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Case Report
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Suspected Monoclonal Gammopathy of Renal Significance in an HIV-Positive Patient with End-Stage Renal Disease and Non-Biopsiable Kidneys

Juby-Ebersey Jade, Kimberley Shira, Hoosen Siddeeq and Rapiti Nadine*

Department of Health, Victoria Mxenge Hospital, KZN, South Africa

Abstract

Background: Monoclonal gammopathy of renal significance (MGRS) describes kidney disease caused by nephrotoxic monoclonal immunoglobulins produced by small B-cell or plasma cell clones that do not meet criteria for overt hematologic malignancy. Renal biopsy is essential for definitive diagnosis but may be contraindicated in specific patient cases. This case highlights the importance of early screening, diagnosis, and treatment to prevent progression to end-stage renal disease (ESRD).

Case Presentation: A 46-year-old HIV-positive female with long-standing viral suppression on renal-friendly antiretroviral therapy presented with end-stage renal disease. Serum protein electrophoresis revealed two monoclonal paraproteins and markedly elevated immunoglobulin G levels. Extensive evaluation excluded plasma cell and lymphoproliferative neoplasms. Renal biopsy was contraindicated due to bilaterally small kidneys. A diagnosis of suspected MGRS was made, and clone-directed therapy was initiated. Although a biochemical response was achieved, renal function did not recover.

Conclusion: This case highlights the diagnostic and therapeutic challenges of suspected MGRS in patients presenting with advanced renal disease where histologic confirmation is not feasible, emphasizing the importance of early recognition to prevent irreversible kidney injury.

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Correspondence:
Dr. Juby-Ebersey Jade, Department of Health, Victoria Mxenge Hospital, KZN, South Africa, Tel: 0790853481; E-mail: jadejubyy@gmail.com

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Introduction

Monoclonal gammopathy of renal significance (MGRS) encompasses a heterogeneous group of renal disorders caused by nephrotoxic monoclonal immunoglobulins secreted by small B-cell or plasma cell clones that do not fulfill diagnostic criteria for multiple myeloma or other overt lymphoproliferative malignancies [1]. Despite the limited clonal burden, these monoclonal proteins can induce progressive and irreversible renal injury [1, 2].

Timely recognition of MGRS is critical, as renal outcomes are strongly associated with early initiation of clone-directed therapy [2, 3]. Renal biopsy with comprehensive immunopathologic assessment remains the gold standard for diagnosis and classification of the underlying lesion [3]. However, in some patient's renal biopsy may be contraindicated due to small kidney size and increased procedural risk. In such cases, clinicians must rely on clinicopathologic correlation and exclusion of alternative etiologies to guide management [3].

We report a case of suspected MGRS in an HIV-positive patient presenting with end-stage renal disease (ESRD) in whom renal biopsy was not possible, highlighting the diagnostic uncertainty and limited renal recovery associated with late presentation.

Case Presentation

A 46-year-old HIV-positive female presented with established end-stage renal disease. She had been diagnosed with HIV infection more than ten years earlier and was chronically virally suppressed on renal-friendly antiretroviral therapy. Her medical history included hypertension, which was well controlled and managed in the context of advanced renal disease. There was no history of diabetes mellitus, systemic autoimmune disease, or opportunistic infections.

Renal imaging demonstrated bilaterally small kidneys, rendering renal biopsy unsafe. Laboratory evaluation revealed two monoclonal paraproteins on serum protein electrophoresis, with monoclonal paraprotein 1 measuring 3 g/L and monoclonal paraprotein 2 measuring 7

Table 1: Longitudinal summary of patient laboratory parameters, treatment, and renal function.

Date	MP 1 / MP 2 (g/L)	γ-Globulin (g/L)	IgG (g/L)	Kappa (mg/L)	Lambda (mg/L)	K:L ratio	Therapy	Renal function (eGFR mL/min/1.73 m²)
Aug – Dec 2022	2 / 8	42	46	672	302	2.2	None	10
Feb 2023	2 / 4	–	35	355	250	1.42	Thal + Dex	10
Jun – Jul 2023	2 / 5	–	32	241	178	1.35	VAD 1	9–13
Nov 2023 – Jan 2025	Nil	13	17.91	95.4	107.6	0.89	VAD 5 / Lenalidomide	10

Table 1. Longitudinal summary of monoclonal protein levels, immunoglobulins, free light chains, treatment, and renal function. Despite clear biochemical response to clone-directed therapy, renal function remained severely impaired, and the patient never required dialysis.

g/L. Serum immunoglobulin analysis showed a markedly elevated immunoglobulin G (IgG) level of 46.45 g/L.

Comprehensive hematologic evaluation, including assessment for plasma cell dyscrasia and lymphoproliferative disorders, was negative, and diagnostic criteria for multiple myeloma or lymphoma were not met. In the setting of unexplained ESRD associated with a significant monoclonal gammopathy and exclusion of alternative causes, a diagnosis of suspected monoclonal gammopathy of renal significance was made. The specific renal lesion subtype could not be determined due to the absence of renal histology.

The patient was treated with clone-directed therapy consisting of vincristine, doxorubicin, and dexamethasone, followed by thalidomide maintenance. Serial serum protein electrophoresis demonstrated a biochemical response with reduction in monoclonal paraprotein levels. Despite hematologic improvement, renal function did not recover. The patient was not requiring dialysis at any point before or during her treatment.

Discussion

This case illustrates the diagnostic and therapeutic challenges of MGRS in patients presenting with advanced renal disease. MGRS is defined by renal injury mediated directly by monoclonal immunoglobulins, allowing even small or indolent clones to cause severe kidney damage [1, 2].

