Dense deposit disease in association with monoclonal gammopathy of unknown significance

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Abstract

Several renal pathologic entities have been reported in patients with lymphoplasmacytic disorders with their typical excess immunoglobulin production. We report dense deposit disease in a patient who was discovered to have an IgG kappa monoclonal protein without clinical evidence of underlying lymphoplasmacytic malignancy during investigation for chronic renal failure with associated nephrotic range proteinuria. This case is unusual since dense deposit disease occurs only rarely in older patients and has not been reported in association with monoclonal gammopathy of unknown significance. Because of the diversity of renal lesions associated with lymphoplasmacytic disorders, renal biopsy is necessary to assess the type of renal lesion in this patient population.

Key words: Dense deposit disease; nephrotic proteinuria; monoclonal gammopathy of unknown significance

Introduction

A large spectrum of renal lesions have been described in patients with lymphoplasmacytic disorders with their associated dysproteinaemias [1-11]. Classically, myeloma kidney and renal amyloidosis are cited, however, a more heterogeneous group of lesions ranging from nodular glomerulosclerosis, proliferative glomerulonephritis, crescentic glomerulonephritis, and in some cases even minimal change nephropathy has been reported.

In this paper we are reporting an unusual renal lesion not previously described in association with any dysproteinaemia. This patient was found to have a monoclonal IgG kappa protein during the course of investigation of newly discovered renal failure with nephrotic range proteinuria. His bone marrow studies were essentially unremarkable with no evidence of a plasma cell dyscrasia. Renal biopsy revealed membranoproliferative glomerulonephritis type II (dense deposit disease) which is an extremely unusual lesion in this patient's age group and has not been reported in association with any form of monoclonal gammopathy.

A kidney biopsy was essential in establishing the renal diagnosis in this case and is an important adjunct to the information gained from the bone marrow studies in patients with abnormal monoclonal proteins.

Case report

A 53-year-old white male was referred for assessment of renal insufficiency. This previously healthy male reported a 4-week history of a flu-like illness with dry cough and sore throat in December 1993. The cough and sore throat both settled by mid-January, however, he continued to feel unwell with reduced energy level. He did not report any gross haematuria or periorbital/peripheral oedema. He visited his family doctor in September 1994 complaining of generalized pruritus. At this time, routine laboratory screen revealed his serum creatinine to be elevated at 1143 umol/l and urea at 44.8 mmol/l. When seen in consultation in October 1994 he had continued to feel somewhat poorly with decreased energy level and pruritus without any systemic symptoms. His only medications were an antihistamine, a topical steroid, and a multivitamin preparation. Physical examination revealed: height 178 cm, weight 105 kg, blood pressure 185/115 mmHg and pulse rate 80/min. He did not have any periorbital or peripheral oedema and his JVP was not elevated. The heart sounds were normal with the exception of a soft fourth heart sound. The remainder of the examination was unremarkable and the patient did not have any classical signs of dense deposit disease. Urine examination revealed 4+ blood and > 3 g/l of protein on dipstick and microscopic examination revealed numerous RBCs (many of which were dysmorphic) and a few coarse granular casts; no RBC casts were seen. Laboratory examination revealed his creatinine to be elevated at 927 umol/l, urea at 39 mmol/l with low calcium (1.70 mmol/l), high phosphorus (2.55 mmol/l), low bicarbonate (18 mmol/l), and high anion
gap (24). Albumin was 44 g/l and total protein 72 g/l both within normal range. Alkaline phosphatase and AST were both marginally elevated. His serum cholesterol was elevated at 7.86 mmol/l. He had a normocytic normochromic anemia with haemoglobin 72 g/l without any abnormalities on smear. Hepatitis C antibody and hepatitis B surface antigen were both negative. ANA titre was 1/100 homogeneous pattern. Complements C3 and C4 were both normal. Specimen was too lipoaemic to test for cryoglobulins. Quantitative immunoglobulins revealed IgG 7.0 g/l, IgA 1.2 g/l, IgM 1.4 g/l, kappa 6.7 g/l, lambda 2.8 g/l (slightly decreased), and kappa/lambda ratio 2.39. Serum protein electrophoresis showed total protein to be elevated with a monoclonal peak in the gamma region. Immunofixation confirmed the presence of an IgG kappa monoclonal protein. Urine protein electrophoresis revealed mainly albuminuria with no monoclonal peak, and immunoelectrophoresis showed IgG and IgA kappa and lambda, as well as free kappa and lambda light chains. His 24-h urinary protein excretion was estimated at ~ 3 g using a spot urine protein/creatinine ratio. Renal ultrasound revealed his right kidney to measure 12.3 cm and the left 10.3 cm with bilateral loss of corticomedullary differentiation. Additional information obtained during an admission in November 1994 included negative HIV serology, normal chest X-ray and skeletal survey and normal PT/PTT. Repeat serum protein electrophoresis and immunofixation reconfirmed the previous findings. Bone marrow aspirate revealed a slightly hypercellular but otherwise unremarkable marrow with no evidence of a plasma cell dyscrasia and cell surface markers showed a normal, mixed population of marrow cells with no evidence of myeloma. The bone marrow biopsy revealed slight hypercellularity but no evidence of plasma cell proliferation.

