DOI: https://doi.org/10.5281/zenodo.20087441

ISR Journal of Medical Case Reports (ISRJMCR)

Homepage: https://isrpublisher.com/isrjmcr/

Volume 02, Issue 02, February 2026 ISSN: 3107-5576 (Online)

Renal Thrombotic Microangiopathy in Multiple Myeloma: A Case Report

C. Congera[1]*, B. Jihane[1], S. Karci[1], S. Mazghi[1], N. Hamouche[1], M. Chettati[1], W. Fadili[1], I. Laouad[1]

[1]Nephrology, Hemodialysis and Kidney Transplantation Department of the Mohammed VI University Hospital of Marrakech, Morocco

***Corresponding author:** C. Congera
Nephrology, Hemodialysis and Kidney Transplantation Department of the Mohammed VI University Hospital of Marrakech, Morocco

Article History

Received: 18-12-2025

Accepted: 02-02-2026

Published: 05-02-2026

Abstract: **Case Report**

Thrombotic microangiopathy (TMA) associated with multiple myeloma is a rare but serious condition involving complex mechanisms including endothelial light chain toxicity, complement activation, and iatrogenic factors. We report the case of a 44-year-old woman with severe renal failure revealing multiple myeloma, complicated by histologically confirmed TMA. The absence of prior treatment suggests a direct role of monoclonal gammopathy. Initial management resulted in partial improvement of renal function. A review of the literature highlights the importance of early diagnosis based on renal biopsy. Treatment focuses on controlling the myeloma and, in some cases, on complement-targeted therapies.

Keywords: Multiple Myeloma, Thrombotic Microangiopathy, Renal Involvement.

I. INTRODUCTION

Thrombotic microangiopathy (TMA) is a rare but serious clinicopathological syndrome characterized by the combination of mechanical hemolytic anemia, peripheral thrombocytopenia, and tissue ischemia due to microcirculatory occlusion by platelet thrombi [1, 2]. Histopathologically, it is defined by the presence of microthrombi obstructing capillaries and arterioles, leading to multi-organ involvement, primarily affecting the kidneys and the central nervous system [1]. The main forms include thrombotic thrombocytopenic purpura (TTP), linked to a severe ADAMTS13 deficiency, and hemolytic uremic syndrome (HUS), characterized by predominant renal involvement [2]. However, secondary TMAs represent a heterogeneous group of pathologies associated with various contexts, including infections, autoimmune diseases, cancers, and certain therapies [3]. Multiple myeloma is a malignant hematological disorder characterized by the clonal proliferation of plasma cells producing monoclonal immunoglobulin or free light chains. Renal involvement is a frequent and major complication of this disease, occurring in approximately 20% to 40% of patients during its course. The classically described mechanisms include myeloma cast nephropathy, AL amyloidosis, and monoclonal light chain deposition. However, rarer forms of renal involvement have been reported, including thrombotic microangiopathy, the recognition of which often remains difficult in clinical practice [4]. The occurrence of thrombotic microangiopathy (TMA) in multiple myeloma

represents a distinct entity. Its pathophysiology remains incompletely understood and appears to be multifactorial. It notably involves direct endothelial toxicity from monoclonal light chains, complement activation, and iatrogenic factors related to treatments, particularly proteasome inhibitors or anti-angiogenic agents [4, 5]. Furthermore, the progression of the hematological disease itself can be a trigger for TMA [4].

Clinically, TMA associated with multiple myeloma most often manifests as acute, sometimes severe, renal failure, associated with signs of mechanical hemolysis and thrombocytopenia. However, the presentation may be incomplete or atypical, making diagnosis difficult, especially since these abnormalities can be attributed to other myeloma complications or its treatments [4]. In this context, renal biopsy plays a central role in confirming the diagnosis and guiding management.

The significance of this entity lies in its potential severity and the therapeutic implications it raises. Indeed, thrombotic microangiopathy (TMA) constitutes a medical emergency, the management of which relies on both specific treatment of the microangiopathy and control of the underlying disease. Early identification is therefore essential to improve renal and overall prognosis. The objective of this work is to review current data concerning thrombotic microangiopathy associated with multiple myeloma, focusing on the pathophysiological mechanisms, diagnostic aspects, and therapeutic strategies.

