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Authors

Arzoo, Karo
Berkowitz, Maurice

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CLINICAL VIGNETTE

A Rare Case of a Proliferative Glomerulonephritis with Monoclonal Immunoglobulin Deposition

Karo Arzoo, MD and Maurice Berkowitz, MD

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.

REFERENCES

1. **Lusco MA, Fogo AB, Najafian B, Alpers CE.** AJKD Atlas of Renal Pathology: Proliferative Glomerulonephritis With Monoclonal Immunoglobulin Deposits. *Am J Kidney Dis.* 2016 Mar;67(3):e13-5. doi: 10.1053/ j.ajkd.2016.01. 003. PubMed PMID:26916379.
2. **Nasr SH, Satoskar A, Markowitz GS, Valeri AM, Appel GB, Stokes MB, Nadasdy T, D'Agati VD.** Proliferative glomerulonephritis with monoclonal IgG deposits. *J Am Soc Nephrol.* 2009 Sep;20(9):2055-64. doi: 10.1681/ASN. 2009010110. Epub 2009 May 21. PubMed PMID: 19470674; PubMed Central PMCID: PMC2736767.
3. **Leung N, Drosou ME, Nasr SH.** Dysproteinemias and Glomerular Disease. *Clin J Am Soc Nephrol.* 2018 Jan 6;13(1):128-139. doi: 10.2215/CJN.00560117. Epub 2017 Nov 7. PubMed PMID: 29114004; PubMed Central PMCID: PMC5753301.
4. **Bhutani G, Nasr SH, Said SM, Sethi S, Fervenza FC, Morice WG, Kurtin PJ, Buadi FK, Dingli D, Dispenzieri A, Gertz MA, Lacy MQ, Kapoor P, Kumar S, Kyle RA, Rajkumar SV, Leung N.** Hematologic characteristics of proliferative glomerulonephritides with nonorganized monoclonal immunoglobulin deposits. *Mayo Clin Proc.* 2015 May;90(5):587-96. doi: 10.1016/j. mayocp. 2015.01.024.PubMed PMID: 25939936.
5. **Sethi S, Rajkumar SV.** Monoclonal gammopathy-associated proliferative glomerulonephritis. *Mayo Clin Proc*. 2013 Nov;88(11):1284-93. doi: 10.1016/j.mayocp. 2013.08.002. Review. PubMed PMID: 24182705.
6. **Fujita E, Shimizu A, Kaneko T, Masuda Y, Ishihara C, Mii A, Higo S, Kajimoto Y, Kanzaki G, Nagasaka S, Iino Y, Katayama Y, Fukuda Y.** Proliferative glomerulonephritis with monoclonal immunoglobulin G3κ deposits in association with parvovirus B19 infection. *Hum Pathol.* 2012 Dec;43(12):2326-33. doi:10.1016/j.humpath. 2012.04.004. Epub 2012 Jul 21. PubMed PMID:22819999.
7. **Nasr SH, Sethi S, Cornell LD, Fidler ME, Boelkins M, Fervenza FC, Cosio FG, D'Agati VD.** Proliferative glomerulonephritis with monoclonal IgG deposits recurs in the allograft. *Clin J Am Soc Nephrol*. 2011 Jan;6(1):122-32. doi:10.2215/CJN.05750710. Epub 2010 Sep 28. PubMed PMID: 20876681; PubMed Central PMCID: PMC3022233.
8. **Barbour SJ, Beaulieu MC, Zalunardo NY, Magil AB.** Proliferative glomerulonephritis with monoclonal IgG deposits secondary to chronic lymphocytic leukemia. Report of two cases. *Nephrol Dial Transplant.* 2011 Aug;26(8):2712-4. doi: 10.1093/ndt/gfr251. Epub 2011 Jun 1. PubMed PMID: 21633102.
9. **Yamada T, Arakawa Y, Mii A, Kashiwagi T, Kaneko T, Utsumi K, Masuda Y, Shimizu A, Iino Y, Katayama Y.** A case of monoclonal immunoglobulin G1-lambda deposition associated with membranous feature in a patient with hepatitis C viral infection. *Clin Exp Nephrol.* 2012 Jun;16(3):468-72. doi: 10.1007/s10157-011-0579-x. Epub 2012 Jan 19. PubMed PMID: 22258557.
10. **Nasr SH, Markowitz GS, Stokes MB, Seshan SV, Valderrama E, Appel GB, Aucouturier P, D'Agati VD.** Proliferative glomerulonephritis with monoclonal IgG deposits: a distinct entity mimicking immune-complex glomerulonephritis. *Kidney Int.* 2004 Jan;65(1):85-96. PubMed PMID: 14675039.
11. **Ohashi R, Sakai Y, Otsuka T, Ohno D, Masuda Y, Murasawa T, Sato N, Shimizu A.** Proliferative glomerulonephritis with monoclonal IgG2κ deposit successfully treated with steroids: a case report and review of the literature. *CEN Case Rep.* 2013 Nov;2(2):197-203. doi: 10.1007/s13730-013-0064-3. Epub 2013 Feb 26. PubMed PMID:28509293; PubMed Central PMCID:PMC5411552.

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