CLINICAL VIGNETTE

A Rare Case of a Proliferative Glomerulonephritis with Monoclonal Immunoglobulin Deposition

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Introduction

A 56-year-old male presented with the unusual diagnosis of proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID). The PGNMID is characterized by deposition of monoclonal immunoglobulins in the glomerulus.[1] Patients present with nephrotic range proteinuria (median of 5.7 g/d) and may have decreased glomerular filtration rates (median Scr of 2.8 g/dl) and hematuria.[2,3] Approximately 80% of cases lack a describable M-protein and/or a clonal origin of the monoclonal immunoglobulins.[4] The monoclonal immunoglobulins result in proliferative glomerulonephritis via an immune complex-mediated. The disease pathology appears to be the direct deposition of the immunoglobulins in the mesangium and capillary walls.[5]

History of Present Illness

A 56-year-old HIV/HIC negative, Caucasian male with remote history of right tonsillar stage IV squamous cell cancer treated with concurrent radiation and chemotherapy was hospitalized with increasing creatinine and peripheral edema. On admission, he was febrile, had anasarca and nephrotic range proteinuria. UA revealed 3+ proteinuria and evidence of pathologic casts. The urine protein to creatinine ratio revealed a 17.7 g of proteinuria and a creatinine of 3.15 (the creatinine 6 months prior was 1.81) and a BUN of 51. Serologies included a cryocrit, ANCA, ANA , c3 c4, GBM AB, SPEP, serum immunofixation and parvovirus B 19 studies. All studies were normal. 24-hour urine immune electrophoresis revealed two faint, ill-defined bands in the IgG region. There was no evidence of an overt monoclonal gammopathy.

Further evaluation included a renal biopsy, a bone marrow biopsy, as well as a metastatic imaging surveys. Renal biopsy revealed diffuse proliferative glomerulonephritis with monoclonal IgG3 kappa immune complex deposits and focal crescents. There was evidence for mild tubular necrosis and moderate artero- and arteriolonephrosclerosis. The bone marrow biopsy and imaging studies were unremarkable.

Upon admission, the patient was placed on high dose steroids and a one-time dose of cyclophosphamide (1 g/m2). Upon discharge, the repeat protein to creatinine ratio was estimated to be 1g and the creatinine was 1.61. He was then started on the CyBorD (cyclophosphamide, bortezomib and dexamethasone) treatment protocol.

Discussion

PGNMID is a rare glomerular disease that is found in both native (0.17%) and in allograft kidney biopsies.[6] The patients present with hematuria (77%), decreased renal function (60%) and/or nephrotic proteinuria (50%).[7] The etiology of this disorder remain elusive but PGNMID has been associated with infectious (HCV and parvovirus B19) and hematologic (lymphoproliferative disorders) processes.[6,8-9] An M-protein/ spike and/or a monoclonal band on immunofixation studies are typically absent in majority of the cases.[4]

The diagnosis of PGNMID requires three specific pathologic criteria: 1) glomerular monoclonal IgG deposits restricted to a single IgG subclass and a single light chain isotype; 2) presence of membranous, membranoproliferative, or endocapillary proliferative features; and 3) detection of immune complex deposits by electron microscopy.[10] It is more common in older Caucasian women.

The prognosis of PGNMID is poor. In native kidneys, there is at least 25% rate of dialysis progression within 3 years of the diagnosis. The various modalities of therapy in native kidneys may result in partial responses (reduction of proteinuria by 50%) and rarely a complete remission (resolution of proteinuria and renal dysfunction). The prognosis of PGNMID in kidney allografts is poorly understood.[2]

Given the paucity and non-uniformity of cases in both native and allograft kidneys, there is a lack of well-established treatment algorithms or protocols. Experts suggest myeloma treatment regimens for PGNMID cases in which a monoclonal protein is detectable. For PGMID cases without a detectable monoclonal band, the decisions to employ chemotherapy or biologics may be difficult. PGNMID patients have been treated with various modalities including: steroids, angiotensin-converting enzyme inhibitors, cyclosporine, mycophenolate, cyclophosphamide, bortezomib and rituximab. Rituximab appears to be useful in IgM-mediated disease regardless of the presence of a detectable monoclonal protein.[2,5,11]

Monoclonal proteins, in their various incarnations, are well known causes of renal disease. These proteins can cause injury in all areas of kidney, including tubular, vascular and glomerular components. PGNMID is a proliferative glomerulonephritis characterized by non-organized Ig deposits. The prognosis is of PGNMID is poor and the treatments are

non-standardized. To date, the treatment choices are based on clinical experience and data from anecdotal case reports. We hope future publications trigger prospective and well planned studies to address the treatment needs of PGNMID patients.

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