Proliferative glomerulonephritis with monoclonal immunoglobulin deposits of lambda chains

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ABSTRACT

Increasingly, monoclonal gammopathies of renal significance (MGRS) are being described as unique, distinct disease states. We describe a type of MGRS with proliferative glomerular lesions with monoclonal immunoglobulin deposits of rarely reported IgG2 lambda chains.

KEYWORDS Acute kidney injury; antineutrophil cytoplasmic antibodies; blood urea nitrogen; chronic kidney disease; lambda chains; monoclonal gammopathies of renal significance; proliferative glomerulonephritis with monoclonal immunoglobulin deposits

The monoclonal gammopathies of renal significance (MGRS) are a group of kidney diseases that are defined by deposition of monoclonal immunoglobulin but no obvious systemic multiple myeloma process.¹ The MGRS group is gaining increasing interest as knowledge of the spectrum of disease is available. We describe a unique case of proliferative glomerulonephritis with monoclonal immunoglobulin deposition (PGNMID) in a patient with acute kidney injury and a negative serologic workup.

CASE DESCRIPTION

A 75-year-old white man with hypertension, coronary artery disease, and peripheral vascular disease was admitted with azotemia, fatigue, anorexia, and headaches. Admission laboratory values revealed a serum creatinine of 4.1 mg/dL and blood urea nitrogen of 95 mg/dL. His creatinine and blood urea nitrogen had been 1.1 mg/dL and 18 mg/dL 12 days prior. He reported no history of contrast exposure, nonsteroidal antiinflammatory use, or antibiotics. Vital signs were within normal limits. Urinalysis showed 100 red blood cells per high-powered field, 30 to 50 white blood cells per high-powered field, and a urine protein-creatinine ratio of 1.3. A renal ultrasound was within normal limits. Hepatitis B and C, antinuclear antibody, double-stranded deoxyribonucleic acid, anti-Sjögren syndrome A and B, anti-neutrophil cytoplasmic antibody, anti-glomerular basement membrane antibody, and cryoglobulins were all negative. Complement levels showed a normal C4, although C3 was low at 63 mg/dL (normal range, 90–180). Serum protein

electrophoresis showed decreased total protein and no M spike. Serum immunofixation revealed normal-range levels of IgG (1007 mg/dL), IgA (276 mg/dL), and IgM (51 mg/dL), with very faint monoclonal lambda immunoglobulins present. Serum free kappa and lambda light chains were mildly elevated but with a normal free kappa-lambda ratio of 1.66. Urine protein electrophoresis showed a positive M spike of 5.5 mg/dL. Hemodialysis was initiated with a tunneled catheter for uremia.

The light microscopic examination of a kidney biopsy revealed two out of 15 glomeruli with global sclerosis, a diffuse endocapillary and mesangial proliferative pattern without crescents, and 30% interstitial fibrosis and tubular atrophy. The immunofluorescence study revealed a lambda-restricted staining pattern with IgG2 only. Electron microscopic examination showed abundant subendothelial and mesangial deposits. The patient was diagnosed with MGRS and PGNMID pattern (*Figure 1*). He was started on immunosuppressive therapy with oral cyclophosphamide 100 mg daily and prednisone 1 mg/kg/day. The patient stopped hemodialysis after 6 weeks and completed immunosuppression therapy as an outpatient.

DISCUSSION

MGRS includes a cluster of conditions caused by a monoclonal immunoglobulin deposition in the kidney.² This definition signifies no serologic or clinical evidence for overt multiple myeloma or B-cell proliferation systemically. The commonly known disease state of monoclonal gammopathy of unknown significance (MGUS) differs from MGRS in that the latter contains objective

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Figure 1. A kidney biopsy with (a) hematoxylin and eosin $\times 400$ and (b) Jones methenamine silver $\times 400$ reveal diffuse mesangial proliferation. (c) Immunofluorescence studies and (d) lambda $\times 400$ and (e) IgG2 $\times 400$ show an IgG2-lambda-restricted staining pattern. (e) Electron microscopy demonstrates abundant subendothelial deposits with endocapillary hypercellularity.

evidence of renal involvement, indicating end-organ damage. The spectrum of MGRS disorders is wide and includes primary amyloidosis, light and heavy chain deposition disease, immunotactoid glomerulopathy, PGNMID, and C3 glomerulopathy.

The diagnosis of PGNMID is confirmed with a kidney biopsy, and 75% of published cases report a negative serum protein electrophoresis, negative urine protein electrophoresis, and normal ratio of serum free light chains.³ The IgG3 subclass is the most common immunoglobulin found in PGNMID.⁴ Our case is rare without any evidence of IgG3 on immunofluorescence and a predominance of the IgG2-lambda subclass, with very few cases reported previously.⁵

The “benign” MGUS diagnosis requires careful monitoring with no cytotoxic treatment. The finding of MGRS on kidney biopsy alternatively necessitates intervention to prevent ongoing deposition and end-organ damage.² In the largest case series of only 37 patients with PGNMID, only 38% experienced complete or partial recovery of renal function.⁴ Our patient received immunosuppressive therapy with

cyclophosphamide and daily oral prednisone in a conservative regimen given his advanced age. He showed great response and was able to come off renal replacement therapy after 6 weeks. The patient is being monitored closely for further improvement of kidney function and the potential eventual serologic detection of disease.

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