Saudi Journal of Medical and Pharmaceutical Sciences **ISSN 2413-4929 (Print)**
Scholars Middle East Publishers **ISSN 2413-4910 (Online)**
Dubai, United Arab Emirates
Website: https://saudijournals.com/

Acute Interstitial Nephritis Associated Multiple Myeloma: A Case Report

Hassani Mohamed[1]*, El Akramine Maroua[2]
[1]Nephrology and Hemodialysis Department, Moulay Ismail Military Hospital Meknes
[2]Faculty of Medicine and Pharmacy of Fes - University Sidi Mohamed Ben Abdellah of Fes

Case Report

***Corresponding author**
Hassani Mohamed

Article History
Received: 11.04.2018
Accepted: 22.04.2018
Published: 30.04.2018

DOI:
10.36348/sjmps.2018.v04i04.010

Abstract: Patients with multiple myeloma may present a variety of renal manifestations as a result of damage from circulating light chain immunoglobulin components. The renal alterations can interest any of the renal compartments, and in certain cases more than one compartment can be affected. The resulting high serum concentrations of these proteins often lead to tubular interstitial injuries as endocytic receptors in the proximal tubules are overwhelmed. A 46-year-old white man with a history of left hip pain was diagnosed as multiple myeloma. Imaging including MRI and PET scan showed a left pelvic heterogenous mass causing bone destruction and compressing the adjacent organs. He was referred to the nephrology department due to the onset of acute kidney injury requiring hemodialysis. A kidney biopsy was performed and showed patterns of acute interstitial nephritis and focal linear staining for kappa light chains along tubular basement membranes on immunofluorescence. After glucocorticoids for acute interstitial nephritis and chemotherapy (Bortezomib - Cyclophosphamide - Dexamethasone) directed against the clone, the renal function partially improved and the patient got off hemodialysis support. Conclusion: Acute kidney injury may be the first clinical presentation in patients with multiple myeloma. Could interstitial nephritis be the only manifestation of MM without myeloma cast nephropathy and whether it was glucocorticoid or chemotherapy directed against the clone that has resulted in a significant improvement in renal function.

Keywords: multiple myeloma; acute interstitial nephritis; acute kidney injury; hemodialysis.

INTRODUCTION

Renal disease in multiple myeloma (MM) most often presents as renal insufficiency and proteinuria. Renal lesions that are seen in patients with MM include myeloma cast nephropathy; light chain AL amyloidosis; monoclonal Ig deposition disease (MIDD); and, less frequently, cryoglobulinemic glomerulonephritis and proliferative glomerulonephritis [1].

Although tubulointerstitial nephritis is a recognized pattern of kidney injury in plasma cell dyscrasias [10-11], association between light chain deposition in the kidney and tubulointerstitial nephritis has rarely been reported.

We report a case of a 46-year-old man with a history of left hip pain that developed proteinuria and impaired kidney function and was diagnosed as multiple myelomas. Renal biopsy demonstrated acute interstitial nephritis and kappa light chain deposition in tubular basement membrane.

CASE REPORT

A 46-year-old white man with a history of smoking and left hip pain that was getting worse with the effort without neurologic manifestations but denied other medical or chirurgical problems

Laboratory assays revealed anemia with Hb at 12 g/dl, serum calcium at 102 mg/l, an M spike on urine protein electrophoresis and on serum protein electrophoresis in alpha-2 globulins with abnormal free light chain kappa/lambda ratio at 336,48 and. Serum and urine immunofixation were for IgG kappa. The bone marrow aspirate showed 6% plasma cells and the bone marrow biopsy showed diffuse plasm cells infiltration CD138+ with kappa monotype. Cytogenetic analysis did not detect translocation t(4,14). Other laboratory tests are summarized in Table 1. Extensive imaging including MRI and PET scan showed a left pelvic heterogeneous mass causing bone destruction and compressing the adjacent organs (Figure 1). The patient was diagnosed as multiple myeloma.

During the investigation, the onset of acute kidney injury (AKI) before initiating treatment of myeloma, delayed and modified the chemotherapy protocol to Bortezomib-Cyclophosphamide-Dexamethasone (VCD). The 24-hour urine protein at 1,20 g/l and creatinine level was 55 mg/l on admission to the nephrology department with recent baseline of 11

mg/l. During the course of hospitalization creatinine was trending upwards, reaching 114 mg/l. The etiology of AKI was first thought to be cast nephropathy and the renal function did not improve despite daily 3 liters intravenous saline fluid therapy. On renal ultrasound, kidneys were normal sized with normal cortical thickness. The patient was started on hemodialysis for uremia and a kidney biopsy was performed two weeks after. Twelve glomeruli were available for evaluation by light microscopy. Glomeruli showed a moderate mesangial cell proliferation (Figure 2). Mild thickening of arteriolar and capillary walls was shown. Features of light chain deposition disease or amyloidosis were not noted in the glomerular or vascular compartments. The interstitial process presented as multiple foci with inflammatory infiltrates, which were composed predominantly of lymphocytes and plasma cells. Interstitial edema and rare eosinophils were present (Figure 2). No multinucleated giant cell reaction or recognizable myeloma casts was seen and no evidence for crystals. Two glomeruli were available for immunofluorescence examination. Scarce presence of C3 was found in the vasculature. No specific glomerular staining for light chains or immunoglobulins was identified. Focal linear staining for kappa light chains along tubular basement membranes was noted (Figure 2). The diagnosis of acute interstitial nephritis was made.

