Membranous glomerulonephritis—an under-reported histological finding in multiple myeloma

Sir,

Plasma cell dyscrasias are characterized by clonal proliferation of plasma cells derived from B-lymphocytes. Renal involvement is well recognized in patients with all types of plasma cell dyscrasias including multiple myeloma. In patients with ‘myeloma kidney’, the commonest histological finding described is tubular light-chain deposition disease. Tubulo-interstitial nephritis, amyloid deposition and infarcts have also been demonstrated but the presentation with membranous glomerulonephritis has never been reported. Herein we describe two patients who had nephrotic syndrome associated with multiple myeloma and were found to have membranous glomerulonephritis.

An 80-year-old male presented with pedal oedema and proteinuria of 7.77 g/day, serum creatinine of 113 µmol/l, creatinine clearance of 81 ml/min and serum albumin of 19 mmol/l. Renal histology confirmed membranous glomerulonephritis, without any sign of amyloid deposition (Figure 1). Serum electrophoresis detected a biclonal IgA lambda at 3.2 g/l and 0.8 g/l, with IgG levels of 3.40 g/l (normal range 6.0–16.0 g/l), IgA 9.20 g/l (0.8–4.0 g/l) and IgM 0.40 g/l (0.5–2.0 g/l). Bence Jones protein was detected in urine. Skeletal survey did not reveal lytic lesions but the excess of abnormal plasma cells in his bone marrow was consistent with a diagnosis of multiple myeloma. The patient’s nephrotic syndrome resolved with chemotherapy for his myeloma.

The second patient was an 87-year-old lady who was noted to have 0.4 g/l Bence Jones paraprotein (kappa band) in her urine upon investigation of her proteinuria. Her renal function and serum calcium, serum electrophoresis and skeletal survey were normal. A bone marrow aspirate at the time revealed <5% plasma cells. However, a year later she developed nephrotic range proteinuria, with a 24-h urine protein of 13.11 g/day, a serum creatinine of 98 µmol/l, creatinine clearance of 83 ml/min and a serum albumin of 28 g/l. Renal histology revealed membranous glomerulonephritis. Her nephrotic syndrome resolved spontaneously. The urine-free light chains were monitored regularly, with no change in the blood counts or renal function. Six years after this presentation, she was referred with back pain. A repeat screen for multiple myeloma showed a definite increase in plasma cells to 15% but again, without lytic lesions on skeletal survey or abnormalities in blood counts or renal excretory function. However, she did have a recurrence of her nephrotic syndrome. There was a detectable serum kappa light chain band of 273 mg/l (normal range 3.3–19.4 mg/l) with a kappa/lambda ratio of 16.3 (normal range 0.26–1.65) and urine light chain quantified at 0.04 g/l. The patient was given treatment for her myeloma, with which her proteinuria resolved. This patient remains under active monitoring, but her paraproteinaemia remains stable and repeated checks for amyloidosis remain negative. She has had no recurrence of her nephrotic syndrome. Her urine protein excretions stabilized at 0.15 g/l.

Renal insufficiency affects >50% of patients with multiple myeloma at the time of diagnosis, and renal failure is the second most common cause of mortality. Renal involvement is often characterized by casts or nephropathy but glomerular, interstitial or vascular diseases have also been noted [1]. However, membranous glomerulonephritis has not been previously reported in myeloma patients. In a recent report, Komatsuda et al. reviewed 5443 renal biopsies and identified three patients with monoclonal immunoglobulin deposition disease associated with membranous features. Renal insufficiency was not a feature in any individual and only one had nephrotic syndrome. Two of the patients had IgG3-κ deposits and one had IgG1-κ deposits without paraprotein in either serum or urine [2]. Unlike this series, both our patients developed nephrotic syndrome and monoclonal paraproteinaemia, which instigated kidney biopsies that demonstrated membranous glomerulonephritis.

