Multiple Myeloma with Plasmacytomas Restricts Ambulation

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Background

Multiple myeloma (MM) is the abnormal proliferation of plasma cells that produce monoclonal immunoglobulin. Proliferation occurring in the bone marrow leads to osteolytic lesions, osteopenia, fractures. It is usually seen in men (1.4:1 ratio), of African American, with median age of diagnosis of 65.
Clinical presentation consists of the popular "CRAB" mnemonic:

- hyperCalcemia (bone demineralization)
- Renal insufficiency (light chain nephropathy, amyloidosis, drug-induced),
- Anemia (normocytic, normochromic; erythropoietin deficiency, dilution due to large IgM, bone marrow replacement)
- Bone disease and pain involving the central skeleton (pathologic/compression fractures, osteolytic lesions)

But can also include neurologic disease, such as spinal cord compression, hyperviscosity, radiculopathy, peripheral neuropathy; and infection due to immune dysfunction from impaired lymphocyte function, suppression of normal plasma cell function, hypogammaglobulinemia.
Plasmacytoma may occur as a single, solitary lesion, or concurrently with MM.

Case Presentation

This is a 59 year old male with a past medical history of meningioma status post (s/p) right-side brain resection (in 2006), tubular adenoma of the colon (2018), seizures (on Keppra and oxcarbazepine) who presented to the Emergency Department (ED) for low back pain for the last 2 months. Specifically right lower back. Described as 10 out of 10 pain, constant, and sharp. Associated with radiation down the right lower extremity. Had multiple ED visits in the last month, where he was diagnosed with sciatica/musculoskeletal back pain. He was prescribed Flexeril and lidocaine patches, without improvement of symptoms. Also tried tylenol and ibuprofen, without pain relief. At time of presentation, patient was barely able to ambulate. Denied any saddle anesthesia, bowel or bladder incontinence, recent trauma or fall, lifting heavy objects. Pertinent physical exam findings included tenderness to palpation of the lumbar spine, with range of motion limited by pain. Labs were significant for elevated blood urea nitrogen (BUN) 25, creatinine (Cr) 1.5, calcium (Ca) 12, total serum protein 9.6, hemoglobin (Hgb) 9.1.

Case Presentation Continued

Magnetic resonance imaging (MRI) of the lumbar spine was completed, showing numerous foci of marrow edema in the spine and pelvis, suspicious for diffuse osseous metastases; large L5 metastatic focus causing mass effect on the exiting L5 nerve; compression fractures of L5 and L1.
Given the MRI findings, Hematology/Oncology and Neurosurgery were consulted. Patient started on intravenous (IV) dexamethasone. Pain management consulted.
On day two of admission, computed tomography (CT) scans of the chest/abdomen/pelvis/lumbar confirmed numerous multifocal lucent foci suspicious of metastatic disease or myeloma; multiple compression fractures at T6, L1, L2, L5. MRI of the cervical/thoracic/lumbar spine with numerous marrow edema/enhancement. Bone marrow biopsy was completed.
Further workup revealed:

- Serum electrophoresis with immunofixation (SPEP), Urine electrophoresis with immunofixation (UPEP):
  - **Total protein = 8.8 (elevated)**
  - Albumin = 4.4
  - Alpha-1 = 4.4
  - Alpha-2 = 0.8
  - Beta-1 = 0.4
  - Beta-2 = 0.30
  - **Gamma = 2.8 (elevated)**
  - **Paraprotein = 2.6 (elevated**
  - **IgG quant: 3,880 (elevated)**
  - IgA quant: <33
  - IgM quant: <21
- Beta-2 microglobulin: **4.2 (elevated)**
- Serum free light chains (FLC)
  - Kappa FLC 0.73, Lambda FLC 0.35 (decreased)
  - **Kappa/lambda FLC ratio 2.09 (abnormal)**
- Lactate dehydrogenase (LDH): 180
- Prostate-specific antigen (PSA): 1.34

Bone biopsy resulted with atypical malignant plasma cell proliferation consistent with plasma cell dyscrasia; positive CD138 and CD 56.

The diagnosis of IgG kappa multiple myeloma with plasmacytomas was made.