ANCA, ANA, anti-dsDNA and the remaining immunologic study as screening for viral infections (HCV, HBV and HIV) were negative. Patient was treated with glucocorticoids prednisone 1 mg/kg/d for one month. Then, the VCD treatment was initiated and completed 6 weeks after.

After 20 sessions of hemodialysis and 4 months later, renal function partially improved with serum creatinine achieving 35 mg/l with complete resolution of M-spike. The patient was referred to the hematology department to complete hematopoietic stem cell transplant assessment.

Table-1: Laboratory data

Parameter	Value	Reference Range
Hemoglobin g/dl	12	13-18
Leukocyte x10^3/uL	9,83	4-10
Neutrophils x10^3/uL	5,58	1,80-7,50
Lymphocytes x10^3/uL	3,15	1-4
Eosinophilis x10^3/uL	0,23	0-0,5
Platelet x10^3/Ul	343	150-400
Ferritin µg/L	59	20-300
Creatinine mg/L	11	7-12
Urea g/L	0,40	0,18-0,55
Potassium mmol/L	4,3	3,7-5,3
Bicarbonate mmol/L	23	22-29
Chloride mmol/L	106	95-110
Calcium mg/L	102	80-105
Phosphorus mg/L	34	25-50
PTH intact (1-84)	44	15-65
C-reactive protein g/L	4,86	0-4,5
CA19-9 U/mL	21,98	0-39
ACE µg/L	2,13	0-3,4
Alpha Foeto Protein IU/mL	3,10	0,5-5,8
P.S.A Total µg/L	1,230	0,5-5,5
Serum IgA g/L	2,32	0,4-4
Serum IgG g/L	4,41	7-16
Serum IgM g/L	0,24	0,4-2,3
Serum protein electrophoresis		
Protein g/L	67	64-83
Albumin g/L	40	34-45
Alpha-1 globulins g/l	4,3	2,1-3,5
Alpha-2 globulins g/l	11,3	5,1-8,5
Beta-1 globulins g/l	4,1	3,4-5,2
Beta-2 globulins g/l	4,3	2,3-4,7
Gamma globulins g/l	5,2	8,0-13,5

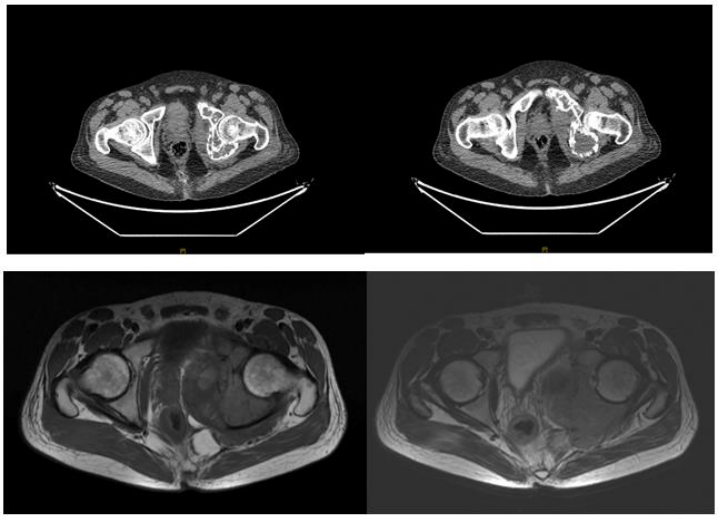

Fig-1: PET scan and IRM, Large heterogeneous mass encompassing the acetabulum, the obturator frame and the left ilio-ischio-pubic branches reaching the pubic symphysis, hypo T1 moderate hyper T2

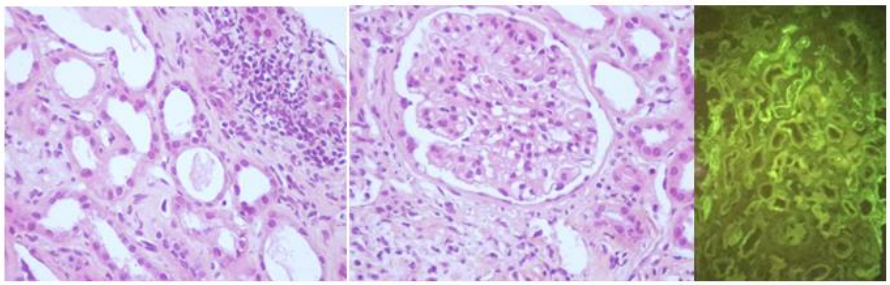

Fig-2: Light microscopy: inflammatory tubular interstitial process, which is typical of the tubular interstitial nephritis pattern (HES). Immunofluorescence: Focal linear staining for kappa light chains along tubular basement membranes

DISCUSSION

Renal failure may be the presenting manifestation of MM and the serum creatinine concentration is increased in almost one-half of patients at diagnosis of MM [4,5]. Two major causes of renal insufficiency in patients with MM are light chain cast nephropathy and hypercalcemia. Patients who do not secrete light chains are not at risk for myeloma kidney.

