MYELOPROLIFERATIVE DISORDERS

Group of disorders that result from an unchecked, autonomous clonal proliferation of cellular elements in the bone marrow

CLASSIFICATION

- Based on most affected Cell Line
  - Chronic Myelocytic Leukemia CML
  - Myelofibrosis with Myeloid Metaplasia MMM
  - Polycythemia Vera PV
  - Essential Thrombocythemia ET

PATHOPHYSIOLOGY

- Increased Stem Cells
- Abnormal Stem Cells expand until overtake normal hematopoiesis

GENERAL FEATURES

- Middle age or older
- Hemorrhage, Thrombosis, Infection, Pallor Weakness
- Anemia or Polycythemia, leukoerythroblastosis, Leukocytosis, Thrombocytosis with bizarre platelets
- Decreased Bone Marrow Iron
- Bone Marrow Hypercellular then Fibrotic

CHRONIC MYELOCYTIC LEUKEMIA

- Three Phases
  - Chronic
  - Accelerated Transition
  - Blast Crisis
- Philadelphia Chromosome
  - T(9;22)(q34;q11)

CML CLINICAL FINDINGS

- 40-59 years of age
- Men and Women
- Insidious onset – weakness, fever, sweats, weight loss, GI bleeding, retinal hemorrhages
- Organ infiltration

CML LABORATORY FINDINGS

- Peripheral Blood
  - Leukocytosis >100X10^9/L
  - Thrombocytosis (50%) variation in shape
  - Normocytic, Normochromic Anemia
  - Pseudo-Pegler Huet
  - Decreased LAP
- Bone Marrow
  - 90-100% Cellular, ↑M:E Ratio
  - Small Megakaryocytes

CML PROGRESS & THERAPY

- 30-40 months then transition accelerated then blast crisis
- Therapy
  - Reduce leukocytes – cytotoxic drugs, leukophoresis
  - Bone Marrow Transplant
  - Interferon-alpha
  - Gleevec

DIFFERENTIAL DIAGNOSIS

- Leukemoid Reaction
  - Neutrophils and bands
  - Toxic Granulation, Cytoplasmic Vacuoles, Döhle Bodies
  - LAP↑
- CML
  - Blast, Promyelocytes
  - ↑Monocytes, Eosinophils, and Basophils
  - ↓ LAP
  - Philadelphia Chromosome
  - Splenomegally

DISEASES SIMILAR TO CML

- Juvenile CML
- Chronic Eosinophilic Leukemia
- Chronic Basophilic Leukemia
- Chronic Neutrophilic Leukemia

MYELOFIBROSIS WITH MYELOID METAPLASIA

- Unregulated proliferation of hematopoietic cells, extramedullary hematopoiesis and fibrosis
- Synonyms – Agnogenic myeloid Metaplasia, idiopathic myelofibrosis, primary myelofibrosis, aleukemic myelosis, myelosclerosis, splenomegalic myelophthisis, Leukoerythroblastic Anemia

MMM PATHOPHYSIOLOGY

- ? Neoplastic Disorder
- ? Toxic Agent that injures hematopoietic cells
- Fibrosis secondary reactive event

MMM CLINICAL FINDINGS

- >50 years old
- Male & Female
- Early no symptoms
- Symptoms- weakness, wt loss, loss of appetite, night sweats, pain in extremities
- Myeloid Metaplasia in spleen, liver and other places

MMM LABORATORY FINDINGS

- Peripheral Blood
  - Moderate Leukoerythroblastic Anemia usually normochromic, normoblastic
  - Aniso & Poik, dacrocytes, elliptocytes, ovalocytes, basophilic stippling
  - LAP 'or normal
- Bone Marrow
  - Dry tab often

MMM PROGNOSIS & THERAPY

- 4-5 years
- No cure or specific treatment

DIFFERENTIAL DIAGNOSIS

- Leukocyte count usually lower
- Shift to Left, Poik
- BM Fibrous, ↑Megakaryocytes
- LAP normal or↑

POLYCYTHEMIA VERA

- Unregulated proliferation of the erythroid elements in the bone marrow and increased erythrocytes in the blood
- Must determine if the increase in the red cell tests are due to an absolute increase in RBC mass or a decrease in plasma volume
  - Three Groups
    - Polycythemia Vera
    - Secondary Polycythemia
    - Relative Polycythemia

PATHOLOGY

- Clonal Stem Cell Defect
- Increased sensitivity to EPO, insulin-like growth factor and maybe Interleukin-3
- Increased Bcl-$x_{(L)}$ inhibits apoptosis

CLINICAL FINDINGS

- 40-60 years old
- Males
- Headache, weakness, pruitus, weight loss, fatigue, 33% thrombotic or hemorrhagic episodes
- Plethora- a red florid complexion
- Spent Phase transition to AML

LABORATORY FNDINGS

- Absolute erythrocytosis – 6-10 $x10^{12}/L$
- Norm/Norm becomes Micro/Hypo
- Retic – Norm or↑
- ESR – does not exceed 2-3 mm/hr
- Leukocytosis 2/3 cases
- Megakaryocytes Hyperplasia
- BM – moderate to marked increase in cellularity
- Oxygen sat – normal
- Uric Acid may be increased

PROGNOSIS AND THERAPY

- Phlebotomy
- Myelosuppressive Therapy

DIFFERENTIAL DIAGNOSIS

- Diagnosis Criteria
  - Total Blood Volume
  - Arterial Oxygen Saturation
  - Spleen Size
  - EPO measurement

SECONDARY POLYCYTHEMIA

- Polycythemia due to an increase in EPO as a normal response to tissue hypoxia
- Polycythemia due to an inappropriate, nonphysiologic increase in EPO
- Familial polycythemia associated with high oxygen affinity hemoglobin variants
- Neonatal polycythemia associated with intrauterine hypoxia or late cord clamping

RELATIVE POLYCYTHEMIA

- Dehydration
- Hemoconcentration
- Gaisbock's syndrome

ESSENTIAL THROMBOCYTHEMIA

- Extreme thrombosis in the peripheral blood along with thrombocytopathy
- Pt count usually > 1,000 x 10^9/L

PATHOPHYSIOLOGY

- Clonal Disorder of pluropotential stem cell
- Surface receptor for thrombopoietin decreased, serum levels increased
- Clonal cells hypersensitive to IL-3, IL-6

CLINICAL FINDINGS

- 50-60 and 20-30 years of age
- Bleeding or thrombosis
- Occasionally splenomegally

LABORATORY FINDINGS

- Extreme Thrombocytosis
- Abnormalities in pt aggregation and adhesiveness
- Leukocytosis 27-40 x 10^9/L
- BM – hyperplasia, increased Megakaryocytes
- PT & PTT usually normal
- Increase in serum cobalamin, uric acid, LDH, acid phos, potassium

PROGNOSIS AND TREATMENT

- 50% longer than 5 yrs
- Plasmaphoresis

DIFFERENTIAL DIAGNOSIS

- Secondary Thrombocytosis – Plt count not as high and function normal
- Criteria for ET
  - Plt count > 600 x 10^9/L
  - Hgb < 13 gm/dl
  - Stable Iron in BM
  - Absence of Philadelphia Chromosome
  - Absence of Fibrosis
  - No know cause for reactive thrombosis