When Does MGUS Become MGRS?

By Jyotsana Thakkar

Monoclonal gammopathy of unknown significance (MGUS), commonly considered a benign condition, is characterized by a low level of detectable monoclonal immunoglobulin (Ig) in the serum (<30 g/L) and <10% monoclonal plasma cells on bone marrow biopsy. Assuming these low levels of circulating Igs do not cause any end organ damage, treatment is usually not recommended for MGUS. However, in some patients with MGUS, these low levels of Ig or kappa/lambda light chains can cause direct kidney deposition or activation of complements leading to kidney diseases. Because of this, in 2012, the term "monoclonal gammopathy of renal significance" (MGRS) was coined to recognize the spectrum of kidney diseases from MGUS and to treat accordingly (1).

In a recently published retrospective study in the *Clinical Journal of the American Society of Nephrology*, Yong and colleagues (2) describe the histopathological and clinical features of this entity. In this single-center study (performed in China), approximately 700 patients with monoclonal gammopathy who underwent single kidney biopsy were retrospectively examined over a period of 21 years (1999–2020). Thirty-eight percent of patients were classified as having a MGRS-related lesion, whereas the rest (62%) did not have MGRS.

Ig monoclonal protein-related amyloidosis was the predominant kidney lesion seen in most patients (63%), followed by monoclonal immune deposition disease (9%) and thrombotic microangiopathy (8%). In the non-MGRS group, membranous nephropathy (40%) was the most common, followed by IgA nephropathy (14%) and diabetic nephropathy (9%).

In the MGRS group, a higher percentage of patients had proteinuria >1.5 g/d (81% vs. 70%) and a higher prevalence of hypoalbuminemia <3 g/dL (61% vs. 52%) compared with the patients with a non-MGRS lesion. The prevalence of hypertension, diabetes, and hematuria was less in the MGRS group. A free light-chain ratio (normal range 0.2–2.9) was significantly abnormal (odds ratio, 5.57; 95% confidence interval, 2.90–10.69; $P = 0.001$) in the MGRS subgroup, which had been verified by a previous study done at the Mayo Clinic (3). The authors also compared clinical data for patients with Ig amyloidosis and non-amyloidosis MGRS. Patients with amyloidosis were significantly older and more likely to have hypoalbuminemia and nephrotic-range proteinuria than the non-amyloidosis group.

The authors concluded that the presence of abnormal free light chains, advanced age, and proteinuria >1.5 g/dL is the potential clinical indicator and can point toward the diagnosis of MGRS.

Yong et al. (2) reported similar findings as the Mayo Clinic, except that the hematuria was also significantly associated with MGRS in the Mayo Clinic study (3). This is contrary to the study by Yong et al. (2), where incidence of hematuria was less in the MGRS group than in the non-MGRS group. One possible explanation for such a difference could be a higher incidence of glomerulonephritis and IgA nephropathy in the Chinese population, leading to more hematuria in the non-MGRS group.

The Yong et al. (2) study found a high incidence of an MGRS-related lesion (approximately 40% vs. 60% non-MGRS) in patients with monoclonal gammopathy and kidney diseases, thus necessitating the need for kidney biopsy to diagnose otherwise missed cases of MGRS. We cannot rule out the possibility of diagnostic bias, since all patients with MGRS underwent kidney biopsies in the study. The salient clinical characteristics differentiating MGRS from non-MGRS kidney biopsy lesions include older age, greater proteinuria (>1.5 g/d), and an abnormal free light-chain ratio among the MGRS group. Nephrologists should be aware of these clinical associations to help in the diagnosis and management of MGRS with kidney disease. ■

Jyotsana Thakkar, MD, is with the Division of Nephrology, Department of Medicine, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY.