II. PHYSIOPATHOLOGICAL MECHANISMS OF RENAL DAMAGE

Endothelial Toxicity of Monoclonal Immunoglobulins

From a pathophysiological standpoint, several mechanisms can explain the occurrence of TMA in multiple myeloma. First, monoclonal immunoglobulins or their fragments, particularly circulating free light chains, can exert direct toxicity on endothelial cells. This toxicity leads to endothelial activation, loss of the physiological anticoagulant properties of the endothelium, and increased exposure of procoagulant factors, thus promoting the formation of microthrombi in capillaries and arterioles. Furthermore, some studies suggest that monoclonal light chains can induce oxidative stress and mitochondrial dysfunction within endothelial cells, contributing to their apoptosis and impaired vascular integrity [1].

Complement Activation and Immune Dysregulation

Another important mechanism involves the activation of the complement system. In some cases, TMA associated with multiple myeloma resembles a complement-mediated thrombotic microangiopathy, similar to atypical hemolytic uremic syndrome. Monoclonal immunoglobulins can interfere with complement regulation, either by acting as autoantibodies directed against regulatory proteins (notably factor H), or by promoting excessive activation of the alternative pathway [3]. This uncontrolled activation leads to persistent endothelial injury.

Role of Pro-Inflammatory Cytokines

The role of pro-inflammatory cytokines is also central to the pathophysiology of TMA associated with myeloma. Plasma cells produce mediators such as IL-6 and TNF-α, which promote endothelial activation, the expression of adhesion molecules, and platelet aggregation. This pro-inflammatory environment contributes to microvascular thrombosis.

Role of antimyeloma treatments

Multiple myeloma treatments are a major triggering factor. Proteasome inhibitors, particularly carfilzomib, are frequently implicated. The mechanisms include direct endothelial toxicity, disruption of von Willebrand factor, and complement activation [4]. Decreased ADAMTS13 activity has also been suggested [5]. Other treatments, such as immunomodulators, may also be involved.

III. ANATOMOPATHOLOGICAL ASPECTS

Histopathologically, renal TMA is characterized by involvement of the glomerular capillaries and arterioles. Lesions include endothelial swelling, narrowing of the vascular lumen, and the presence of fibrin-platelet thrombi. Chronic forms show double contours of the basement membrane and interstitial fibrosis [2]. Immunofluorescence is generally poor, which aids in differential diagnosis.

IV. CLINICAL AND BIOLOGICAL MANIFESTATIONS

The clinical presentation is heterogeneous. It may involve microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure. Hemolysis is confirmed by the presence of schistocytes, elevated LDH, and decreased haptoglobin. Renal involvement manifests as renal failure, proteinuria, and sometimes hematuria [1].

V. DIAGNOSTIC APPROACH

The diagnosis is based on a combination of clinical and biological findings. ADAMTS13 measurement is essential to rule out thrombotic thrombocytopenic purpura. In TMA associated with myeloma, its activity is generally preserved [5]. Complement testing may suggest complement-mediated TMA.

VI. THERAPEUTIC MANAGEMENT

Management is based on identifying and stopping the triggering factor, particularly in cases of drug toxicity. Treating myeloma is essential to reduce the production of monoclonal immunoglobulins.

Plasma exchange has variable efficacy. Complement inhibitors, such as eculizumab, represent a promising option in certain forms [3, 4].

VII. PROGNOSIS AND OUTCOME

The prognosis remains guarded, with a high risk of progression to end-stage renal disease [5]. Recovery depends on early diagnosis and control of the myeloma. Iatrogenic forms may be reversible if identified quickly.

VIII. OBSERVATION

A 44-year-old female patient, with a history of multinodular goiter treated with levothyroxine and chronic headaches treated with analgesics, was hospitalized in our department from December 9th to 27th, 2023, for severe renal failure. She had initially consulted in November 2023 for inflammatory polyarthralgia with hair loss in the context of a decline in her general health. Severe renal failure was diagnosed, and the patient was referred to our department for further management.