Renal biopsy is central to confirming MGRS and defining the pattern of renal injury, which has important prognostic and therapeutic implications [3]. In patients with advanced CKD and bilaterally small kidneys, however, biopsy may be contraindicated, limiting definitive diagnosis. Similar challenges have been described in prior MGRS cohorts, particularly among patients presenting late in the disease course [2, 3].

The coexistence of HIV infection adds complexity to the diagnostic evaluation of renal disease. While HIV-associated nephropathy and immune complex–mediated kidney disease are well recognized, sustained viral suppression on renal-friendly antiretroviral therapy reduces the likelihood of these entities. In this context, the presence of a significant monoclonal paraproteinemia raised concern for a nephrotoxic monoclonal process contributing to renal failure [1].

Table 1 shows the observed biochemical response to clone-directed therapy that supports the presence of an active monoclonal process. However, the absence of renal recovery highlights a key principle in MGRS: once chronic and irreversible structural kidney damage has occurred, hematologic response may not translate into improvement in renal function [2, 4, 5]. This observation is consistent with published series demonstrating that renal outcomes are closely linked to disease stage at diagnosis and baseline kidney function [2, 5].

Hypertension as a confounding factor in suspected MGRS

Hypertension is a common comorbidity in patients presenting with chronic kidney disease and may confound the clinical interpretation of renal dysfunction in individuals with monoclonal gammopathy. Hypertensive nephrosclerosis is frequently considered in patients with long-standing hypertension and reduced kidney function; however, the presence of a circulating monoclonal protein should prompt consideration of monoclonal protein–mediated renal injury. In MGRS, kidney damage results from nephrotoxic monoclonal immunoglobulins produced by a small plasma cell or B-cell clone that does not meet diagnostic criteria for overt hematologic malignancy [1, 2]. Because these clones are often small and associated paraprotein levels may be modest, renal disease may initially be attributed to more common causes such as hypertensive nephropathy. Failure to recognize the potential role of monoclonal proteins may delay diagnosis and treatment, allowing progressive and potentially irreversible renal injury to occur [2].

HIV coinfection and monoclonal gammopathy

HIV infection has been associated with a range of immunologic abnormalities, including polyclonal hypergammaglobulinemia and an increased prevalence of monoclonal gammopathies. Chronic immune activation and B-cell dysregulation in HIV infection may contribute to the development of monoclonal plasma cell expansions [3]. Although some monoclonal gammopathies in HIV-positive individuals may resolve with effective antiretroviral therapy, persistent monoclonal protein production can occur and may lead to plasma cell dyscrasias or monoclonal gammopathy–related renal disease [3, 4]. Renal disease in patients with HIV is multifactorial and includes HIV-associated nephropathy, immune complex–mediated kidney disease, drug-related nephrotoxicity, and hypertensive nephrosclerosis. Consequently, monoclonal protein–mediated kidney injury may be overlooked in this population. In patients with well-controlled HIV infection and unexplained renal dysfunction accompanied by monoclonal gammopathy, MGRS should therefore be considered in the differential diagnosis.

Clone size and renal recovery in MGRS

A defining feature of MGRS is that the underlying clonal disorder is typically small and does not meet criteria for multiple myeloma or lymphoma. Bone marrow plasma cell infiltration is often less than 10%, and circulating monoclonal protein levels may be relatively low [1]. Despite the small clone size, the monoclonal immunoglobulin produced may possess nephrotoxic properties capable of causing significant renal injury. Consequently, the severity of kidney disease in MGRS does not necessarily correlate with the burden of the underlying hematologic clone [1, 2]. Treatment strategies therefore focus on clone-directed therapy aimed at reducing production of the pathogenic monoclonal protein. Studies have shown that achieving a deep hematologic response improves the likelihood of renal

response; however, recovery of kidney function is highly dependent on the degree of irreversible structural damage present at the time of diagnosis [5]. Patients presenting with advanced chronic kidney disease frequently experience stabilization rather than improvement in renal function despite successful control of the monoclonal clone [5]. This highlights the importance of early recognition and treatment of monoclonal protein–mediated kidney disease before the development of end-stage renal injury.

Conclusion

Suspected MGRS should be considered in patients with unexplained advanced kidney disease and monoclonal gammopathy, even when renal biopsy is not feasible [1, 3]. This case demonstrates that delayed presentation may limit renal recovery despite successful control of the monoclonal clone, emphasizing the importance of early recognition and multidisciplinary management [2, 5].

Declarations

Ethics approval and consent to participate and Consent to publish

Written informed consent was obtained from the patient for publication of this case report and any accompanying data. All identifying information has been removed to preserve patient anonymity. Formal institutional ethics committee approval was not required for this single anonymized case report in accordance with institutional guidelines.

Data availability

Data was obtained from the patients' medical records.

Competing interests

None.

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None.

Authors' contributions

J.E. (Jade Ebersey) contributed to data collection, compilation of clinical information, and drafting of the manuscript, and was involved in the ongoing clinical care of the patient.

K.S. (Kimberley Shira) contributed to patient management and clinical care, and assisted with manuscript review.

H.S. (Siddeeq Hoosen) supervised the study, contributed to manuscript editing and critical revision, and was involved in the patient's care as a consultant haematologist.

R.N. (Nadine Rapiti) provided senior oversight, contributed to manuscript editing and critical revision, and was involved in the patient's care as a consultant haematologist and head of department.

All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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