Proliferative Glomerulonephritis with Monoclonal IgG Deposits

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Abstract

Proliferative glomerulonephritis with monoclonal IgG deposits (PGNMID) is a recently described disorder that belongs to the class of monoclonal gammopathy of renal significance with the incidence of 0.17%. Monoclonal IgG deposits in glomeruli can produce a proliferative glomerulonephritis that mimics immune-complex mediated glomerulonephritis by light microscopy (LM) and electron microscopy (EM). Proper recognition of this disease requires confirmation of monoclonality by immunofluorescence (IF) staining. We present here a 50 year old female patient presented with nephrotic range proteinuria and normal renal function. Renal biopsy showed endocapillary and mesangial proliferation by LM. IF showed Ig G (+2) and C3 (+2) with positivity for Lambda light chain and Kappa light chain is negative consistent with PGNMID.

Introduction

Glomerular diseases related to monoclonal gammopathies is characterized by organized deposits (type 1 cryoglobulinemia, immunotactoid glomerulonephritis and rarely fibrillary glomerulonephritis) and granular electron-dense deposits, and monoclonal immunoglobulin deposition disease (MIDD) which include light and heavy chain deposition disease (LHCDD), light chain deposition disease (LCDD) and heavy chain deposition disease (HCDD).[1] We report here a patient diagnosed to have PGNMID.

Case Report

A 50 yr- old-lady presented with edema legs and decreased urine output of two weeks duration. Her blood pressure was 100/60 mm Hg, heart rate - 90 beats /min and respiratory rate -20/ min. There was no lymphadenopathy or skin lesions. Systemic examination revealed bilateral pleural effusion with moderate ascites. Laboratory data was given in Table 1. Ultrasound showed normal sized kidneys and no other organomegaly. Serum complements were normal, antinuclear antibody, hepatitis B surface antigen, HIV, hepatitis C antibody, and rheumatoid factor were negative.

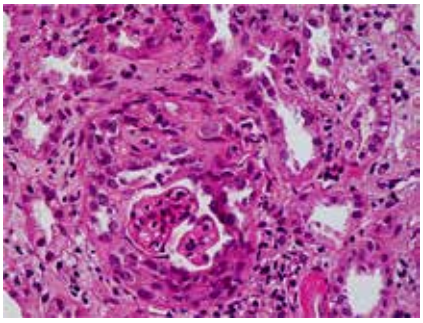

Fig. 1a: Renal biopsy showing crescents (HandE)

Renal biopsy revealed 10 enlarged glomeruli with endocapillary and mesangial proliferation. Basement membrane were irregular and showed double contours focally. Early cellular crescent was seen in 1 glomerulus (Figure 1a). IF revealed granular positivity for IgG (+2) and C3 (+2) show a along the capillary walls and focally over the mesangium. Kappa light chain is negative and Lambda light chain is positive (Figure 1b). IgM, Ig A and C1 q are negative consistent with diagnosis of PGNMID.

Further work up for monoclonal gammopathies including skeletal survey, serum electrophoresis, immunofixation and bone marrow examination was normal. Serum cryoglobulin titers and antiphospholipid antibodies were negative.Serum free light chains,kappa chain : 0.68 (normal 0.33–1.94 mg/dL), and lambda chain : 1.29 (normal 0.57–2.63 mg/dL) were normal. She received oral steroids (0.5 mg/kg/day) tapered and stopped over six months, six intravenous monthly cyclophosphamide pulse of 500 mg and anti-proteinuric measures. She is still on follow-up for 1.5 years with partial remission and serum creatinine of 1.5 mg/dl.

Discussion

PGNMID is a rare entity described by Nasr et al. in 2004.[2] Clinical presentations included renal insufficiency (80%), nephrotic syndrome (44%), and microhematuria (60%).The diagnostic criteria[3] include (a) immune deposits staining positive for IgG, with negativity for IgA and IgM indicating restriction to a single immunoglobulin class,(b) positive staining for a single IgG subclass (IgG1, IgG2, IgG3, or IgG4), (c) positive staining for a single light chain isotype (kappa or lambda), indicating monoclonality, (d) predominant granular electron-dense deposits in mesangial, subendothelial, and/or subepithelial locations by electron microscopy, resembling immune complex glomerulonephritis, and (e) no clinical or laboratory evidence of cryoglobulinemia. The pathogenesis of PGNMID remains elusive.Probable mechanism involves a clonal proliferation of B lymphocytes or plasma cells that hypersecrete abnormal IgG capable of self-aggregation and deposition in the glomerulus.

