CLINICAL VIGNETTE

Multiple Myeloma Presenting with Sub-acute Kidney Injury and No Proteinuria

Ramya Malchira, MD and Michael Shye, MD

Case Presentation

A 75-year-old female with a history of rheumatoid arthritis, essential hypertension and hyperlipidemia was referred for evaluation of elevated serum creatinine. Upon initial evaluation, the patient was on methotrexate for rheumatoid arthritis, ibuprofen for arthritis, and daily losartan 50 mg for hypertension. Her serum creatinine on presentation was 1.5 mg/dL within patient's baseline serum creatinine of 0.91 mg/dL.

The Ibuprofen was stopped and she was tapered off the methotrexate. However her serum creatinine continued to increase over the next six months and peaked at 2.7 mg/dL. Her initial urinalysis revealed no protein, no microscopic hematuria or pyuria. The initial serum calcium level was borderline elevated at 10.5 mg/dL and on repeat was normal at 9.8 mg/dL. Infectious serologies including hepatitis B and C was negative. Autoimmune labs including negative ANA, double-stranded DNA, and ANCA. Rheumatoid factor was elevated at 21. Serum Immunofixation showed poorly defined area of increased kappa reactivity which may represent a monoclonal protein. Urine immunofixation showed a monoclonal free lambda light chain consistent with light chain disease. During this time her spot urine protein creatinine ratio was 0.09 grams and urine albumin to creatinine ratio was less than 30 mg.

Renal ultrasound showed right kidney was 9.7 cm and left kidney 10.2 cm with cortical thickness 13 mm and mild kidney echogenicity with multiple bilateral cysts. Kidney biopsy showed kappa light chain deposition disease. Acute tubular injury with interstitial inflammation, arterial and arteriolar nephrosclerosis was also noted. The initial kappa and lambda free light chain ratio was 70.7. (Normal 0.26 to 1.65).

The patient was evaluated by hematology oncology and had a bone survey which showed a tiny non-specific lucent focus involving the calvarium. No other lytic lesions were identified within the axial and appendicular skeleton. Bone marrow biopsy showed kappa restricted plasma cell dyscrasia about 10% of marrow cellularity, Congo red staining was negative in vessels providing no support for vascular amyloidosis. Her diagnosis was consistent with stage I multiple myeloma and she was initiated on treatment due to her underlying nephropathy. Patient was initially started on Dexamethasone and Bortezomib. She responded well, however, developed paresthesia and numbness and was changed to Lenalidomide. The patient showed significant improvement with her kidney function. The serum creatinine peaked at 2.7 and following treatment her creatinine stabilized at 2.0 to 2.1. During the whole course of patient's diagnosis and treatment she did not have any proteinuria. After a month of chemotherapy the patient's kappa and lambda free chains decreased to 7.09 and is stable at 1.5.

Discussion

Multiple myeloma (MM) is a malignant plasma cell disorder that accounts for approximately 10% of all hematologic malignancies. It is defined by the presence of a serum monoclonal spike (M-spike) of more than 3 g/dL or more than 10% clonal plasma cells in the bone marrow and at least one of the myeloma defining events such as CRAB (hyperCalcemia, Renal impairment, Anemia and Bone lesions). Patients meeting the M-spike or bone marrow plasma cell requirement but not having CRAB defining events are classified as having smoldering multiple myeloma.[1]

The kidney is a major target organ in myeloma. Up to 40 percent of patients will develop kidney impairment and 10 to 15 percent will require dialysis. The incidence is highest in patients with advanced stage disease. Kidney impairment has a significant effect on the overall survival (OS) of these patients. A study from Spain found that patients with acute kidney injury (AKI) had a median OS of 8.6 months whereas patients who never developed AKI had a median OS of 34.5 months ($P < 0.001$). Of note is the poor prognosis was reversible if kidney function was restored.[1] Median OS increased to 28.3 months in patients who recovered their kidney function vs 3.8 months in those who had irreversible kidney failure.

Kidney disease in myeloma can present as myeloma cast nephropathy, amyloidosis, monoclonal immunoglobulin deposition disease, acute tubular necrosis, myeloma infiltration, and light chain Fanconi Syndrome. Monoclonal Immunoglobulin deposition disease (MIDD) represents a group of kidney diseases that includes light-chain deposition disease (LCDD), light heavy-chain deposition disease (LHCDD), and heavy chain deposition disease (HCDD).[2]

The most common MIDD is LCDD. It is characterized by amorphous to granular deposition of monoclonal immunoglobulin or its components. In autopsy studies of patients with MM, MIDD is seen in 5% of MM patients. The median age of presentation ranges from 51 to 57 years. Roughly two thirds of the patients are male. Proteinuria is present in almost all patients.[2,3]. The

median proteinuria is 2.7 to 4.1 g/day with approximately 40% of patients with nephrotic-range proteinuria. Patients with HCDD appear to have a higher degree of proteinuria. Microscopic hematuria is common (62%), but gross hematuria is rare (3%). Kidney insufficiency is also nearly universal, with an average serum creatinine of 3.8 mg/dL. Our patient had no proteinuria or microscopic hematuria.

In patients who have multiple myeloma or CLL with MIDD, the treatment should be based on the standard treatment for each disease. In patients with MGRS or monoclonal gammopathy of renal significance (≤10% bone marrow plasma cells), treatment with cytotoxic therapy is still necessary because MIDD will result in ESRD. In one study, the patient survival at 5 years was 71% whereas kidney survival was only 40%. The authors believed that inadequate treatment of the MGRS was the reason for the high rate of ESRD (end stage renal disease).[1] However, because these patients do not have a malignant condition, minimizing chemotherapy-related toxicity is as important as efficacy. Bortezomib-based therapies have been used in the treatment of patients with LCDD.[4,5] Our patient did develop significant adverse effects with Bortezomib based therapy and was eventually switched to Lenalidomide.

Conclusion

It is important to recognize that patients with multiple myeloma can present with progressively worsening kidney function and need not have any proteinuria. Early diagnosis and appropriate treatment is important for preserving renal function and delays time to development of end stage renal disease.

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