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Case Report

# Monoclonal Gammopathy of Renal Significance: A Case Report of Nephrotic Syndrome Due to IgG Kappa Light Chains

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**Abstract**

Monoclonal Gammopathy of Renal Significance (MGRS) is a group of pathologies that includes all renal disorders caused by the abnormal presence of a monoclonal immunoglobulin (MIg) secreted by plasma cells or other B cells in patients without diagnostic criteria for Multiple Myeloma. This article describes the case of a patient with nephrotic syndrome who was diagnosed with MGRS by Immunoglobulin G (IgG) kappa light chain, with progression to a renal disease requiring dialytic support, highlighting the importance of an adequate clinical diagnosis to guide treatment given the significant morbidity.

**Keywords:** Monoclonal Gammapathy; Renal Insufficiency; Nephrotic Syndrome; Immunoglobulin G; Case report

## Introduction

Monoclonal Gammopathy of Renal Significance (MGRS) has a prevalence of 0.7% in the general population and increases with age. Annual incidence varies between 4 and 15 cases per 100,000 inhabitants, reaching 169 cases per 100,000 inhabitants in those over 80 years old [1]. Monoclonal gammopathies are disorders in which plasma cells in the bone marrow produce an excessive amount of an abnormal monoclonal protein. The monoclonal component can be formed by a heavy chain (usually γ chain, and less frequently α, μ, δ, ε chains) along with a light κ or λ chain, isolated light chains, and exceptionally only heavy chains [2]. These monoclonal proteins can have different characteristics and structures, associated with various diseases [1].

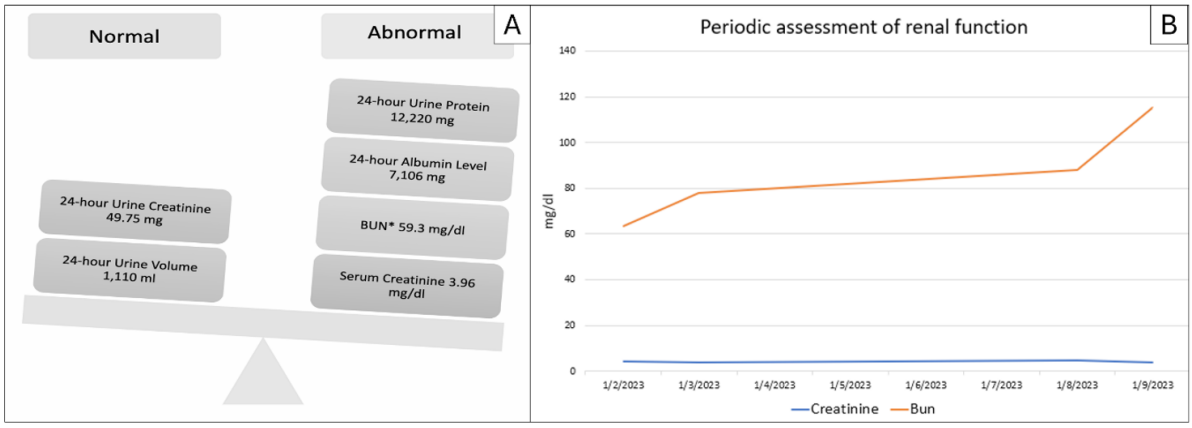
MGRS is a significant cause of renal injury, where monoclonal proteins may deposit in the kidneys and cause damage. This disease is associated with a variety of glomerular, tubulointerstitial, and vascular lesions within the kidney [3]. Common lesions include immunoglobulin-related amyloidosis, light chain deposition disease, fibrillary glomerulonephritis, and immunotactoid glomerulonephritis [3]. Neoplastic transformation (myeloma or lymphoma) of these monoclonal gammopathies is estimated at 1% annually. Factors determining this risk include an abnormal ratio between free kappa and lambda light chains, monoclonal component other than immunoglobulin (light or heavy chains), or IgA type, and concentration of monoclonal protein ≥15 g/L.

If these three factors are met, the risk of neoplastic progression reaches 58% in 20 years, compared to only 5% if none of these characteristics are present [1].

Treatment strategy is based on chemotherapy tailored to the underlying clone, whether lymphocytic or plasmacytic, renal function, and the presence or absence of extrarenal involvement. Rapid suppression of nephrotoxic MIg secretion has been shown to favorably affect renal and patient survival in most diseases associated with MGRS, including AL amyloidosis, Light Chain Deposition Disease (LCDD), immunotactoid glomerulopathy, and Proliferative Glomerulonephritis with Monoclonal Ig Deposits (PGNMID). Early recognition and rapid characterization of the MGRS type are crucial, as they determine the therapeutic strategy and strongly impact renal prognosis [2].