On examination, she was conscious, cooperative, breathing normally, afebrile, with a blood pressure of 130/70 mmHg, no edema, and a normal urine output of 1.5 L/100km. Urine dipstick testing revealed proteinuria (1 X) and hematuria (3 X). Laboratory tests revealed severe renal insufficiency (creatinine 85 mg/L, MDRD clearance 5 mL/min); urea 2.1; sodium 129; potassium 3.7; chloride 102; acidosis (bicarbonate 10); uric acid 129; total protein 64; albumin 35; calcium 85.8; phosphorus 69; CRP 1.6; vitamin D deficiency (vitamin D 8); and normochromic normocytic anemia (hemoglobin 7.5 g/dL); platelet count 211,000 (decreasing to 164,000 and then 113,000); white blood cell count 7,870. Immunological tests were negative for ANA, anti-DNA antibodies, ANCA, and anti-GBM. Serum supplements were not consumed. There were no associated viral infections, specifically no hepatitis, HIV, or syphilis. Liver and lipid profiles were normal. Urine culture showed a red blood cell count of 600,000/ml and a white blood cell count of 550,000/ml with a positive polymicrobial culture. The protein/creatinine ratio was 0.9 g/g. Serum protein electrophoresis revealed a monoclonal peak in the gamma globulin region. Bone marrow aspirate showed 34% plasma cells.

Renal ultrasound revealed both kidneys to be of normal size, measuring 10 x 4.4 cm on the right and 10.5 x 5 cm on the left, with regular, undifferentiated contours and no dilation of the renal pelvis and calyces. The renal biopsy revealed dense deposits of non-granular kappa on the arteries, arterioles, and especially the tubular basement membrane and some casts. The morphological and immunological findings initially suggested thrombotic microangiopathy (TMA) or Shu syndrome with suspected light chain disease.

In our case, the diagnosis of thrombotic microangiopathy in the context of renal involvement in multiple myeloma was made based on severe renal failure, the results of the bone marrow aspirate (plasma cell count of 34%), and the renal biopsy (TMA with suspected light chain disease); in the absence of other factors explaining the occurrence of TMA in multiple myeloma, particularly the absence of chemotherapy.

Therapeutic management during hospitalization consisted of rehydration with corticosteroid therapy, and the patient's condition showed marked improvement in renal function (serum creatinine decreasing from 85 to 45 mg/L), persistent anemia, and progressive thrombocytopenia. The patient was then referred to the hematology department for initiation of chemotherapy.

IX. DISCUSSION

Thrombotic microangiopathy associated with multiple myeloma is a rare but increasingly recognized entity within the spectrum of renal involvement linked to monoclonal gammopathies. The reported case illustrates an atypical presentation, marked by severe initial renal failure in the absence of prior antimyeloma treatment, suggesting a mechanism directly related to the disease itself rather than drug toxicity. In the literature, thrombotic microangiopathy (TMA) in multiple myeloma can occur either de novo or secondary to treatments, particularly proteasome inhibitors such as carfilzomib [6]. However, several recent observations have highlighted cases of TMA preceding any chemotherapy, suggesting a direct pathogenic role of monoclonal immunoglobulins or their fragments [7]. In our case, the absence of exposure to potentially toxic agents reinforces this hypothesis. From a pathophysiological standpoint, monoclonal light chains, particularly of the κ type as in our case, can induce direct endothelial damage, promoting coagulation activation and microthrombi formation [8]. Furthermore, recent data suggest that these immunoglobulins can interfere with complement regulation, especially the alternative pathway, leading to uncontrolled activation and persistent endothelial damage [9]. Although complement levels remained normal in our patient, this does not preclude local or functional complement activation, as described in some forms of TMA associated with monoclonal gammopathies [10].