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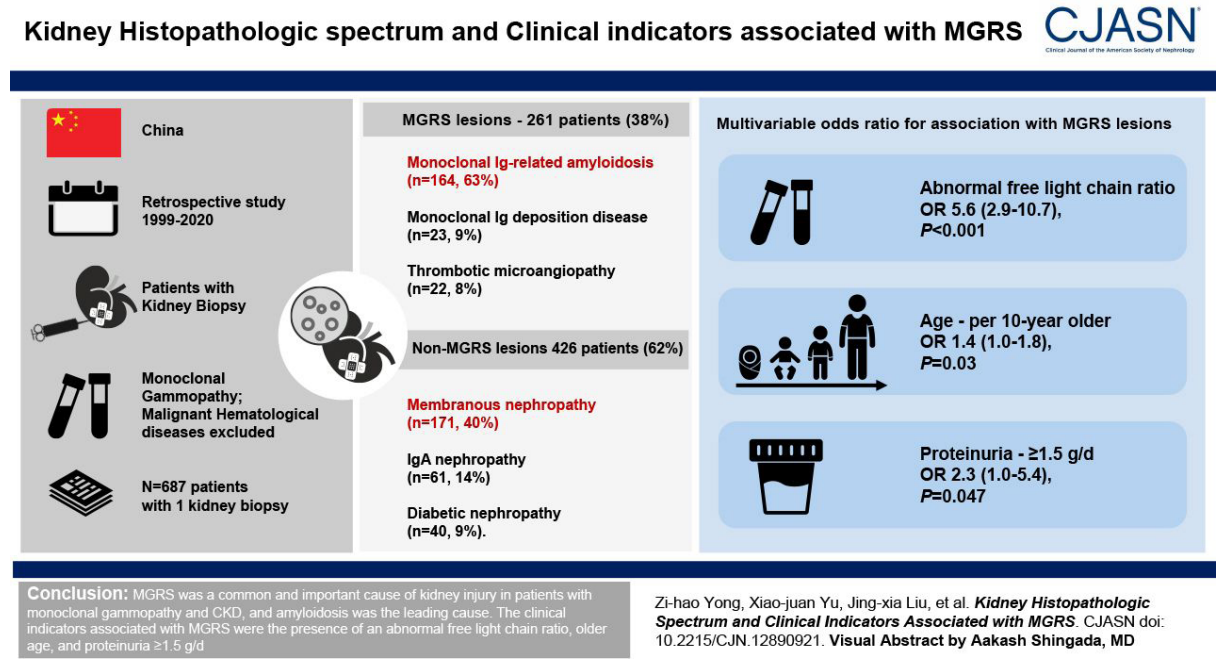

Reconsidering All Aspects of Nephrology's Future

By Melissa West

Earlier this year, ASN received requests from the American Board of Internal Medicine (ABIM) and Accreditation Council for Graduate Medical Education (ACGME) that taken separately would impact the future training of nephrologists. After careful consideration and thought, the ASN Council responded with a request for 8 months to convene the community and reconsider all aspects of the future of the specialty of nephrology.

"This is a unique opportunity to respond to the requests of ABIM and ACGME. Nephrology has evolved over the last 5 to 10 years as more options to treat patients earlier have become available," said former ASN President Mark E. Rosenberg, MD, FASN. "Advancing American Kidney Health focused the community on patient choice, including options for home dialysis, reforming transplant policy, accelerating innovation, and eliminating disparities."

Dr. Rosenberg is chairing the ASN Task Force on the Future of Nephrology, which is charged with meeting the society's commitment to ABIM and ACGME. The task force includes a diverse cross-section of ASN members, such as current and former nephrology fellowship training program directors, nephrologists in private practice, leaders in academic medicine, and early career nephrologists. According to Dr. Rosenberg, the task force will interact with representatives from ABIM and ACGME as appropriate."

The ASN Task Force on the Future of Nephrology is not intended to serve as a representative panel of every constituency within nephrology. Rather, ASN will facilitate deep dives and opportunities for community members to provide their input. Some of the groups that the task force will be interacting with include the chiefs of nephrology divisions at academic institutions, nephrology fellowship training program directors, patients and care partners, representatives from nephrology practices, ASN's committees, and leaders of kidney organizations. As mentioned previously this year in an April *Kidney News* article (1), conversations about required procedures or program requirements have been going on for many years. As such, the task force will focus on defining the big picture as it relates to the future of nephrology and then work backward into requirements for training, certification, and recertification.

"As we face a crisis in the nephrology workforce, now is the time to think big and strategically about the specialty's role in the broader health care system," said ASN Executive Vice President Tod Ibrahim. "Nephrologists care for some of the most complex patients, but the specialty is too often undervalued by the broader system."

To learn more about the task force and its charge, please refer to the article in the April issue of *Kidney News* (1). Regular updates will be provided in *Kidney News* through October 2022. To provide your thoughts and ideas on the future of nephrology, please email Melissa West, ASN's Senior Director for Strategic Relations and Patient Engagement, at mwest@asn-online.org. ■

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ASN Task Force on the Future of Nephrology

Sharon Anderson, MD, FASN
Samira S. Farouk, MD, MS, FASN
Keisha L. Gibson, MD, FASN, MPH, ASN Council Liaison
Robert S. Hoover, Jr., MD, FASN
Benjamin D. Humphreys, MD, PhD, FASN
Janis M. Orlowski, MD
Mark E. Rosenberg, MD, FASN, Chair
Suneel M. Udani, MD, FASN
Joshua S. Waitzman, MD, PhD