

Content available at: <https://www.ipinnovative.com/open-access-journals>

IP Archives of Cytology and Histopathology Research

Journal homepage: <https://www.achr.co.in/>

## Short Communication

# Monoclonal gammopathy of renal significance: An overview

Iffat Jamal <sup>1</sup>\*<sup>1</sup>Dept. of Hematology, Indira Gandhi Institute of Medical Sciences, Patna, Bihar, India

### ARTICLE INFO

#### Article history:

Received 27-11-2023

Accepted 12-11-2023

Available online 08-01-2024

This is an Open Access (OA) journal, and articles are distributed under the terms of the [Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License](https://creativecommons.org/licenses/by-nc-sa/4.0/), which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: [reprint@ipinnovative.com](mailto:reprint@ipinnovative.com)

## 1. Introduction

Monoclonal gammopathy of renal significance (MGRS) encompasses kidney disorders resulting from a monoclonal protein (M-protein) secreted by a small clone of plasma cells or other B-cell groups in patients not meeting multiple myeloma or other B-cell malignancy criteria. Typically, the underlying condition in MGRS patients aligns with monoclonal gammopathy of undetermined significance (MGUS). The spectrum of MGRS-related kidney disorders is diverse and continuously expanding. These disorders may present as glomerular diseases, tubulopathies, or vascular involvement, exhibiting diverse clinical manifestations. Due to this broad spectrum, diagnosing MGRS poses challenges, especially in establishing a direct pathogenic link between the presence of M-protein or serum free light chains and kidney diseases. Complicating accurate diagnosis further is the high occurrence of MGUS and/or kidney disorders, unrelated to MGRS, in elderly patients. However, MGRS significantly impairs kidney function, highlighting the critical importance of early recognition. A combined approach involving hematology and nephrology is essential to determine the causative role of M-protein in kidney disease. Directed therapy targeting the clone, including autologous stem cell transplantation for eligible patients, often yields improved outcomes.<sup>1–4</sup>

Approximately 3% of individuals aged 50 and above have a circulating M-protein, a figure that increases to 5% after 70 years. Those with this protein are diagnosed with MGUS if the M-protein is < 30 g/l and bone marrow examination shows < 10% monoclonal plasma cells without organ damage or other events defining multiple myeloma. Monoclonal gammopathies may remain asymptomatic in MGUS cases but can sometimes cause severe organ damage without meeting overt multiple myeloma or other malignant lymphoproliferative disorder criteria. To address this, the term MGRS was introduced in 2012 by the International Kidney and Monoclonal Gammopathy Research Group (IKMG) to describe kidney diseases stemming from M-protein secretion by small B-cell, lymphoplasmacytic, or plasma cell clones not meeting specific hematologic therapy criteria. Recently updated by IKMG, MGRS now encompasses B-cell or plasma cell proliferative disorders producing nephrotoxic M-proteins, including smoldering MM, smoldering WM, monoclonal B-cell lymphocytosis (MBL), low-grade B-cell lymphomas, and low-grade CLL associated with renal disease. These M-proteins can directly or indirectly harm the kidneys, such as by complement activation. Treatment guidelines generally advise against anti-tumor therapy for MGUS, smoldering myeloma, or asymptomatic WM patients, opting for monitoring unless symptoms emerge. However, in MGRS cases, where the M-protein directly influences kidney disease despite a low tumor burden, a different approach is needed due to the increased risk of progression to end-stage

\* Corresponding author.

E-mail address: [iffatjamal111@gmail.com](mailto:iffatjamal111@gmail.com) (I. Jamal).

renal disease (ESRD). Therefore, an interdisciplinary evaluation involving nephrologists, hematologists, and nephropathologists well-versed in MGRS is ideal for managing these cases.

## 2. Etiopathogenesis

Excessive monoclonal protein, either the entire immunoglobulin or light chain (rarely heavy chain), may be present in the kidney or systemic microcirculation, forming misfolded proteins and depositing as fibrils, crystals, or activating complement pathways.

Immunoglobulins or complement deposition in the glomerulus, sometimes with or without monoclonal light chains (e.g., C3 glomerulopathy).

Presence of inflammatory cells and proliferation of resident glomerular cells or visceral epithelial cells in glomeruli with monoclonal light chain or sole complement deposition, forming crescents.

Prevalence of kappa light chain clone in MGRS lesions, except for AL amyloidosis where lambda is more common.

Cases resulting from paraprotein disrupting the complement pathway without direct kidney paraprotein deposition.

## 3. Laboratory Diagnosis

1. Urinalysis, 24-hour urine collection.
2. Detection of monoclonal free light chains (kappa or lambda) in blood or urine.
3. Kidney biopsy via light microscopy, immunofluorescence, and electron microscopy.
4. Bone marrow examination, flow cytometry, cytogenetics, FISH studies, immunoelectron microscopy, laser dissection tandem mass spectrometry (LDTMS).<sup>5</sup>

Various indicators such as increased urinary protein, microscopic hematuria, altered serum creatinine, electrolyte imbalances, renal tubular acidosis, Bence-Jones protein in urine, abnormal serum/urine protein electrophoresis, abnormal kappa or lambda light chain, elevated free kappa or lambda light chain, altered serum complement levels, cryoglobulin levels, and specific blood/bone marrow flow cytometry or cytogenetics/FISH studies.<sup>6</sup>

The goal of MGRS treatment is to maintain or enhance kidney function by targeting the B-cell or plasma

cell clone. Consensus favors clone-directed over general immunosuppressive therapy. Bortezomib is recommended for patients with plasma cell clones and MGRS, while rituximab-based therapy suits those with B-cell clones expressing CD20. Supportive care for hypertension, proteinuria, and mineral metabolism impairment is also essential.

## 4. Source of Funding

None.

## 5. Conflict of Funding

None.

## References

1. Rajkumar SV, Dimopoulos MA, Palumbo A, Blade J, Merlini G, Mateos MV, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol.* 2014;15(12):548–48.
2. Kyle RA, Therneau TM, Rajkumar SV, Larson DR, Plevak MF, Offord JR, et al. Prevalence of monoclonal gammopathy of undetermined significance. *N Engl J Med.* 2006;354(13):1362–9.
3. Van De Donk N, Palumbo A, Johnsen HE, Engelhardt M, Gay F, Gregersen H, et al. The clinical relevance and management of monoclonal gammopathy of undetermined significance and related disorders: recommendations from the European Myeloma Network. *Haematologica.* 2014;99(6):984–96.
4. Fermand JP, Bridoux F, Dispenzieri A, Jaccard A, Kyle R, Leung N, et al. Monoclonal gammopathy of clinical significance: a novel concept with therapeutic implications. *Blood.* 2018;132(14):1478–85.
5. Kyle RA, Durie BG, Rajkumar SV, Landgren O, Blade J, Merlini G, et al. Monoclonal gammopathy of undetermined significance (MGUS) and smoldering (asymptomatic) multiple myeloma: IMWG consensus perspectives risk factors for progression and guidelines for monitoring and management. *Leukemia.* 2010;24(6):1121–7.
6. Angioi A, Amer H, Fervenza FC, Sethi S. Recurrent Light Chain Proximal Tubulopathy in a Kidney Allograft. *Am J Kidney Dis.* 2016;68(3):483–7.

## Author biography

Iffat Jamal, Assistant Professor  <https://orcid.org/0000-0001-5574-5569>

**Cite this article:** Jamal I. Monoclonal gammopathy of renal significance: An overview. *IP Arch Cytol Histopathology Res* 2023;8(4):296-297.