Early stage IgD multiple myeloma in a 50-year-old man

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ABSTRACT

We present the case of a 50-year-old Hispanic man who presented to the emergency department with an acute right femur fracture after 3 months of intermittent discomfort in the right leg. He was eventually diagnosed with immunoglobulin D (IgD) multiple myeloma, a rare class of myeloma that is often of advanced stage at diagnosis. Fortunately, our patient was stage I at diagnosis and did not have hypercalcemia, anemia, or renal insufficiency, as is common with myeloma. This report describes a rare case of an uncommon condition and highlights the fortunate aspects of this patient's unfortunate diagnosis.

KEYWORDS IgD; M-spike; multiple myeloma; pathologic fracture

Multiple myeloma is a neoplastic disorder characterized by the clonal proliferation of malignant plasma cells. IgD myeloma is rare, accounting for about 2% of multiple myeloma cases worldwide.¹ It is often associated with advanced disease at diagnosis. Patients will often have the trappings of multiple myeloma, which include hypercalcemia, renal insufficiency, anemia, and lytic bone lesions, known as “CRAB” symptoms. We report a case of IgD myeloma that, fortunately for the patient and contrary to the norm, was diagnosed at an early stage.

CASE REPORT

A 50-year-old Hispanic man with a history of hypertension and prediabetes presented to the emergency department with acute right thigh pain. The pain initially began 3 months prior when he stepped in a hole while working. While walking in to work the morning of presentation, he heard a “crack” and experienced a sharp pain in his right proximalateral thigh and had to brace himself to stay upright. He denied other areas of bony tenderness.

The patient had no family history of malignancy or blood disorders. His social history was unremarkable. He was employed as a cafeteria manager. Home medications included lisinopril and recent prescriptions for cyclobenzaprine and ibuprofen. Physical exam revealed an obese

middle-aged man lying in bed with a traction splint applied to his right lower extremity. Laboratory studies showed a hemoglobin of 13.6 g/dL, serum creatinine of 0.9 mg/dL, and calcium of 9.2 mg/dL. Blood glucose was mildly elevated, but other laboratory tests, including a complete blood count and comprehensive metabolic panel, revealed values within normal limits. Plain films revealed an acute minimally comminuted fracture of the proximal right femur diaphysis (*Figure 1*). Computed tomography scan of the right lower extremity showed irregularity of the margins and small adjacent osseous fragments consistent with a pathologic fracture. A focal soft tissue mass was identified within the marrow cavity.

The orthopedic service took the patient for open reduction and internal fixation with biopsy the following day. Confusingly, intraoperative frozen section revealed only acute and chronic inflammation without evidence of malignancy. Subsequent laboratory studies showed a beta-2 microglobulin of 1.35 mg/L, albumin of 3.7 g/dL, and lactate dehydrogenase of 176 U/L. Peripheral blood flow cytometry eventually revealed a monoclonal plasma cell population making up 1% of cells analyzed. Serum and urine protein electrophoreses revealed M-spikes of 0.4 g/dL and 8.8 mg/dL, respectively. Serum immunofixation revealed a monoclonal IgD population. The lambda and kappa free light chain levels were 543.43 mg/L and 7.95 mg/L, respectively. Bone marrow biopsy was performed and revealed plasma cell dyscrasia with 20% to 25% lambda-clonal plasma cells (*Figure 2*).

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Figure 1. Radiograph of the right femur showing an acute, oblique, minimally comminuted fracture of the proximal right femur diaphysis.

Fluorescence in situ hybridization was positive for immunoglobulin heavy chain gene rearrangement and monosomy 13. Ultimately, the right femur biopsy revealed a lambda-restricted plasma cell neoplasm.

The patient established outpatient care with the hematology service after discharge and was started on a regimen of lenalidomide, bortezomib, and dexamethasone. After four cycles, he had evidence of a very good partial response with residual disease only detectable by a positive urine immunofixation. M-protein levels were undetectable on electrophoresis, and bone marrow biopsy showed no evidence of residual myeloma. He underwent autologous hematopoietic stem cell transplant and was subsequently started on lenalidomide maintenance, which he will continue for a planned 2 years. At the time of submission of this article, the patient

Figure 2. Bone marrow aspirate smear.

was doing well overall and had no clear evidence of disease progression.

DISCUSSION

Immunoglobulin D multiple myeloma is rare, with an incidence of about 2% of all patients diagnosed with myeloma. Before Bladé et al² described 53 patients with IgD myeloma in 1994, only seven series reported five or more patients with this particular class. Classically it was thought to be associated with a poorer prognosis compared to other myelomas; however, with the use of modern therapies, outcomes have been shown to be similar to other myeloma classes.¹⁻³ IgD myeloma tends to present at a younger age, favor male gender, be of more advanced stage, and have more features of high-risk disease vs others.^{3,4} Unlike other myelomas, lambda light chain predominance is a characteristic feature of IgD myeloma and is seen in 70% to 90% of cases.^{4,5} Furthermore, IgD myeloma has been shown to present with higher rates of renal failure and Bence Jones proteinuria compared to other myelomas.³ Because the serum concentration of physiologic IgD is present at a much lower concentration (0–10 mg/dL) compared to IgG (1020–1460 mg/dL) and IgA (210–350 mg/dL), the M-spike on electrophoresis is often very small or even unrecognizable in IgD myeloma.^{4,5}

In the current era, patients diagnosed with myeloma are staged based on the revised International Staging System, developed by Palumbo et al⁶ and the International Myeloma Working Group in 2015. Stage I disease (14.3% of cases) includes patients with a beta-2 microglobulin of <3.5 mg/L, albumin of ≥ 3.5 g/dL, lactate dehydrogenase within normal limits, and absence of high-risk chromosomal abnormalities by fluorescence in situ hybridization: del(17p), t(4;14), or t(14;16). Stage III disease (61.2% of cases) includes those with beta-2 microglobulin ≥ 5.5 mg/L and elevated lactate dehydrogenase or the presence of one of the aforementioned chromosomal abnormalities. Patients not meeting criteria for either of the other stages are classified as stage II (24.5% of cases).⁴ The group found median overall survival

and progression-free survival for revised International Staging System stages I to III of [not reached] and 66 months, 83 and 42 months, and 43 and 29 months, respectively.

Our case is unusual due to the patient's early disease at presentation, a beneficial status uncommon in IgD myeloma. The patient was stage I at presentation, with a normal beta-2 microglobulin, albumin, and lactate dehydrogenase and no high-risk chromosomal abnormalities. Monosomy 13 was identified on bone marrow biopsy in 72% of the cells examined and, while not used in the staging or stratification of myeloma patients, does confer a worse prognosis.⁷ These findings, coupled with a lactate dehydrogenase within normal limits and no features of primary plasma cell leukemia, place our patient in the "standard risk" category. The "high risk" category includes patients with any of the high-risk chromosomal abnormalities previously mentioned along with the addition of t(14;20) and gain of 1q, those with a lactate dehydrogenase >2 times the upper limit of normal, and those with features of primary plasma cell leukemia. Initial treatment differs for the two risk categories.

While a pathologic fracture is never a pleasant experience, the presence of our patient's bone lesion leading to this fracture allowed him to be diagnosed at an early stage of disease. Given this, despite being diagnosed with the generally less favorable IgD class, his prognosis is better than had he

presented with the typical CRAB symptoms that are hallmarks of multiple myeloma.

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