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

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Clinical History

A 59-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 bleeds. Patient's ESRD is secondary to focal glomerular sclerosis post kidney transplant in 1993 that was rejected in recent years. Two colonoscopies and an esophagogastroduodenscopy 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 other recent abnormal bleeding. No petechiae or bruising observed. No reported fevers, night sweats, recurrent infections, lymphadenopathy or unintentional weight loss. Degree of anemia observed is disproportionate to clinical documentation of bleeding. Baseline hemoglobin (hgb) levels over the past two years range from 5-10 g/dL. Recent platelet counts have dropped to ranges of 100,000-189,000/uL. Epogen administration three times weekly at dialysis and IV Iron do not have any impact on hgb results. Benign hematology requested base line labs, as well as iron studies, thyroid stimulating hormone (TSH), folate and B12. A bone marrow biopsy procedure was also requested to rule out hematologic malignancy or other bone marrow disorder.

Laboratory results

Baseline laboratory results were consistent with reported patient history (**inset 1**), and TSH, folate and B12 results ruled out a deficiency as a cause of the anemia (**inset 1**). Further, Iron Studies showed that the cause of anemia was chronic disease. Bone marrow results came back two week after base line labs were collected with a reported diagnosis of Plasma Cell Myeloma (**inset 2, Figure 1**). 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 Beta2-Microglobulin. Protein electrophoresis results indicated a monoclonal gammopathy. Protein IFE revealed two monoclonal bands present (**Figure 2**). Flow cytometry showed kappa-skewed plasma cells, which are CD200(subset+) and CD56(subset+) (**Figure 3**).

Results

▸ **Inset 1:** Laboratory Testing Results

- **CBC Results**

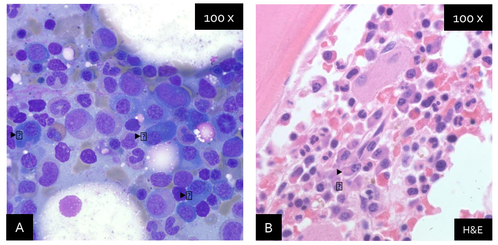
WBC: 6.7 x 10e3/uL
RBC: 2.9 x 10e3/uL **(L)**
HGB: 8.7 g/dL **(L)**
HCT: 29% **(L)**
MCV: 102 fL
MCHC: 30 g/dl **(L)**
PLT: 138 x 10e3/uL **(L)**
MPV: 10.9 fL
Unremarkable differential
Reticulocyte: 1.7%

- **Chemistry Results**

BUN: 37 mg/dL **(H)**
Creatine: 6.02 mg/dL **(H)**
Total Protein: 8.3 g/dL **(H)**
Ferritin: 133.3 ng/mL
Folate: >20.0 ng/mL
TSH: 2.040 uIU/mL
Vitamin B12: 818 pg/mL
Iron Panel Results:
Iron: 31 ug/dL **(L)**
TIBC: 296 ug/dL
% Iron Saturation: 10% **(L)**
UIBC: 265 ug/dL

▸ **Inset 2:** Bone Marrow Biopsy Testing Results

- **FISH Studies for MDS and Lymphoma/Burkitts, MM**: All studies normal
- **Flow Cytometry**: **0.20%** population of plasma cells, 80% are CD19(-), subset positivity for CD56 and CD200 (overall intracellular Kappa:Lambda = 5.7), 74% granulocytes, 8.4% monocytes, 3.5% erythroid elements, 0.38% immunophenotypically unremarkable myeloid blasts, 2.3% T cells, 0.60% NK cells. 0.19% mature B cells (Kappa:Lambda = 1.0), and 0.37% maturing B cell precursors.
- **Interpretation of Aspirate, touch imprint, Core Biopsy, Clot section**: Plasma Cell Myeloma. Core Biopsy is 50% cellular. Plasma cells comprise approximately 15-20% of core biopsy cellularity by CD138 immunohistochemistry.
- **Aspirate Differential**: Demonstrates 10% plasma cells.



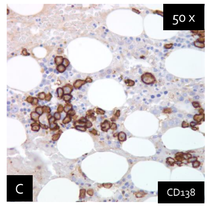


Figure 1. Bone marrow biopsy. A, Aspirate smear demonstrates increased plasma cells with moderately dispersed chromatin. **B, Core biopsy** shows increased plasma cells with dispersed chromatin and distinct nucleoli. **C, CD138 immunohistochemistry** demonstrates approximately 15-20% plasma cells.

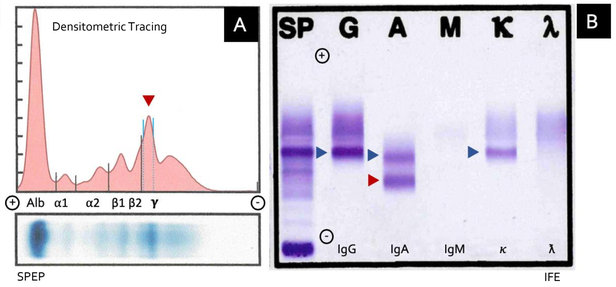


Figure 2. Serum electrophoresis. There is a single, large (2.83 g/dL) M-protein peak (red arrow head on densitometric tracing (**Panel A**)). The M-protein was identified by immunofixation electrophoresis (IFE) (**Panel B**) as IgG Kappa and biclonal IgA.

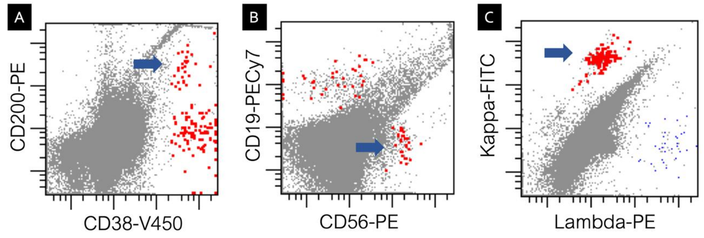


Figure 3. Flow cytometric diagrams of case (**A-C**) illustrating the antigens expression on plasma cells. The plasma cell population represented 0.20% of events. **A-B,** Blue arrow demonstrates a subset of CD56(+) and CD200(+) plasma cells. **C,** Kappa-skewed plasma cells (overall ic kappa : ic lambda = 5.7). Plasma cells, *red; and polytypic 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 (hyper**c**alcemia, renal dysfunction, **a**nemia, and **b**one 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 (1). 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, paraprotein 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 2018, who confirmed diagnosis. Due to co-morbidities, monitoring until progression occurs.

References

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