



## MGUS: It's about the protein, not just the marrow

Monoclonal gammopathy of undetermined significance (MGUS) has always been a favorite topic on internal medicine teaching rounds and is sometimes used to challenge residents. It is a relatively uncommon cause of some common laboratory and clinical anomalies. Thus, residents must field questions such as, “What is a cause of a high erythrocyte sedimentation rate with a concurrently normal C-reactive protein level and a low anion gap?” And for internists who love probabilistic assessments, there are now data and flowcharts to help predict the likelihood that a patient with MGUS will develop myeloma, Waldenström macroglobulinemia, or other malignant clonal proliferative disorder that will warrant therapy.

In the past decade, it has been increasingly recognized that these clonally produced proteins—entire immunoglobulins or free light chains—may be directly pathogenic, independent of any pathologic effect of cellular clonal expansion and infiltration. Brouet class 1 cryoglobulinemia (in which a monoclonal paraprotein precipitates in cooler temperatures and acts as a source of complement, activating the immune complex) and light chain (usually lambda)-related amyloidosis have been recognized for much longer. But a newer concept, monoclonal gammopathy of renal significance (MGRS), has attracted significant attention and to some extent has modified our approach to patients with either known MGUS or unexplained chronic kidney disease.

Finding MGUS still warrants a parsimonious evaluation for possible progression to myeloma or other proliferative disorder, as discussed by Khouri et al in this issue of the *Journal* (page 39). But it should also prompt a thoughtful assessment of renal function, including estimating the glomerular filtration rate and looking for proteinuria, hematuria, and unexplained glucosuria or inappropriate urine pH. While typical light chain-induced renal tubular injury is usually associated with high levels of proteins such as those seen with myeloma, other patterns of glomerular, vascular, and mixed renal disease are associated with deposition of proteins that, once considered in the differential diagnosis, warrant renal biopsy to diagnose and direct appropriate therapy. That MGUS and MGRS occur more frequently in older patients, who are already at greater risk of multiple common causes of kidney disease, complicates clinical decision-making.<sup>1</sup> Some of these disorders are associated with other initially subtle or seemingly disconnected clinical symptoms such as polyneuropathy, rash, and carpal tunnel syndrome, but many are at least initially limited to the kidneys.

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As we enter a new calendar year, we at the *Journal* send our best wishes to all of our readers, authors, and peer reviewers, and we thank you for sharing in our medical education ventures. I personally hope that we have added some joy, enthusiasm—and some knowledge—to your professional activities, and I hope that we all can participate in some way to refashion a more civil and peaceful world in 2019.



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1. Rosner MH, Edeani A, Yanagita M, et al. Paraprotein-related kidney disease: diagnosing and treating monoclonal gammopathy of renal significance. *Clin J Am Soc Neph* 2016; 11(12):2280–2287. doi:10.2215/CJN.02920316