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A Mystery Intensive Care Admission with Renal Failure: A Rare Case of Monoclonal Gammopathy of Renal Significance

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Abstract

This report presents the case of a 54-year-old woman admitted to the intensive care unit with severe acute kidney injury of an initially undetermined source, complicated by hypotension and lactic acidosis requiring continuous renal replacement therapy. An unexplained protein gap and markedly elevated serum free kappa light chains prompted a paraprotein workup and kidney biopsy, which demonstrated proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID) with IgG3-kappa restriction. Because the bone marrow contained only a small (approximately 5%) kappa-restricted plasma cell clone that did not meet criteria for multiple myeloma, and the glomerular deposits matched the circulating clone, the patient was diagnosed with monoclonal gammopathy of renal significance (MGRS). Competing causes of shock-associated renal failure, light chain cast nephropathy, ischemic acute tubular necrosis, sepsis, nephrotoxin exposure, and obstruction, were systematically excluded. The patient was treated with a bortezomib-based clone-directed regimen. This case highlights the protein gap as a diagnostic clue, the indispensability of kidney biopsy in linking a monoclonal protein to renal injury, the reconciliation of an MGRS diagnosis with a low-burden clone, and the role of clone-directed therapy in preserving kidney function.

Keywords

Renal Failure, Kidney Injury

1. Introduction

Monoclonal gammopathy refers to the production of a structurally identical (monotypic) immunoglobulin or immunoglobulin fragment by an expanded

clone of plasma cells or B lymphocytes, detectable in serum and/or urine. Monoclonal gammopathies span a clinical spectrum from the premalignant monoclonal gammopathy of undetermined significance (MGUS) to overt malignancies such as multiple myeloma, Waldenstrom macroglobulinemia, and other B-cell lymphomas. Even in the absence of a malignant tumor burden, a monoclonal immunoglobulin can inflict end-organ injury when its intrinsic physicochemical properties render it nephrotoxic [1].

The term monoclonal gammopathy of renal significance (MGRS) was introduced by the International Kidney and Monoclonal Gammopathy Research Group (IKMG) in 2012 and refined in a 2019 consensus report to distinguish clonal disorders that cause kidney disease through a nephrotoxic monoclonal immunoglobulin, but that do not meet hematologic criteria mandating treatment of the clone itself, from MGUS, which by definition lacks end-organ damage [2] [3]. The distinction is clinically pivotal: MGUS is generally observed, whereas MGRS warrants clone-directed therapy to preserve renal function.

Diagnosis of MGRS requires two elements: 1) a kidney biopsy lesion attributable to a monoclonal immunoglobulin, demonstrated by light microscopy, immunofluorescence, and electron microscopy, with the monoclonal protein detected in serum and/or urine ideally matching the immunoglobulin identified in the biopsy; and 2) an underlying B-cell or plasma-cell clone that does not meet criteria for treatment of multiple myeloma, lymphoma, or other overt malignancy [2] [4].

The histopathologic spectrum of MGRS is broad and is classified by the composition and ultrastructural organization of deposits. It includes immunoglobulin-related amyloidosis, monoclonal immunoglobulin deposition disease (MIDD), light chain proximal tubulopathy, crystal-storing histiocytosis, type I cryoglobulinemic glomerulonephritis, proliferative glomerulonephritis with monoclonal immunoglobulin deposits (PGNMID), immunotactoid glomerulonephritis, C3 glomerulopathy with monoclonal gammopathy, and thrombotic microangiopathy associated with monoclonal gammopathy [5].

PGNMID, a recently characterized entity within the MGRS spectrum, is renal-limited and usually presents in the sixth decade with chronic glomerular disease, proteinuria, and declining renal function; acute nephritic or severe acute kidney injury (AKI) presentations are uncommon. Histologically, it most often shows a membranoproliferative pattern, with granular glomerular-restricted deposits of a monotypic immunoglobulin, most commonly IgG3 with kappa restriction, admixed with complement. A distinguishing feature is that a circulating paraprotein or an abnormal bone marrow clone is detectable in only approximately 30% of patients, which makes both diagnosis and clonal attribution challenging [2] [3].

Because comprehensive studies of diagnosis, severity, and treatment of MGRS remain limited, diagnosis is often delayed. We present a 54-year-old woman who presented to the intensive care unit with severe AKI of undetermined source accompanied by hypotension and lactic acidosis, prompting continuous renal replacement therapy, ultimately diagnosed as PGNMID-associated MGRS.

