Unclassified Myelodysplastic/Myeloproliferative Neoplasm: A Case Report

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Introduction

An incidental finding of an elevated WBC count , ranging from 13 to 100 K/μL in an asymptomatic patient prompts workup for a number of clinical disorders. Apart from infection and leukemoid reaction, Chronic Myeloid Leukemia (CML) is often suspected. Of all adult leukemias, CML constitutes 15-20%. However, a number of other disorders may present in a similar manner, including Juvenile Myelomonocytic Leukemia (JMML), Chronic Myelomonocytic Leukemia (CMML), "Atypical CML" (aCML,) and Unclassified MDS/MPN. This patient illustrates the challenges in diagnosing and differentiating between these various disorders and to highlight a rare case of MDS/MPN-U.

Case Presentation

Our patient is a 76 yo Male Veteran with PMH of Hypertension who presented to the Emergency Department in June 2019 for poorly-controlled blood pressure. Admission labs showed an incidental finding of abnormal leukocytosis, with a WBC count of 53.4, concerning for CML. A baseline CBC one year prior showed a normal WBC count of 8.6. The patient denied fevers/chills, fatigue or malaise, and recent weight loss. He denied any recent illness, and 12-point review of systems was negative. He denied any past surgical history or known allergies. Family history was not significant for any malignancy or blood disorder. His only medication was Amlodipine 5mg daily. Social history was significant for being born and raised in South Korea prior to moving to the United States, and also included a history of significant alcohol and tobacco-use, however the patient quit smoking "a few years ago." He served in the Military from 1975-1979 during the Vietnam War Era. His physical examination was unremarkable.

Summary of Significant Lab Findings

Table 1. Initial Complete Blood Count

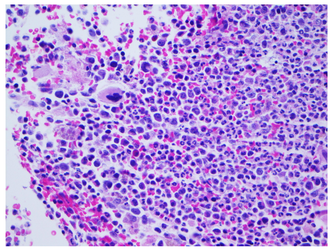
	Hgb	WBC	Platelets
Baseline	8.6 g/dL	13.2 K/μL	103 K/μL
Presentation	13.1 g/dL	53.4 K/μL	245 K/μL

LDH = 588 U/L
PSA = 0.74 ng/mL
Leukocyte Alkaline Phosphatase (LAP) = 26

Peripheral Blood Smear

- RBC: Normal
- WBC: blast cells, myelocytes, metamyelocytes, bands, PMNs, hypogranular PMNs, monocytes, large granular lymphocytes
- Platelets: Giant platelets

Bone Marrow Aspirate



H and E, 40 x, Hypercellular bone marrow

Molecular Testing

Table 2. Demonstrating mutations characteristic of Myeloproliferative and Myelodysplastic Disorders. Mutations observed in this patient are bolded.

Clinical entity	BCR-ABL1	MPN	MDS
CML	Positive	+ JAK2	None
CMML	Not present	+/- JAK2	+ TET2, ASXL1, **SRSF2**, RUNX1
Atypical CML	Not present	+/- JAK2	+ NRAS, KRAS, TET2, **CBL**, CSF3R, SETBP1, ETNK1
MDS/MPN-U	**Not present**	+/- **JAK2**	**+ ASXL1, + TET2**

Discussion

An asymptomatic elderly patient found to have a significantly elevated WBC count warrants further work-up for CML and other myeloproliferative disorders. Evaluation consists of Peripheral Blood Smear and Bone Marrow Aspirate, Cytogenetics/FISH sequencing, PCR for *BCR-ABL1*, and Myeloid Mutation Panel Testing.

CML is distinguished from the MDS/MPN disorders by a positive *BCR-ABL1* test and the absence of significant dysplasia on peripheral blood smear, suggesting a primary proliferative disorder. The 5 MDS/MPN entities are characterized by a negative *BCR-ABL1*, often have <20% blasts in the blood and bone marrow, and may have dysplasia in one or more lineages. Genetic mutations may be seen in TET2, SRSF2, JAK2V61, CSF3R, and SETBP1.

In this clinical case, it was challenging to distinguish aCML from MDS/MPN-U. This patient had myeloproliferative features of disease, and was also noted to have dysplastic cells on blood smear. *BCR-ABL1* was negative, and proliferation of specific cell lines was not observed, as would be seen in CMML or JMML. Myeloid mutations potentially suggestive of aCML include increased RAS mutations, and fewer JAK2 mutations. He had mutations seen with MDS (TET2, ASXL1) and myeloproliferative disease (JAK2). In summary, MDS/MPN-U is diagnosed as patients with both features of myeloproliferative neoplasms and myelodysplastic syndromes who do not meet the criteria for CMML, JMML, or ACML. There are currently. no specific cytogenetic or molecular markers that distinguish MDS/MPN-U from the other entities.

References

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