The severe renal involvement observed in our patient is consistent with the literature, where the kidney is the organ most frequently implicated in TMA [8]. Renal biopsy plays a key role in diagnosis, revealing the characteristic lesions of thrombotic microangiopathy (TMA), associated in our case with κ light chain deposits, suggesting a dual microangiopathic involvement linked to a light chain disorder. This association has been described in the context of monoclonal gammopathy of renal significance (MGRS), where the same monoclonal protein can induce different types of renal lesions [7]. Clinically, the initial absence of severe thrombocytopenia and its progressive evolution highlight the sometimes incomplete or evolving nature of the TMA presentation, making diagnosis more difficult. This profile is reported in several recent series, where incomplete or atypical forms of TMA are frequent, particularly in the context of monoclonal gammopathies [10].

Management is primarily based on treating the underlying cause. In our case, the partial improvement in renal function under symptomatic measures (rehydration,

corticosteroid therapy) is encouraging, but remains insufficient in the absence of specific treatment for myeloma. The literature emphasizes the importance of rapid control of plasma cell proliferation to limit light chain production and reduce endothelial damage [8]. Furthermore, the use of complement inhibitors, such as eculizumab, has been proposed in certain forms of TMA associated with myeloma, particularly when complement activation is suspected, with variable results [9, 10]. The renal prognosis depends primarily on early diagnosis and the rapid initiation of appropriate treatment. Despite this, the risk of progression to chronic kidney disease remains high, especially in cases of advanced histological lesions [6].

This case highlights the importance of considering TMA in any case of severe acute kidney injury associated with a monoclonal gammopathy, even in the absence of prior treatment. Renal biopsy and hematological evaluation are essential for an accurate diagnosis. A multidisciplinary approach involving nephrologists and hematologists is indispensable to optimize management and improve prognosis.

X.CONCLUSION

Thrombotic microangiopathy in multiple myeloma is a rare but serious condition with a poor renal and overall prognosis. Its pathophysiology is multifactorial, involving tumor activity and/or certain therapeutic agents. Early diagnosis, based on biological and histological findings, is essential to rapidly implement an appropriate treatment strategy.

BIBLIOGRAPHY

1. Duveau, A., & Lerolle, N. (2011). Microangiopathie thrombotique en réanimation—Prise en charge initiale chez l'adulte. *Médecine Intensive Réanimation*, *20*(Suppl. 2), 332-337.
2. McFarlane, P. A., Bitzan, M., Broome, C., Baran, D., Garland, J., Girard, L. P., ... & Licht, C. (2021). Making the correct diagnosis in thrombotic microangiopathy: a narrative review. *Canadian Journal of Kidney Health and Disease*, *8*, 20543581211008707.
3. Coppo, P. (2017). Microangiopathies thrombotiques secondaires. *Rev Med Interne*, *38*(11), 731–736.
4. Gavriatopoulou, M *et al*., (2019). Thrombotic microangiopathies in multiple myeloma. *Leuk Res*, *85*, 106195.
5. van Doorn, D. P., Abdul-Hamid, M. A., Frenken, L. A., van Paassen, P., Timmermans, S. A., & Limburg Renal Registry. (2024). The spectrum of thrombotic microangiopathy related to monoclonal gammopathy. *Clinical Kidney Journal*, *17*(1), sfad306.
6. George, J. N., & Nester, C. M. (2014). Syndromes of thrombotic microangiopathy. *New England Journal of Medicine*, *371*(7), 654-666.
7. Bridoux, F., Leung, N, *et al*., (2015). Monoclonal gammopathy of renal significance. *Kidney Int*, 2015.
8. Leung, N., Bridoux, F., Batuman, V., Chaidos, A., Cockwell, P., D'Agati, V. D., ... & Nasr, S. H. (2019). The evaluation of monoclonal gammopathy of renal significance: a consensus report of the International Kidney and Monoclonal Gammopathy Research Group. *Nature Reviews Nephrology*, *15*(1), 45-59.
9. Fakhouri, F., Zuber, J., Frémeaux-Bacchi, V., & Loirat, C. (2017). Haemolytic uraemic syndrome. *The Lancet*, *390*(10095), 681-696.
10. Catanese, L, *et al*., (2023). Carfilzomib-induced thrombotic microangiopathy treated with eculizumab. *BMC Nephrol*, 2023.