2. Case Presentation

The patient was a 54-year-old woman with a documented baseline serum creatinine of 0.9 mg/dL (estimated glomerular filtration rate greater than 60 mL/min/1.73m^2) recorded in outpatient records approximately four months before admission. Her comorbidities comprised well-controlled hypertension and hyperlipidemia. She had no history of diabetes mellitus, prior chronic kidney disease, autoimmune disease, plasma cell dyscrasia, or prior proteinuria. Her regular medications were amlodipine and atorvastatin. She reported no recent use of nonsteroidal anti-inflammatory drugs, proton pump inhibitors, herbal or over-the-counter products, and no recent iodinated contrast exposure. There was no history of intravenous drug use and no family history of kidney disease.

She presented to the emergency department with two weeks of progressive fatigue and decreased urine output, progressing to altered mental status. On arrival, blood pressure was 84/46 mmHg, heart rate 110 beats per minute, respiratory rate 20 breaths per minute, temperature 36.8˚C (98.2 F), and oxygen saturation 97% on room air. She was oriented only to self. Examination revealed bilateral lower-extremity edema; cardiac, pulmonary, and abdominal examinations were unremarkable, with no costovertebral angle tenderness, palpable bladder, or signs of infection.

Laboratory studies demonstrated severe AKI with serum creatinine of 6.4 mg/dL, blood urea nitrogen elevated in proportion, sodium 130 mEq/L, potassium 6.1 mEq/L, and bicarbonate consistent with metabolic acidosis; an elevated lactate accompanied the hypotension. Serum albumin was 3.6 g/dL with total protein of 8.6 g/dL, yielding a protein gap of 5.0 g/dL. Complete blood count showed hemoglobin 9.2 g/dL, white blood cell count 7800/uL without left shift, and platelets 155,000/uL. Serum calcium was within normal limits. Urinalysis showed 3+ protein without dysmorphic red cells and, importantly, no muddy-brown granular casts and no red-cell casts. Renal ultrasound demonstrated normal-sized, non-obstructed kidneys with no hydronephrosis and no nephrolithiasis.

She was admitted to the intensive care unit for uremic encephalopathy and hemodynamic instability requiring vasopressor support. Nephrology initiated continuous renal replacement therapy for refractory hyperkalemia, uremic encephalopathy, and volume overload in the setting of hemodynamic instability.

Because the patient presented with hypotension, lactic acidosis, and severe AKI, common causes of shock-associated renal failure were systematically evaluated and excluded.

She was afebrile and normothermic with a normal white-cell count and no leukocytosis or bandemia; blood, urine, and respiratory cultures were obtained and returned negative, and no source of infection was identified. Procalcitonin and the overall trajectory did not support sepsis as the primary driver.

Although transient hypotension was present, the urinary sediment lacked the muddy-brown granular casts and renal tubular epithelial cells characteristic of ischemic ATN, and the degree of AKI, the heavy glomerular-range proteinuria, and

the subsequent biopsy findings were disproportionate to and inconsistent with pure ischemic injury.

A careful medication reconciliation identified no nephrotoxic agents; there was no recent iodinated contrast, aminoglycoside, or NSAID exposure, and no evidence of tumor lysis or hypercalcemia.

Post-renal obstruction was excluded by renal ultrasound showing no hydronephrosis and normal caliber collecting systems.

The unexplained severe AKI with heavy proteinuria and an elevated protein gap prompted a paraprotein workup: serum protein electrophoresis (SPEP) with immunofixation, quantitative immunoglobulins, serum free light chain (FLC) assay, and 24-hour urine total protein with urine protein electrophoresis (UPEP) and immunofixation. SPEP revealed a monoclonal spike in the gamma region; serum immunofixation identified an IgG-kappa monoclonal protein. The serum FLC assay demonstrated markedly elevated kappa light chains at 485 mg/L with a kappa/lambda ratio of 42.5. A 24-hour urine collection contained 4.2 g of protein, with urine immunofixation positive for kappa light chains.

Bone marrow aspirate and biopsy demonstrated a low-level (approximately 5%) kappa-restricted plasma cell clone by immunohistochemistry and flow cytometry, without lytic lesions, hypercalcemia, anemia attributable to marrow infiltration, or other CRAB features, and thus did not meet criteria for multiple myeloma. FDG-PET/CT identified no lytic bone disease or plasmacytoma.

Kidney biopsy was performed on hospital day 5. Findings across the three diagnostic modalities were a membranoproliferative pattern of glomerular injury with global endocapillary hypercellularity, mesangial expansion and hypercellularity, and thickened capillary walls with double-contour ("tram-track") formation on silver stain. There was no evidence of fractured tubular casts with a giant-cell/cellular reaction to exclude cast nephropathy, and Congo red staining was negative, excluding amyloidosis.