## Case Presentation

An 84-year-old male patient with a history of right renal hypoplasia, arterial hypertension, chronic kidney disease stage G4 under outpatient nephrology management, Alzheimer's dementia, and thrombocytopenia. Admitted to the institution on January 23, 2023, due to oedema in upper and lower limbs, as well as ascites. Vital signs were blood pressure 166/75 mmHg, mean arterial pressure 96, heart rate 63 beats/min, respiratory rate 18 breaths/min, oxygen saturation 93%, temperature: 36.08°C. Paraclinical reports showed chronic kidney disease G5, with nephrotic range proteinuria (Figure 1).




*BUN (Blood Urea Nitrogen)

**Figure 1:** Paraclinical report.

The following etiological diagnoses for nephrotic syndrome were considered: amyloidosis vs. Waldenstrom's macroglobulinemia vs. multiple myeloma. Imaging studies reported long bone X-rays: skull: No bone lesions were observed in the vault, and the sella turcica was normal. Long bones: Antero-posterior X-rays were taken of humeri, forearms, femurs, and legs, showing demineralization in the observed bones. Degenerative phenomena are seen in the left humerus's greater tuberosity, and a pseudo-cystic image is present in the distal end of the right radius with involvement of the articular surface. Figure 2A illustrates the immunological studies.