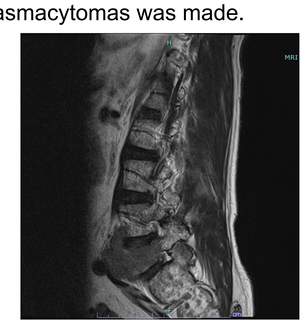

Figure 1: MRI T2 weighted imaging of lumbar spine with lesion at L5 has extraosseous extension into left prevertebral space measuring up to 5.6 cm and likely causing mass effect on L5

Discussion

Multiple myeloma is an abnormal proliferation of plasma cells producing monoclonal immunoglobulins. Because this proliferation occurs in the bone marrow, it results in osteolytic lesions, osteopenia, and pathologic fractures. MM predominantly occurs in males, those of African American descent, with median age of diagnosis at 65.
The patient can present with "CRAB," as previously discussed, although not limited to. Other symptoms include neurologic disease: spinal cord compression (from extramedullary plasmacytoma), radiculopathy, peripheral neuropathy; and even infection due to immune dysfunction from impaired lymphocyte function and suppression of normal plasma cell function.
This patient presented with radiculopathy and nerve compression due to the plasmacytoma, with imaging and lab findings resulting in high suspicion for plasma cell dyscrasias. Unclear if MM had developed primarily with later formation of plasmacytoma. Only a small percentage of patients develop plasmacytomas during the course of MM.

Workup includes SPEP and UPEP with immunofixation to determine presence of M protein ("M spike"), indicating underlying clonal plasma call or lymphoproliferative disorder (gamma, beta, alpha proteins), and bone marrow (or soft tissue, plasmacytoma) biopsy. Subtype distribution can be categorized by specific immunoglobulin subtype (IgG, IgA, IgM most commonly) and serum FLC. Additionally, serum FLC of kappa and lamba ratio, normal being 0.25-1.65, aid in diagnosis and monitoring of MM, as well as other non-secretory or oligosecretory myeloma, amyloidosis types.
Other workup includes peripheral smear (reveals rouleaujx formation, leukopenia, thrombocytopenia), urinalysis (revealing etiology of damage, proteinuria).

The diagnostic criteria for MM is biopsy with plasma cells ≥10% and either CRAB or biomarker with near progression to end organ damage (>60% clonal plasma cells in bone marrow, involved/uninvolved FLC ratio of 100 or more, MRI with >1 focal lesion (bone or bone marrow).

The differential for lymphoproliferative disorders include light chain myeloma (only FLC present with normal/decreased total serum protein), oligo-secretory myeloma (FLC abnormal with decreased serum and urine M protein), nonsecretory myeloma (normal SPEP/UPEP/FLC, M protein present in neoplastic plasma cells), monoclonal gammopathy of undetermined significance, smoldering MM, solitary plasmacytoma, metastatic carcinoma, reactive plasmacytosis.

Discussion continued

Staging for MM is based on the Revised International Staging System (R-ISS), consists of stages I to III, which uses serum Beta-2 microglobulin (B2M), LDH, and bone marrow fluorescence in situ hybridization (FISH) results.

Stage I	Stage II	Stage III
Includes all of the following: B2M < 3.5 mg/l Albumin ≥ 3.5g/100/ml Normal LDH By FISH: No del(17p), t(4;14), or t(14;16)	Does not fit stage I nor stage III	B2M ≥ 5.5 mg/l and elevated LDH And/or by FISH del(17p), t(4;14), or t(14;16)

There is increased risk in mortality based on multiple characteristics, including abnormal karytopes (example: deletion of chromosome 13, monosomy), presence of genetics via FISH (listed above), high plasma cell labeling index.
Response to treatment and progression of MM is monitored by repeated SPEP, UPEP, FLC ratios, bone marrow plasma cell percentage, "CRAB."

Conclusion

The patient was diagnosed with IgG kappa myeloma with plasmacytoma given the findings of the bone biopsy, SPEP/UPEP. The patient first started radiotherapy to the L5 lesion with the goal to decrease the size, improve pain and ambulation. Eventually, started on chemotherapy regimen VRd (bortezomib, lenalidomide, low dose dexamethasone), with the ultimate goal to undergo hematopoietic cell transplant (HCT).

Acknowledgements

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