It is unclear why the association between membranous glomerulonephritis and myeloma has not been observed before. The most common renal pathology in myeloma is cast nephropathy. In these patients, the absence of glomerulonephritis suggests that the abnormal immunoglobulins do not bind to the basement membrane. Glomerular involvement does occur in the rare presentations of amyloid and light chain deposition disease [3]. The diffuse pattern of deposition that also involves the mesangial and subendothelial compartments makes it less likely to be caused by antibodies targeted against the basement membrane. The same is true of cryoglobulinaemia [4]. Our patients’ histology demonstrated no pathology other than subepithelial deposits with focal foot process effacement. This picture ties in with other researchers’ conclusion that different mechanisms cause differing renal disease in myeloma patients [5]. Our patients’ nephrotic syndrome was probably caused by a process of immunoglobulin binding to glomerular basement membrane antigens such as M-type phospholipase A2 receptor or neutral endopeptidase, similar to that noted in some instances of idiopathic membranous glomerulonephritis [6,7]. The rarity of this presentation in myeloma patients could then be explained by the low probability, amongst all the possible light chain combinations, of forming an antibody that is competent enough to bind with podocyte antigen and trigger the complement cascade.

As demonstrated in our two patients, membranous glomerulonephritis does occur in association with multiple myeloma and does respond to therapy. The resolution of our
patients’ nephrotic syndrome with treatment of the plasma cell dyscrasia further adds to our premise that their glomerulonephritis was caused by their myeloma.

Conflict of interest statement. None declared.

Editorial Note: Dr Komatsuda et al. had no further comments on this letter.

1Department of Haematology
University of Liverpool
2Department of Haematology
University Hospital Aintree
3Department of Pathology, Royal
Liverpool University Hospital, UK
4Department of Nephrology,
University Hospital Aintree
E-mail: a.abraham@aintree.nhs.uk

Fig. 1. Electron microscopy ×8800 showing subepithelial deposits separated by spikes of the basement membrane and focal foot process effacement, consistent with membranous glomerulonephritis.

Natural killer cells in continuous ambulatory peritoneal dialysis patients

Sir,

You have published a very interesting paper by Vacher-Coponat et al. [1] indicating that haemodialysis (HD) duration and renal function are factors influencing natural killer (NK) cell count and NK cell activity in HD patients. Lower cell counts characterize immune disorders in HD patients. In our study [2], we determined the influence of continuous ambulatory peritoneal dialysis (CAPD) course on lymphocyte subset count (SLC) including lymphocytes T (CD3), lymphocytes B (CD19), helper lymphocytes (CD4), cytotoxic-suppressor lymphocytes (CD8) and NK cells (CD16+56). Uraemic patients started CAPD therapy with decreased SLC, excluding NK cell count that was within the normal range in the predialysis period. In the first year of CAPD therapy, a significant increase in SLC and CD4:CD8 ratio was observed, concomitantly with an improvement in nutritional status. In the following years, CD3, CD4, CD8 and CD19 cell counts decreased, but not NK cell count. In patients on CAPD for more than 36 months, an increase in the number of NK cells over the normal range was shown. An increase in NK cells above the normal range may reflect chronic sterile or infectious inflammatory response, which stimulated NK cells. That finding accords with the study performed in CAPD patients by Palop et al. [3]. When the examined patients were distributed according to age, decreasing values of SLC with ageing in younger (35.5±5.4 years) and older (67.2±5.1 years) CAPD groups were shown, but age did not influence a number of NK cells [4]. In this study, a decrease in SLC was significantly related to CAPD duration only in younger patients: negative correlations were seen between dialysis duration and CD3, CD19 and CD4. NK cell count was not associated with CAPD duration neither in younger nor in older patients.

Treatment of CAPD patients with angiotensin-converting enzyme inhibitors (ACEIs) can influence lymphocyte count over the course of CAPD. In our study [5], patients receiving ACEI demonstrated negative correlation between summarized ACEI (enalapril, captopril, perindopril) dose and NK cell count. In this study, correlation was not seen between NK cells count and erythropoietin dose.

There were no associations between NK cell count and underlying kidney diseases, gender, intake of main food components, residual renal function, dialysate protein losses and CAPD adequacy, but there was negative correlation between NK cell count and blood urea nitrogen [6].