A report of 37 patients by Nasr et al[4] showed membranoproliferative (57%), endocapillary proliferative (35%) and membranous GN (5.4%) in histology with 22% progressed to ESRD. In this series,four had urine and serum paraproteinemia, seven had both urinary and serum

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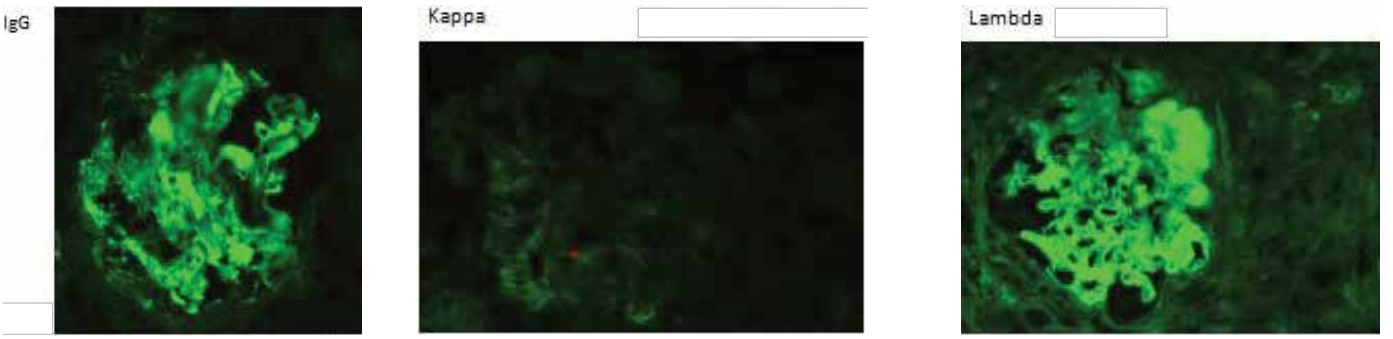

Fig. 1b: Immunofluorescence of renal biopsy showing intense positivity for IgG and Lambda with negative staining for kappa

Table 1: Laboratory data

Urine	
Protein	4+
Protein creatinine ratio	7
Red cells/hpf	5-6
Hemogram	
Hemoglobin	9.2 gm/dl
White cell count	8,600 /cu.mm
Differential count	
Polymorphs	67 %
Lymphocytes	33 %
Platelet count	2,80,000/cu.mm
Serum Biochemistry	
Urea	24 mg/dl
Creatinine	0.8 mg/dl
Sodium	140 meq/L
Potassium	4.1meq/L
Uric acid	5.9 mg/dl
Calcium	8.4 mg/dl
Phosphorus	3.3 mg/dl
Total bilirubin	0.8 mg/dl
Total proteins	6.9 g/dl
Albumin	3.0 g/dl

paraproteinemias, one had multiple myeloma and one had amyloidosis. Higher creatinine at biopsy, percentage of glomerulosclerosis, and degree of interstitial fibrosis but not immune-modulatory treatment or presence of a monoclonal spike correlated with progression to ESRD. The differential diagnosis includes glomerulonephritis with C3 deposits associated with MGUS, infection related glomerulonephritis and C3 glomerulopathy. Serum levels of complements (C3 and C4) and serological tests for MGUS will be helpful in differentiating. Though electron microscopy is not mandatory for the diagnosis of PGNMID, it is helpful in differentiating from other entities. Till date, 60 cases have been reported and this entity does not appear to be a precursor or of significantly associated with an underlying plasma cell dyscrasia. Recurrence of PGNMID in the renal allograft has only recently been described[5] and was treated with high dose prednisone and rituximab / cyclophosphamide and plasmapheresis.

Renal biopsy with careful attention to light chain and IgG isotype staining is essential for diagnosis of PGNMID. This case emphasizes the need for routine use of kappa and lambda in IF.

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