aim was to design a classification scheme that would provide valuable information for clinicians and that at the same time could be easily adopted by pathologists in daily practice”, says Berden.

On the basis of results from prior studies, Berden and colleagues designed a classification system that groups biopsy samples into four categories—focal,



Features of glomerular histology: (left) a normal glomerulus; (middle) a cellular crescent; (right) a sclerotic glomerulus. Images courtesy of A. E. Berden, Leiden University Medical Center, Leiden, The Netherlands.

crencentic, mixed, and sclerotic—according to glomerular pathology as assessed by light microscopy. Biopsy samples were classed as focal if  $\geq 50\%$  of glomeruli were not affected by disease, crescentic if  $\geq 50\%$  of glomeruli had cellular crescents, mixed if they showed a combination of normal, crescentic, and sclerotic glomeruli, or sclerotic if  $\geq 50\%$  of glomeruli were sclerotic.

The researchers also assessed the usefulness of their classification system for the assessment of disease severity and prognosis by performing a validation study in 100 patients who had clinically and histologically confirmed ANCA-associated glomerulonephritis. Biopsy samples with a minimum of 10 whole glomeruli were included.

Berden *et al.* found that the four renal biopsy categories correlated with the degree of renal function at presentation and at 1-year and 5-year follow-up, with category independently predicting estimated glomerular filtration rate at both follow-up points. They also demonstrated a relationship between disease category and risk of end-stage renal disease. “The validation study demonstrated that the phenotypic and numerical order of the scheme’s classes corresponded to the severity of renal function impairment during follow up”, explains Berden. The researchers also found that patients with sclerotic ANCA-associated glomerulonephritis had a higher risk of death than other patients.

The working group believe that their classification system provides a useful tool for assessing disease and patient prognosis at the time of renal biopsy. “This scheme is of clinical relevance because clinical outcomes between patients with ANCA-associated glomerulonephritis are very diverse and are difficult to predict”, stresses Berden. “As might be expected, our study showed that patients with extensive chronic damage stand a lesser chance of renal recovery than patients with a relatively high percentage of nonaffected renal tissue. Interestingly, patients with extensive evidence of disease activity, but not so much scarring in the renal biopsy are likely to present with very impaired renal function, but stand a good chance of recovery.”

The researchers hope that their proposed classification system will be validated by other researchers in independent cohorts. The researchers also plan to investigate the intraobserver and interobserver variation of their scheme in greater detail. “Findings from these analyses will be used to further refine our classification system and increase its usefulness and reliability in daily practice for the benefit of patients worldwide”, they say.

Susan J. Allison

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