Nephroquiz for the Beginner
(Section Editor: M.G. Zeier)

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Light from the renal biopsy

Case

A previously healthy 66-year-old man complained of progressive lassitude, exertional dyspnoea and swollen ankles over 6 weeks. Physical examination was normal apart from oedema affecting the ankles and a blood pressure of 168/84 mmHg. Dipstick testing showed significant haematoproteinuria and the serum electrolytes were: Na 145 mmol/l, K 4.0 mmol/l, urea 11.7 mmol/l, and creatinine 205 μmol/l. Proteinuria was 5.62 g/day, the serum albumin was 36 g/dl, and random glucose 6.2 mmol/l. Haemoglobin was 9.9 g/dl. The following investigations were normal or negative: WBC, platelets, anti-nuclear antibodies, antineutrophil cytoplasmic antibodies (ANCA), antiglomerular basement membrane (GBM) antibody and complement levels. Serum electrophoresis revealed panhypogammaglobulinaemia but no paraprotein. Bence-Jones protein was not detected in the urine. Serum calcium was elevated at 3.08 mmol/l but serum ACE levels were normal. A chest X-ray and a radiological skeletal survey showed no abnormality. The kidneys were of normal size and morphology on ultrasound examination. The renal biopsy appearances are shown in Figures 1 and 2.

Question

What is the most likely diagnosis?

Fig. 1. Light microscopy of renal biopsy. Haematoxyline/eosine stain (×400 magnification).

Fig. 2. Light microscopy of renal biopsy. Silver stain (×400 magnification).
Answer to the quiz on preceding page

Monoclonal immunoglobulin deposition disease (MIDD).

The immune paresis, hypercalcaemia and poorly argyrophilic nodular glomerulosclerosis are characteristic of MIDD. Immunofluorescence and electron microscopy confirmed the diagnosis. Figures 3 and 4 show $\kappa$ light chain deposition around the tubular basement membrane and the diagnosis of ‘non-secretory’ myeloma was substantiated by a bone marrow examination that revealed abnormal plasma cells (20%) with $\kappa$ restriction. In 15–30% of patients with MIDD, there is no detectable monoclonal immunoglobulin in the serum or urine, hence the term ‘non-secretory myeloma’. True non-secretion is probably very rare because, in most cases, the abnormal immunoglobulin is either rapidly degraded or deposited in tissues [1].

Glomerular lesions are heterogeneous but nodular glomerulosclerosis (Figure 1) is most frequently observed. There are similarities with diabetic nodular glomerulosclerosis, but distinctive features of MIDD are: (i) the nodules are evenly distributed and often are poorly argyrophilic (Figure 2); (ii) the exudative lesions (‘fibrin caps’) and extensive hyalinosis of the efferent arterioles, characteristic of diabetes, are not observed. In milder forms of MIDD, glomerular lesions may not be evident on light microscopy, but can be identified by electron microscopy.

Tubular lesions may be more conspicuous than glomerular changes and are characterized by the deposition of a refractile, eosinophilic, PAS-positive, ribbon-like material along the outer part of the tubular basement membrane. Marked interstitial fibrosis develops in advanced disease. Evidence of monotypic light- and/or heavy-chain fixation along the tubular basement membrane is required for the diagnosis of MIDD. Immunostaining of glomeruli is typically less prominent than that observed along the tubular basement membranes. The degree of staining does not always correlate to the actual amount of deposited material, since several cases have been reported in which glomerular immunofluorescence was negative despite the presence of large amounts of granular glomerular deposits demonstrated by electron microscopy [4]. The most characteristic ultrastructural feature is the presence of finely- or coarsely-granular electron-dense deposits that delineate the outer aspects of the tubular basement membrane and endothelial aspects of the glomerular basement membrane (Figure 4). Electron-dense material deposition is also seen in the mesangium and nodules.

Plasma cell dyscrasia and MIDD must be considered in older patients with hypercalcaemia, immune paresis and evidence of renal injury even in the absence of other features of myeloma. Furthermore, MIDD may be the correct underlying diagnosis in some cases of ‘diabetic glomerulosclerosis’ with no other evidence of diabetes.

References


Mohammed Javed Ansari
Ajay Kumar
John Turney
Department of Renal Medicine
The General Infirmary at Leeds
Leeds, UK