Granular deposits restricted to the glomeruli (capillary walls and mesangium) that were monotypic, staining for IgG with kappa light-chain restriction and negative for lambda, accompanied by C3. IgG subclass staining demonstrated restriction to IgG3. There was no linear basement-membrane staining to suggest MIDD and no staining along tubular basement membranes.

The diagnosis of MGRS was made by satisfying both formal criteria introduced above. First, the kidney biopsy demonstrated a lesion (PGNMID) directly attributable to a monoclonal immunoglobulin, with IgG3-kappa restriction on immunofluorescence concordant with the circulating IgG-kappa paraprotein and the kappa-restricted marrow clone, fulfilling the requirement that the monoclonal protein detected in serum/urine match the immunoglobulin in the biopsy. Second, the underlying clone (approximately 5% kappa-restricted plasma cells, without CRAB features or lytic disease) did not meet criteria for multiple myeloma or another malignancy requiring treatment on hematologic grounds alone.

Given the plasma cell nature of the clone, a bortezomib-based clone-directed

regimen (bortezomib, cyclophosphamide, and dexamethasone) was initiated, with acyclovir prophylaxis and appropriate supportive care. She continued thrice-weekly maintenance hemodialysis after transition off continuous renal replacement therapy.

At early outpatient follow-up after the initial cycles of therapy, the hematologic response was encouraging, with a substantial reduction in the involved serum kappa free light chain and a normalizing kappa/lambda ratio, consistent with progression toward at least a very good partial hematologic response. Her serum creatinine showed a downward trend and urine output began to recover; a plan was made to reassess dialysis dependence with serial creatinine, urine output, and free light chain measurements, recognizing that renal recovery in dialysis-requiring MGRS is contingent on the depth and durability of the hematologic response and may lag behind it. Frequent reassessment of serum FLC, the monoclonal spike, serum creatinine, and proteinuria was scheduled to guide ongoing therapy and to titrate against treatment-related toxicity.

3. Discussion

This case illustrates the diagnostic challenge of MGRS presenting as severe AKI, resulting in hypotension and lactic acidosis, requiring intensive care. MGRS is a relatively recent construct, coined by the IKMG in 2012 and refined in the 2019 consensus report, describing clonal proliferative disorders that produce a nephrotoxic monoclonal immunoglobulin without meeting criteria for overt hematologic malignancy; the distinction from MGUS is central, because MGUS implies absent end-organ damage whereas MGRS directly causes renal injury [2] [3].

Several features of this presentation warrant emphasis. First, the protein gap (total protein 8.6 g/dL with albumin 3.6 g/dL, a gap of 5.0 g/dL) served as a key early clue prompting the paraprotein workup in a patient with otherwise unexplained AKI. In any patient with unexplained renal failure, an elevated protein gap should prompt SPEP, serum immunofixation, and a serum FLC assay, which together identify more than 97% of monoclonal gammopathies [6].

Second, the low marrow clonal burden does not argue against an MGRS attribution in this patient; rather, it is characteristic of PGNMID, in which a circulating paraprotein or abnormal marrow clone is detectable in only approximately 30% of cases, and more than 80% of PGNMID patients, particularly those with IgG3 deposits, have an otherwise negative hematologic evaluation. In this patient, the demonstrable IgG-kappa serum paraprotein, the markedly elevated serum kappa FLC with a skewed ratio, a concordant kappa-restricted marrow plasma cell clone, and matching IgG3-kappa restriction within the glomerular deposits together provide unusually strong evidence that the deposited immunoglobulin derives from a genuine, if small, pathogenic plasma cell clone. This concordance is important because recent high-throughput immunoglobulin repertoire sequencing has shown that many PGNMID-IgG3 cases are oligoclonal or polyclonal and may not derive from a true clonal disorder; the presence here of a matching, light-

chain-restricted plasma cell clone distinguishes this case as authentic clone-driven MGRS rather than a non-clonal PGNMID mimic [3].

Third, the kidney biopsy was decisive, both in establishing the causal link between the monoclonal protein and the renal lesion and in subtyping the lesion. Immunofluorescence and electron microscopy are the cornerstone of PGNMID diagnosis, demonstrating glomerular-restricted granular deposits of monotypic IgG (most commonly IgG3) with light-chain restriction (usually kappa) and complement, with amorphous, non-organized subendothelial and mesangial deposits ultrastructurally [3]. IgG subclass staining and the absence of organized substructure are what separate PGNMID from immunotactoid glomerulonephritis, type I cryoglobulinemic glomerulonephritis, MIDD, and amyloidosis.

Interestingly, anemia is a feature of multiple myeloma or progression to the same, but with a low-burden clone, anemia was deemed to be in the setting of chronic disease.