Renal biopsy

Light microscopy revealed glomerular tuft enlargement with hypercellularity and accentuation of the lobular pattern. There was mesangial expansion, hypercellularity, and irregular thickening of capillary walls; incipient cellular crescents were present in some glomeruli (Figure 1). Silver stain demonstrated double contoured capillary basement membranes (Figure 2). Immunoperoxidase stains for light chains showed moderate staining for Kappa chain in tubular casts and peripheral glomerular foci. Stains for lambda chains were negative. Immunofluorescence showed only granular mesangial deposits of C3, C5 and properdin. Electron microscopic examination disclosed numerous large, elongated, intramembranous electron dense deposits on the glomerular basement membranes (Figure 3). No deposits were noted in the vascular or tubular basement membranes. Diagnosis of membranoproliferative glomerulonephritis Type II (dense deposit disease) was made based on the above findings. The patient did not receive a specific treatment for his monoclonal gammopathy and was started on dialysis for end stage renal disease.

Discussion

Monoclonal gammopathies represent a spectrum of diseases characterized by excessive production of a single type of immunoglobulin or immunoglobulin fragment (M component). As usually typified by multiple myeloma, renal disease occurs commonly. Most of the renal lesions are directly related to the overproduction of monoclonal immunoglobulin or its fragments.
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and the type of renal lesion appears to depend on the intrinsic structure and physiochemical features of these molecules. Renal manifestations may include chronic renal failure, nephrotic syndrome, acute renal failure, and asymptomatic urinary abnormalities with mild proteinuria with or without hematuria [1]. Our patient had nephrotic range proteinuria and renal failure on presentation. Because of commonness of dysproteinemias in older patients, we screen older individuals with uncertain cause for renal disease with serum protein electrophoresis. Since this patient was found to have an abnormal monoclonal protein, he underwent usual myeloma laboratory investigations including bone marrow assessment, however, we were unable to find any underlying lymphoproliferative disorder in association with his monoclonal protein. At this point in time, his disorder would be referred to as monoclonal gammopathy of unknown significance (MGUS). Monoclonal gammopathies are common and increase in frequency with age, reaching 5.7% in individuals aged 80–89 years [11]. They are more common in patients with renal disease than in an age matched population with no clear explanation [11]. The most commonly described renal lesion associated with MGUS is proliferative glomerulonephritis, however, membranous glomerulonephritis and minimal change disease have been reported [4,11]. There is no previous report of membranoproliferative type II (dense deposit
disease) in these patients. There were no IgG deposits in the glomeruli to link this patient’s renal lesion to his abnormal M-protein, however, older age and an essentially unremarkable previous medical history with no other disease association on routine screening would make one very suspicious that these two abnormalities are related and not merely coincidental.

In conclusion, because of high prevalence of dysproteinæmias in older patients and variability of the renal manifestations of these disorders, it would be important to screen elderly patients with renal disease of undetermined aetiology for the presence of one of these conditions with serum and urine protein electrophoresis. Since a large number of glomerular lesions have been described in patients with a monoclonal protein and proteinuria with or without haematuria or renal insufficiency, renal biopsy would be required to determine the exact renal pathology. This is an important adjunct to the bone marrow studies in complete assessment and planning for treatment in these patients.

References


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