An Unusual Presentation of Smoldering Multiple Myeloma in a patient with End Stage Renal Disease

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Clinical History
A 53-year old male presented at a benign hematology clinic with a chief complaint of persistent macrocytic anemia with mild thrombocytopenia of unclear etiology. The patient has an extensive medical history including end stage renal disease (ESRD) on hemodialysis and recurrent gastrointestinal bleed. Patient’s ESRD is secondary to focal glomerular sclerosis post kidney transplant in 1993 that was rejected in recent years. Two colonoscopies and an esophagogastroduodenoscopy have failed to produce a source of bleeding that would explain the prolonged anemia. Patient denies prolonged weakness or progressive fatigue. No melena, hematemesis, epistaxis, hematuria, bleeding from fistula site or prolonged weakness or progressive fatigue. No melena, hematemesis, epistaxis, hematuria, bleeding from fistula site or

Laboratory results
Baseline laboratory results were consistent with reported patient history (inset 1), and TSH, folate and B12 results are listed out in Table 1. Further, Iron studies showed that the cause of the anemia was chronic disease. Bone marrow results came back two weeks after base line labs were collected with a reported diagnosis of Plasma Cell leukemia (inset 2). At follow up appointment, further labs and radiology studies were ordered to make a differential diagnosis between multiple myeloma, plasma cell leukemia, and smoldering multiple myeloma. Immunoglobulin studies showed an increase in IgA, IgG and Betazeta-Microglobulin. Protein electrophoresis results indicated a monoclonal gammopathy. Protein IFE revealed two monoclonal bands present (Figure 1). Flow cytometry showed kappa-skewed plasma cells, which are CD20(++) and CD38(++) (Figure 2). Flow cytometry showed kappa-skewed plasma cells, which are CD20(++) and CD38(++) (Figure 2). Flow cytometry showed kappa-skewed plasma cells, which are CD20(++) and CD38(++) (Figure 2).

Results

- CBC Results
  - WBC: 8.7 x 10^3/uL
  - RBC: 3.9 x 10^6/uL (L)
  - HGB: 8.7 g/dl (L)
  - HCT: 29% (L)
  - MCV: 100 fl
  - MCHC: 30 g/dl (L)
  - PLT: 178 x 10^9/uL (L)
  - MPV: 10.9 fl

- Chemistry Results
  - BUN: 37 mg/dl (H)
  - Creatine: 6.0 mg/dl (H)
  - Total Protein: 8.3 g/dl (H)
  - Ferritin: 135 ng/mL
  - Folate: >20.0 ng/mL
  - TSH: 2.04 uIU/mL
  - Vitamin B12: 818 ng/mL
  - Iron Panel Results
    - Iron: 31 ug/dL
    - Total Iron Binding Capacity: 195 mg/dl
    - Unremarkable differential
      - Reticulocyte: 1.7% 

- Immunoglobulin studies showed an increase in IgA, IgG and Beta2 microglobulin.

- Bone marrow biopsy
  - Aspirate
    - Malignant plasma cells are noted
  - Biopsy
    - Malignant plasma cells are noted

- Flow cytometry was used to identify the monoclonal plasma cell population.

- Immunohistochemistry
  - CD138 immunohistochemistry demonstrates approximately 25-30% of core biopsy cellularity by CD38

- Bone marrow biopsy
  - Aspirate smear demonstrates increased plasma cells with moderately dispersed chromatin. B, Core biopsy shows increased plasma cells with dispersed chromatin and distinct nuclei. C, CD138 immunohistochemistry demonstrates approximately 25-30% plasma cells.

- Densitometric Tracing
  - There is a single, large hyperdense area in the left atrium with typical asymmetric trabeculation and mild left atrial enlargement.

- Isofluran

- FISH Studies for MDS and Lymphoma

- Aspirate differential

- Figure 1. Bone marrow biopsy. A, Aspirate smear demonstrates increased plasma cells with moderately dispersed chromatin. B, Core biopsy shows increased plasma cells with dispersed chromatin and distinct nuclei. C, CD138 immunohistochemistry demonstrates approximately 25-30% plasma cells.

- Figure 2. Serum electrophoresis. There is a single, large (2.83 g/dL) M-protein peak (red arrow head on densitometric tracing (Panel B)). The M-protein was identified by immunofixation electrophoresis (IFE) (Panel B) as IgG kappa and bicalon IgA.

- Figure 3. Flow cytometric diagrams of case (A-C) Illustrating the antigen expression on plasma cells. The plasma cell population represented a 26% of events. A-B, Blue arrow demonstrates a subset of CD56(+) and CD38(+) plasma cells. C, Kappa-skewed plasma cells (overall Ic kappa: Ic lambda = 5:7). Plasma cells, red, and polyclonal plasma cells, blue.

Discussion

Plasma cell myeloma, a disease of older people, is rare in people under the age of 40. The diagnosis of myeloma requires 10% or more monoclonal plasma cells in the bone marrow or a biopsy-proven plasmacytoma. However, patients who meet the criteria may be asymptomatic and stable for years; these patients are considered to have smoldering (asymptomatic or indolent) myeloma (SMM). The diagnosis of symptomatic myeloma, requires the presence of one or more myeloma-defining events (MDEs), such as CRAB features (hypercalcemia, renal dysfunction, anemia, and bone lesions, [1,2]). In our patient, while end-organ damage was present, they could not rule this into their diagnosis because another cause for the organ failure was already present. And since no bone lesions were present, they did not meet the CRAB criteria for diagnosis MM ([1,2]. There isn’t any current research that suggests that treatment during SMM would clinically improve outcomes for patients unless they are at high risk for disease progression ([2]. Treatment normally follows once they progress to full MM.

Patient Outcome

Radiologic findings for the patient were negative for any pathologic lesions. Based on bone marrow, paraa protein studies and radiologic findings, the patient was diagnostic with Smoldering Multiple Myeloma and referred to the malignant hematology-myeloma team on the same campus. Patient was seen by myeloma team in November 2016, who confirmed diagnosis. Due to co-morbidities, monitoring until progression occurs.

References

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