The management of MGRS differs fundamentally from that of both autoimmune glomerular disease and overt hematologic malignancy: therapy is directed by the nature of the underlying clone, and the therapeutic end point is a deep hematologic response sufficient to preserve kidney function. A very good partial hematologic response, defined as a difference between involved and uninvolved free light chains of less than 4 mg/dL or a greater than 90% reduction in the involved free light chain, is the minimum response associated with renal preservation, and deeper responses may further improve renal outcomes [6]. For plasma-cell clones, this is currently best achieved with bortezomib-based regimens, which have demonstrated high hematologic and renal response rates, particularly when initiated early [7]. Emerging evidence supports the addition of the anti-CD38 monoclonal antibody daratumumab, and a recent prospective pilot randomized trial found that both bortezomib-cyclophosphamide-dexamethasone and rituximab produced comparable renal responses in PGNMID, reinforcing that clone-directed rather than lesion-directed therapy is the guiding principle [8]. The requirement for maintenance dialysis in this patient underscores that renal recovery depends on the depth and durability of the hematologic response and reinforces the importance of early recognition and treatment.

4. Conclusion

Severe AKI requiring intensive care can be the presenting manifestation of MGRS, and PGNMID in particular. In this 54-year-old woman with a normal baseline creatinine and no chronic kidney disease, a systematic exclusion of shock-associated causes of renal failure, recognition of an elevated protein gap, and a kidney biopsy with immunofluorescence and electron microscopy established a diagnosis of IgG3-kappa PGNMID attributable to a small but demonstrable kappa-restricted plasma cell clone, satisfying both formal criteria for MGRS despite a low clonal burden. Early clone-directed therapy with a bortezomib-based regimen was associated with an encouraging hematologic and renal trajectory. The case rein-

forces three practice points: an unexplained protein gap in AKI should trigger a paraprotein workup; kidney biopsy is indispensable for linking a monoclonal protein to a specific renal lesion and for excluding cast nephropathy and other mimics; and prompt, clone-directed therapy targeting a deep hematologic response offers the best opportunity to preserve renal function in MGRS.

Patient Consent

Written informed consent was obtained from the patient for publication of this case report.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Bridoux, F., Nasr, S.H., Arnulf, B., Leung, N., Sirac, C. and Jaccard, A. (2024) Renal Manifestations of MGUS. *Hematology*, **2024**, 489-498. https://doi.org/10.1182/hematology.2024000573

[2] Leung, N., Bridoux, F., Batuman, V., Chaidos, A., Cockwell, P., D'Agati, V.D., *et al.* (2018) The Evaluation of Monoclonal Gammopathy of Renal Significance: A Consensus Report of the International Kidney and Monoclonal Gammopathy Research Group. *Nature Reviews Nephrology*, **15**, 45-59. https://doi.org/10.1038/s41581-018-0077-4

[3] Leung, N., Bridoux, F. and Nasr, S.H. (2021) Monoclonal Gammopathy of Renal Significance. *New England Journal of Medicine*, **384**, 1931-1941. https://doi.org/10.1056/nejmra1810907

[4] National Comprehensive Cancer Network (2026) Multiple Myeloma (Version 5.2026), MGRS-1 and MYEL-1. NCCN Clinical Practice Guidelines in Oncology.

[5] Sethi, S., Rajkumar, S.V. and D'Agati, V.D. (2018) The Complexity and Heterogeneity of Monoclonal Immunoglobulin-Associated Renal Diseases. *Journal of the American Society of Nephrology*, **29**, 1810-1823. https://doi.org/10.1681/asn.2017121319

[6] Bao, S., Xun, Z., Bian, W., Wang, D., Liu, H., Li, Y., *et al.* (2026) Renal Amyloidosis Prediction in Kidney Disease Patients Accompanied by Monoclonal Gammopathy. *British Journal of Haematology*, **209**, 580-588. https://doi.org/10.1111/bjh.70565

[7] Javaugue, V., Pascal, V., Nasr, S.H., Bender, S., Derouault, P., Dasari, S., *et al.* (2025) Revisiting Proliferative Glomerulonephritis with Monoclonal Immunoglobulin Deposits through Immunoglobulin Repertoire Sequencing. *Kidney International*, **108**, 1146-1157. https://doi.org/10.1016/j.kint.2025.07.039

[8] Zhang, X., Yu, X., Wang, Z., Qin, A., Wang, J., Guo, D., *et al.* (2026) Bortezomib-Cyclophosphamide-Dexamethasone versus Rituximab in PGNMID. *Nephrology Dialysis Transplantation*. https://doi.org/10.1093/ndt/gfag146