CLINICAL VIGNETTE

Acute Renal Failure, Anemia, and Back Pain: Not to be Taken Lightly

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Introduction

Multiple myeloma (MM) has a wide array of clinical presentations. The classic presentation includes symptomatic hypercalcemia, renal insufficiency, anemia, or lytic bone lesions. "CRAB" symptoms are often caused by plasma cell and protein infiltration. We present a patient who presented with vertebral compression fractures and acute renal failure (ARF) initially thought to be NSAID-induced, who was ultimately diagnosed with light chain multiple myeloma.

Case

A 52-year-old Caucasian man with history of chronic low back pain and alcohol abuse presented to the hospital with one week of fatigue, nausea, and non-bilious non-bloody emesis. Two months prior, he had been seen with low back pain and x-rays showed chronic healing thoracic vertebral compression fractures. Over the last month, he was taking 1600 mg – 2400 mg of ibuprofen per day for the pain and was not taking any other medications or supplements.

On presentation, vitals and physical exam were normal. Laboratory values were significant for creatinine of 6.73 mg/dL (from baseline of 1.0 five months prior), BUN 34, hemoglobin 9.9 g/dL (from 13.6 two months prior), MCV 99, and a mildly depressed folate level. Total protein (6.9 g/dL), protein gap (2.5), calcium (9.9 mg/dL), and ANCA were all unremarkable. Urinalysis significant for 2+ protein and urine/protein creatinine ratio x2 was 0.9 and 2.4. Urine eosinophils were negative. Renal ultrasound showed normal kidneys with normal echogenicity. Given the history and acuity, it was felt that his ARF was most likely NSAID-induced and that his macrocytic anemia was from folate deficiency and possible EtOH abuse. There was no acute indication for hemodialysis (HD), so he was managed conservatively over the next few days with NSAID avoidance. His creatinine subsequently improved on average of 0.5 mg/dL per day.

However, the creatinine did not improve as quickly as expected, prompting a percutaneous kidney biopsy. The biopsy pathology showed acute tubular necrosis (ATN) with light chain casts suspicious for MM. Subsequent SPEP showed a small monoclonal gamma protein band of 0.1 g/dL, serum free light chain (FLC) level elevated at 1,250 mg/dL kappa FLC (ref < 1.94), and a kappa/lambda ratio of 4,808. 24-hour UPEP notable for 32.4% monoclonal protein and 130 mg/dL urine kappa FLCs. Bone marrow biopsy, found 50% focal clonal plasma cells, and he was diagnosed with light chain MM.

Skeletal survey was negative for any osteolytic lesions, and re-demonstrate healing T8 and T10 chronic wedge compression fractures and signs of osteopenia. Immediate treatment was advised to avoid further kidney damage and need for renal replacement therapy, however, for personal reasons, the patient flew to Germany to pursue further treatment. Creatinine on discharge was 3.5 mg/dL.

Discussion

The 2014 International Myeloma Working Group (IMWG) established diagnostic criteria for MM. Greater than 10% bone marrow clonal plasma cells with one of the following: a myeloma defining event (evidence of end organ damage due to plasma cells - anemia, hypercalcemia, renal insufficiency or lytic bone lesions) or a biomarker of malignancy (FLC ratio > 100, > 60% clonal plasma cells in bone marrow, or MRI with focal bone lesion).[1]

Classically, MM is diagnosed with an SPEP showing an isolated band. However, approximately 20% of MM is diagnosed with only free light chains in the serum or urine ("light chain myeloma").[2] These patients typically do not present with elevated protein or protein gap as the clonal plasma cells are only secreting light chains and not heavy chains. In addition, SPEP/UPEP screening has poor sensitivity for free light chains and may not be markedly abnormal. Therefore, it is necessary to also obtain serum and urine FLC.[3] The combination of all three (SPEP/UPEP, IFE, and serum/urine FLC) increase sensitivity to 97%. Since the kidneys clear FLCs, presence of renal injury could potentially affect overall clearance and the measured ratio, leading to decreased specificity.[4]

Twenty to Fifty percent of patients with MM will develop renal injury at some point during their disease, with multiple possible mechanisms. Light chain cast nephropathy and hypercalcemia are the majority.[4] Incidence of renal failure is significantly higher in light chain predominant myeloma as FLCs are fully secreted by the kidneys and often build up in the renal tubules. Approximately 30% of patients with light chain myeloma present with creatinine > 2 mg/dL [2] and if left untreated, most

will progress to kidney failure. With treatment, up to 50% of patients with light chain myeloma can have reversal of kidney failure, but up to 50% of patients with severe renal failure at diagnosis will progress and require renal replacement therapy despite therapy.[4,5] The most significant difference between those who recovered and those who did not was the degree of myeloma cast burden, as determined by histology, as well as having myeloma responsive to chemotherapy.[4] Thus, early recognition of MM and associated renal disease is important for improved outcomes for patients.

Our patient was also found to have osteoporotic compression fractures without any evidence of osteolytic disease or hypercalcemia. Seventy to Ninety percent of patients with MM have bone lesions, which are classically osteolytic.[6] However, 20% can also present with only osteoporosis, pathologic fractures, or compression fractures.[2] The IMWG had previously set the gold standard for evaluation of MM bone disease as whole-body x-ray (WBXR).[7] However, it has since been recognized that WBXR is not sensitive enough to detect all focal or osteolytic lesions or osteoporosis. MRI is more sensitive, detecting lesions in 74% imaged sites, versus WBXR at 56%.[7] Because of MRI ability to distinguish early bone marrow infiltration by myeloma cells prior to creating bone loss, 52% of patients who had a normal WBXR had focal lesions on MRI.[7] Thus, the IMWG developed a new consensus statement in 2014 establishing MRI as the new gold standard for the evaluation of painful lesions, including focal lesions as part of the diagnostic criteria.[7]

This case highlighted the importance of recognizing multiple myeloma as a potential etiology for acute renal failure or osteoporosis in a young male, and to fully evaluate if needed with renal biopsy and MRI.

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