MYELOPROLIFERATIVE DISORDERS

no disclosures
PRIMARY MYELOFIBROSIS

- Progressive generalized reactive fibrosis of bone marrow
- Associated development of hemopoiesis in spleen and liver (myeloid metaplasia)
Primary Myelofibrosis Pathogenesis

- Megakaryocytes release platelet derived growth factor and other cytokines to stimulate fibroblasts
- JAK-2 mutation positive in 50%
- Nonspecific cytogenetic abnormalities in 50%
- Transformation to acute leukemia 10-20%
Primary Myelofibrosis

- Symptoms
  - Weakness
  - Night sweats, weight loss

- Signs
  - Massive hepatosplenomegaly
  - Bone marrow failure
  - Portal hypertension
  - Pulmonary hypertension
Primary Myelofibrosis Lab Findings

- Anemia: tear-drop erythrocytes
- Initial elevation, then decline in WBC & platelet count
- JAK-2 positive in 50%
- Bone marrow fibrosis with increased megakaryocytes
Etiologies of Myelofibrosis

- Infections, ie-TB, osteomyelitis
- Hematological malignancies
- Metastatic cancer, esp breast & prostate
- High exposure to radiation
- Benzene toxicity
- Fluorine toxicity
- Paget's disease-focal fibrosis
- Osteopetrosis
Primary Myelofibrosis Treatment

- Hydroxyurea
- Transfusion as indicated
- Splenic irradiation or splenectomy
- JAK-2 inhibitors
- Erthropoietin
- Androgen therapy
POLYCYTHEMIA VERA

- Clinical Features

  - Symptoms: headaches, dyspnea, blurred vision, night sweats, pruritus (esp after hot shower)

  - Signs: plethoric facies, retinal venous engorgement, splenomegaly, hypertension, gout, thrombosis (arterial or venous), hemorrhage (GI, uterine, cerebral)
Polycythemia Vera

- Laboratory findings
  - Elevated hemoglobin and hematocrit
  - RBC volume increased
  - Leukocytosis-50%
  - Thrombocytosis-50%
  - Hypercellular bone marrow
  - Low erythropoietin
  - JAK-2 positive-95%
Polycythemia Vera

- **Diagnosis**
  - JAK-2 positive-no further work-up needed
  - JAK-2 negative
    - No cause of secondary erythrocytosis
    - Splenomegaly
    - Acquired genetic abnormality
    - Thrombocytosis +/- leukocytosis
Etiologies of Secondary Polycythemia

- Tumor related increase in erythropoietin
  - Renal cell cancer
  - Hepatocellular cancer
  - Uterine fibroids
- Hypoxemia
  - COPD
  - Sleep apnea
  - Massive obesity
  - High altitude
- Increased carboxyhemoglobin levels
  - Smoking
  - Chronic carbon monoxide exposure
- Hemoglobinopathy
Differential Diagnosis of Polycythemia

- **Step 1**
  - H&P, CBC w/diff, ferritin, renal & liver function tests, PFTs, ABG w/carboxyhemoglobin, erythropoietin
  - JAK-2: if negative proceed to step 2

- **Step 2**
  - Bone marrow biopsy w/cytogenetics
  - Abdominal US

- **Step 3**
  - O2 dissociation: heart & lung evaluation
Therapy of Polycythemia

- Phlebotomy to Hct < 45%
- Hydrea for platelet count > 400,000
- Aspirin 81 mg daily
- JAK-2 inhibitors
ESSENTIAL THROMBOCYTHEMIA

- Clinical findings
  - Asymptomatic
  - Thrombosis (venous or arterial)
  - Hemorrhage (abnormal platelet function)
  - Splenomegaly
  - Erythroelalgia-burning sensation of hands & feet
Essential Thrombocythemia

- **Laboratory Findings**
  - Platelet count $>400,000$
  - Abnormal large platelets and megakaryocytic fragments on peripheral smear
  - JAK-2 positive-90%
  - Bone marrow with abnormal megakaryocytes
  - Platelet function studies abnormal
THROMBOCYTOYSIS

Reactive:
- Hemorrhage
- Trauma
- Postoperative
- Chronic iron deficiency
- Malignancy
- Chronic infections
- Connective tissue diseases
- Postsplenectomy

Endogenous:
- Essential thrombocythemia

Can also be seen in:
- Polycythemia vera
- Myelofibrosis
- CML