Understanding MPN

Adult learning styles to recognize myeloproliferative disorders

Mary Jo K. Voelpel, DO,

Objectives

- Define myeloproliferative disorders
- Know diseases included in the category
- Recognize clinical Signs and Symptoms

World Health Organization Classification of MPN's

- Chronic MyelogenousLeukemia-translocation of 9:22
- Chronic Neutrophilic Leukemia-translocation of 15:19
- Chronic Eosinophilic Leukemia-translocation PDGFR-alpha
- Polycythemia Vera: 95% JAK 2
- Primary Thrombasthenia V617F
- Mastocytosis
- MPN unclassified

Historical Perspective

Dameshek initially introduced the term myeloproliferative disorders in 1951 as of a common etiologic agent (Blood 6:372) "Some speculations on the myeloproliferative syndrome,"

At that time we considered terms such as Pseudoleukemia and atypical myelosis.

Today we still share the concept of a multipotential hematopoietic progenitor but we now have evidence of phenotypic heterogeneity. These distinctions allow us to more accurately define the conditions.

Let's Begin

- A 45 yo presents to the emergency room with a cough. (Could be male or female. No medication, no prior medical conditions, just felt exhausted.
- CBC-WBC 23,200 predominantly neutrophils with left shift and one nucleated RBC. Enzymes normal
- Physical exam: coarse breath sounds, 2 finger splenomegaly, the patient swears he doesn't drink, hasn't used cocaine in 2 years, and only smokes one pack a day. CXR was neg. When patient came back from x ray-asked for something for itching.

What Next?

- Consider sepsis, consider smoking, is the splenomegaly from liver disease?
- How can we easily approach this?

What clues suggest this may not be benign

- A leukocyte alkaline phosphatase score can be helpful if available, if its low it suggests the leukocytosis is not related to an infectious or inflammatory process and consideration for a myeloproliferative process is in order.
- A liver spleen scan may be helpful but there is nothing definitive other than confirming the physical exam finding and ruling out an infiltrative disorder.
- Today there are test kits available for a bedside check on BCR/ABL that would quickly identify a problem that required referral.

Case 2

- A 65 yo cau male presents with a sensation of SOB and getting very itchy if he takes a hot shower, it creates a flushing all over that he finds uncomfortable and makes him feel full in his belly. He said he just drank a beer but he doesn't think that's the problem.
- His pulse ox was 97% on room air, he was barrel chested and had 4 finger splenomegaly. :
- Labs- WBC 11,100 HCT 59 Hb 19.3 erythropoietin was low
- What should you do?
-

Case 3

- 38 yo asthenic cau male presented for evaluation after PCP did baseline blood work for his job and found a platelet count over one million.
- He did not have any comorbid conditions, was a non drinker and ran a half marathon last weekend.
- Does he need to worry-his Mom came with him.

Case 4

- This 58 yo cau female presented for second opinion after recently having bone marrow biopsy in florida. She had a history of Primary Thrombasthenia for 10 years and had been on hydrea and anagrelide previously. The bone marrow revealed secondary myelofibrosis.

- She was anemic and had recently been admitted for abdominal pain with a hemoglobin electrophoresis that revealed Sickle Cell Trait.

What are the next steps?

- Evaluate for Sickling, obtain more history
- Check current CBC, and evidence of possible hemolysis
- Address most important symptoms first

MYELOPROLIFERATIVE NEOPLASMS

- The National Cancer Consensus Network (NCCN) recently updated guidelines and treatment. A complete guide can be accessed at NCCN.org
- These broad categories include: Chronic Myelogenous Leukemia, primary myelofibrosis, primary thrombasthenia, polycythemia vera . The diagnosis and management of these disorders has evolved dramatically since identification of BCR/abl, JAK2, CALR, and MPL mutations were identified that have become the major drivers for targeted therapies
- Gerds, Aaron, et al, JNCCN, Vol 20, Issue 9, Sept 22, p1033-1068.

Case 1

- This 46 yo was JAK2 +, has responded to rx, last scan no splenomegaly and no pruritus. His stumbling blocks to longevity will be adherence to medication, and avoidance of addictive scenarios.
- He recently fell thirty feet from a tree he was trimming when his safety harness malfunctioned, extensive bruising, rib fractures, and shoulder injury, but survived, and married recently

Treatment of case 1

- This particular case initially presented with erythrocytosis, thrombocytosis, leukocytosis and splenomeglly. His WBC and Platelets were felt to be reactive to his lifestyle habits and while incarcerated was referred to hematologist for phlebotomies….the patient didn't understand why. His presentation to the ER led to the work up with bone marrow and genetic testing with definitive treatment (3 years after initial symptoms). It is not uncommon to see early symptoms with slow progression and delays in diagnosis in many cases. Care is always targeted to the patient and varies with symptoms. His estimated survival will be 28 years. Goals of care will be symptom management and surveillance.

CASE 2

- This 46 yo presented with flushing, pruritus, and marked abdominal pain with a sensation of SOB, he had marked splenomegaly, eosinophilia, No hypoxia with normal plasma vol and elevated RBCmass, his erythropoietin was low and his bone marrow was hypercellular with no fibrosis. He was treated symptomatically with phlebotomies and ASA, No admissions over a 30 year span , only arthritic problems with shoulders and right knee and in past year development of cognitive impairment from years of martinis. At the age of 76 he is being placed in a memory Care facility.

Case 3

- Bone marrow biopsy did not reveal fibrosis, but there was megakaryocytic clustering and a hypercellular marrow.
- Mutation of the calreticulin gene (CALR) was identified. This is seen in 20-35% of ET patients. CALR type 2 are the most common mutations in ET
- There are many mutations in genes involved in signal transduction chromatn modification, RNA splicing, and tumor suppressor functions that have been reported with the MPN, so there will be many future targets for treatment.
- This patient was placed on hydrea to reduce platelet count to safer levels.

CASE 4

- This case was seen by many specialists over a 20year process. The Sickle cell trait led to episodes of crisis when she was in motorcycle accidents and when she was struck by a Hi-Lo truck at work. She is a blonde haired , blue eyed patient, so when complications arose, no one considered a sickle crisis. She was JAK negative and treated with anagrelide an hydrea over the years. She underwent repeat bone marrow biopsy 2 years ago and has development of myelofibrosis. Prefibrotic myelofibrosis can preceed the diagnosis of myelofibrosis by many years and is difficult to identify in these early stages. Currently there are 3 medications recommended, all with side effects, ruxolitinib, pacritinib, and fedratinib.

Dynamic international prognostic scoring

- Since myelofibrosis has a higher propensity for developing Acute Leukemia it is helpful to address the scoring for severity of symptoms and risks.

Dynamic International Prognostic scoring system

- AGE>65 one point low risk-0
- HB<10 two points intermediate risk 1-1-2 points
- WBC>25 one point intermediate risk 2-3-4 points
- Blasts>1% one point high rsk-5-6 points
- Constitutional symptoms-one pt
- Patients with MPN may benefit from an understanding of their scoring-it's a concrete way to say—0 is good 6 is bad

Bedside testing-has it arrived?

- Hands on clinical testing kit