The renal pathology of cast nephropathy, MIDD, and amyloidosis is diverse, but in each instance, the initial pathogenetic step is the production in the bone marrow of an abnormal Ig light chain by a clone of neoplastic plasma cells. During normal and neoplastic Ig synthesis, plasma cells produce an excess of light chains that are released into the circulation [3]. However, normal light chains are filtered by the glomeruli and are endocytosed and metabolized by the tubules, and they neither deposit in renal structures nor cause pathology [2].

In the absence of other causes of renal failure, a presumptive diagnosis of light-chain cast nephropathy can be made in the setting of high involved free light chain levels. In contrast, renal biopsy should be performed to document typical histologic changes in patients with suspected cast nephropathy, especially if the serum-involved free light chain level is below 500 mg/l [6].

Other causes of renal failure in a patient with MM include concurrent AL amyloidosis, light chain deposition disease, and drug-induced renal damage. However, acute tubulointerstitial nephritis accompanied by neither cast nephropathy nor glomerular lesions has been recently reported in patients with plasma cell dyscrasias [9].

Our findings were consistent with data from Xin GU *et al*. that accumulation of light chains along tubular basement membranes may induce an interstitial process that mimics acute tubular interstitial nephritis [9].

Discontinuation of an offending agent is a universal recommendation for treatment of acute interstitial nephritis. But our patient had no recent history of nephrotoxic medication use, fluid depletion, or hypercalcemia that could explain the AKI. Although the benefits of glucocorticoid therapy are inconclusive, improvement in kidney function has been suggested by several uncontrolled reports [7, 8]. After treatment, our

patient got off hemodialysis support and renal function improved partially.

This pattern is relatively rare, but it should be recognized as an initial manifestation of light chain deposition disease, and adequate treatment should be administered. A high index of suspicion is necessary to make the correct diagnosis, and routine lambda and kappa light chain staining and, if possible, electron microscopic examination is recommended in biopsied cases [12].

CONCLUSION

Acute kidney injury remains an important cause of morbidity and mortality in patients with multiple myeloma. Can we ask if accumulation of light chains along tubular basement membranes may induce an interstitial process that mimics acute interstitial nephritis in multiple myeloma?

This case highlights two important assumptions: could interstitial nephritis be the only manifestation of MM without myeloma cast nephropathy and whether it was glucocorticoid or chemotherapy directed against the clone that has resulted in a significant improvement in renal function.

REFERENCES

1. Markowitz GS (2004): Dysproteinemia and the kidney. Adv Anat Pathol;11: 49–63.
2. Wochner RD, Strober W, Waldmann TA (1967): The role of thekidney in the catabolism of Bence Jones proteins and immunoglobulin fragments. J Exp Med;126: 207–221.
3. Stephen M. Korbet* and Melvin M. Schwartz (2006). Multiple Myeloma. J Am Soc Nephrol;17: 2533–2545,
4. Kyle RA, Gertz MA, Witzig TE, (2003). Review of 1027 patients with newly diagnosed multiple myeloma. Mayo Clin Proc; 78:21.
5. Winearls CG (1995). Acute myeloma kidney. Kidney Int; 48:1347.
6. Hutchison CA, Batuman V, Behrens J. (2011). The pathogenesis and diagnosis of acute kidney injury in multiple myeloma. Nat Rev Nephrol; 8:43.
7. Rossert, J. (2001). Drug-induced acute interstitial nephritis. *Kidney international*, *60*(2), 804-817.
8. Buysen, J. G. M., Houthoff, H. J., Krediet, R. T., & Arisz, L. (1990). Acute interstitial nephritis: a clinical and morphological study in 27 patients. *Nephrology Dialysis Transplantation*, *5*(2), 94-99.
9. Gu X, Herrera GA (2006). Light-chain-mediated acute tubular interstitial nephritis: a poorly recognized pattern of renal disease in patients with plasma cell dyscrasia. Arch Pathol Lab Med. 130:165-9.
10. Rastegar A, Kashgarian M (1998). The clinical spectrum of tubulointerstitial nephritis. Kidney Int. 54:313-27.
11. Venkataseshan, V. S., Faraggiana, T., Hughson, M. D., Buchwald, D., Olesnicky, L., & Goldstein, M. H. (1988). Morphologic variants of light-chain deposition disease in the kidney. *American journal of nephrology*, *8*(4), 272-279.
12. Takahashi, S., Soma, J., Nakaya, I., Yahata, M., Sakuma, T., Yaegashi, H., ... & Sato, H. (2012). Systemic and rapidly progressive light-chain deposition disease initially presenting as tubulointerstitial nephritis. *CEN case reports*, *1*(2), 117-122.