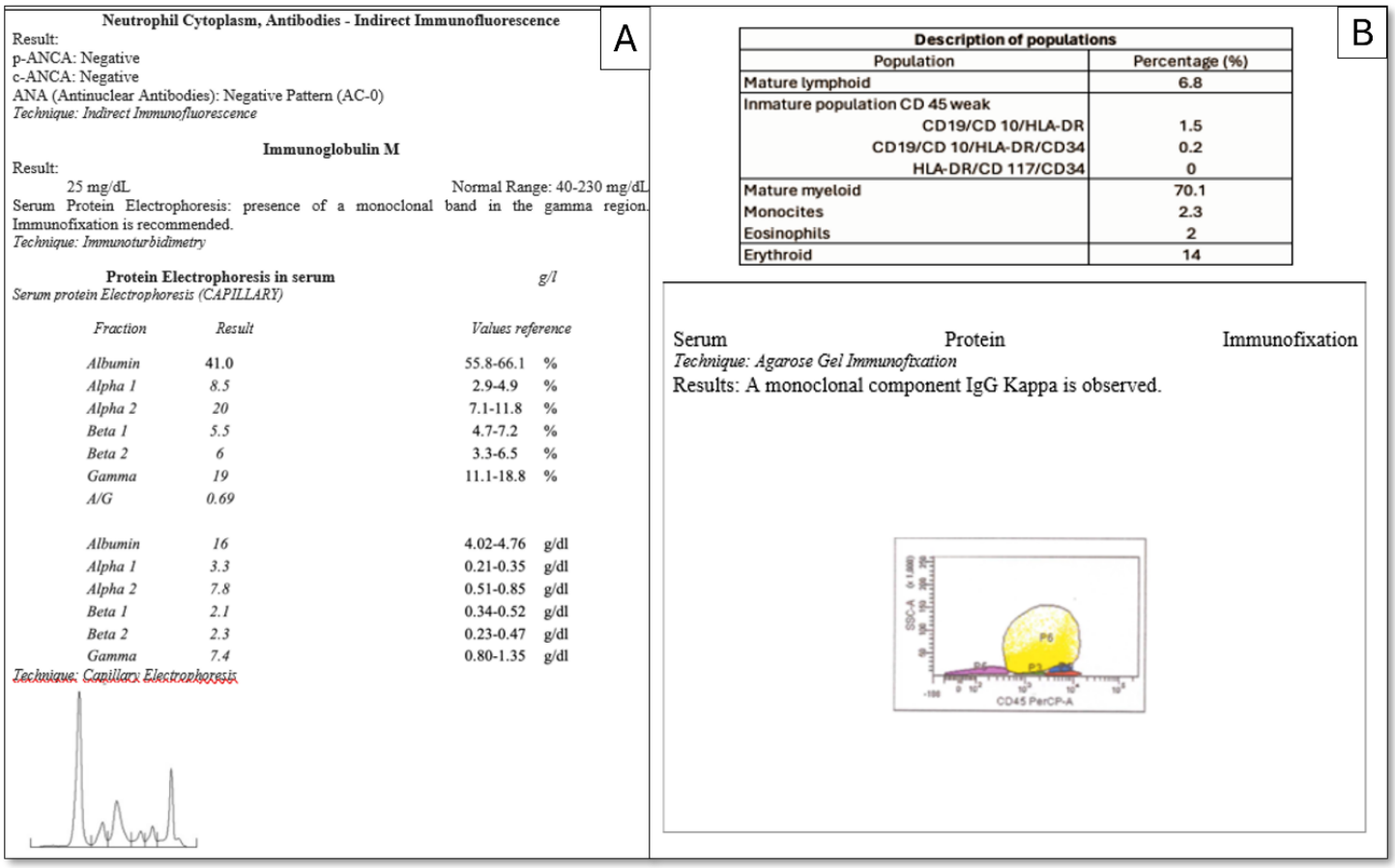



**Figure 2:** Immunological Studies and Flow Cytometry and Protein Immunofixation.

## Management Considerations and Initial Intervention

Considering the high suspicion of multiple myeloma, the decision was made to initiate treatment with methylprednisolone 1 g IV daily. Additionally, a bone marrow aspirate and flow cytometry were scheduled. Following the initiation of corticosteroids, renal function persisted impaired, accompanied by a partial decrease in proteinuria: 5838 mg/24 hours and a volume of 600 ml/24 hours. Consequently, Nephrology recommended the initiation of renal replacement therapy (Figure 1b).

The flow cytometry study did not suggest the presence of a lymphoid or myeloid population. The serum immunofixation on agarose gel revealed a monoclonal component IgG Kappa (light chains) (See Figure 2B).

The results report concluded that the nephrotic-range proteinuria was related and/or caused by MGRS with IgG Kappa light chain. Due to the progression of renal damage, increased azotemia, serositis, and the exclusion of hematologic malignancy, management with oral Prednisone 50 mg per day, associated with intravenous Cyclophosphamide 500 mg every 15 days, was indicated. Following the initiation of treatment, proteinuria control was requested, with a reported value of 6 g/dL.

## Discussion

Nephrotic syndrome in the elderly can result from various etiologies that alter glomerular permeability to proteins, including metabolic, infectious, neoplastic, and hereditary conditions [2]. However, in clinical practice, the focus is primarily on classic metabolic diseases such as diabetes mellitus, hypothyroidism, and, in the presented case, the infectious component. This leads to the use of diagnostic tools, whose results may be delayed, anchored to the technological level of the clinical institution, coupled with administrative procedures, resulting in a delayed start of definitive treatment [4].

In this case, we describe an elderly patient with a history of renal hypoplasia, hypertension, and chronic kidney disease

stage G4, consistent with the literature [5]. Renal biopsy was contraindicated, posing a diagnostic challenge due to the rapid progression of oedema associated with nephrotic-range proteinuria and renal failure. Differential diagnoses such as amyloidosis, Waldenstrom's macroglobulinemia, multiple myeloma [6], systemic lupus erythematosus were considered, requiring a series of clinical and laboratory analyses, as well as the intervention of a multidisciplinary team to guide diagnosis and subsequent therapeutic management.

Monoclonal gammopathies of renal significance end up being a diagnosis of exclusion, despite their increased incidence with age [7]. In this described case, not only metabolic, infectious, hematologic studies, and imaging were necessary but also resulted in a monoclonal IgG Kappa pattern as the cause of proteinuria and its classic manifestation, oedema, with a poor response to corticosteroid management.

The initiation of cytotoxic therapy with cyclophosphamide showed a decrease in proteinuria values in a period of no less than 15 days. However, as reported in the literature, late initiation provides a higher risk of morbidity and mortality [2]. The timeliness in treatment is related to the inclusion of such pathologies in presumptive diagnoses. Thus, the request for corresponding studies allows for a quicker approach to diagnosis and, if necessary, the timely initiation of targeted therapy [8].

The use of cytotoxic therapy poses plausible risks such as leukopenia and thrombocytopenia, increasing the risk of infections and bleeding. This leaves clinicians in a realm of uncertainty about its use when there is no definitive diagnostic reason. With the presentation of this case, we aim to bring greater visibility to Monoclonal Gammopathy of Renal Significance, its diagnosis, and the use of cytotoxic therapy without the possibility of renal biopsy.

## Conclusion

The presented case underscores the complexity and challenges associated with managing nephrotic syndrome in older adults, especially when renal biopsy is not feasible. Monoclonal gammopathy of renal significance emerges as a critical diagnosis, and despite its therapeutic risks, the timely implementation of cytotoxic therapy, as demonstrated in this case, can lead to clinical improvements. However, the uncertainty arising from the lack of a definitive diagnostic confirmation highlights the urgent need for more precise and accessible diagnostic strategies in this context. This scenario emphasizes the importance of a comprehensive and collaborative approach in addressing complex nephrological conditions in the geriatric population, focusing on the promptness and accuracy of the diagnosis to improve clinical outcomes and avoid delays in therapeutic intervention.

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## Ethical Statement

This case report was conducted with the patient's consent, who was adequately informed about the objectives of this study. Furthermore, the authors rigorously conducted the study, strictly adhering to both national and international ethical principles governing scientific research.

**Conflict of Interest:** None

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