Polycthemia Vera (Rubra)
Polycythemia Vera (Rubra)

- Increased red cells
- Clonal
- Myeloid lineages also increased
- 2-13 cases per million
- Mean age: 60 years
Sites of Involvement

- Bone marrow
- Peripheral blood
- Liver and spleen (extramedullary hematopoiesis)
WHO Criteria

- $A_1$ RBCs $>25\%$ above normal, or Hb $>18.5\text{g/dL}$ in men and $>16.5\text{g/dL}$ in women
- $A_2$ No cause of secondary erythrocytosis (hypoxia, abnormal Hgb, familial conditions)
- $A_3$ Splenomegaly
- $A_4$ Clonal genetic abnormalities (but not Ph+)
- $A_5$ Endogenous erythroid colony formation
  
  *in vitro*
WHO Criteria

- $B_1$ Thrombocytosis $>400 \times 10^9/L$
- $B_2$ WBCs $>12 \times 10^9/L$
- $B_3$ BM Bx with panmyelosis, erythroid and megakaryocytic hyperplasia
- $B_5$ Low serum erythropoietin levels
Diagnosis of Polycythemia Vera

- $A_1 + A_2$ and any one of other category A, or
- $A_1 + A_2$ and any two of category B
Clinical Features

- Thrombosis (25%)
- Hemorrhage
- Stroke
- Plethora (70%)
- Splenomegaly (70%)
- Hepatomegaly (40%)
- Leukocyte Alkaline Phosphatase (LAP): normal
Polycythemia Rubra Vera
Clinical Signs and Symptoms

- Plethora, headache, dyspnea or orthopnea, eye complaints
- Epigastric discomfort – risk of Budd-Chiari syndrome
- Abnormal blood flow: MI, stroke
Polycythemia Stage

- Normoblastic erythroid proliferation in BM
- Normochromic, normocytic RBCs in PB
- If bleeding or phlebotomy ➞ RBCs hypochromic and microcytic
- Neutrophilia
- Basophilia
- Thrombocytosis (50%)
Polycythemia Stage

- Proliferative stage
- BM cellularity 35-100% (median 80%)
- Panmyelosis (Erythroid, granulocytic, and megakaryocytic proliferation)
- Blasts not increased
Polycythemia Stage

Megakaryocytes

- Increased, clustered (parasinusoidal and paratrabecular); sinusoids dilated
- Pleomorphic, nuclear hyperlobulation but not dysplastic
- No stainable iron in 95%
Polycythemia Stage

- Only 30% with fibrosis at presentation (reticulin increased)
- Spleen and liver congested
- Extramedullary hematopoiesis minimal
- 10-50% progress to fibrotic stage
Spent Phase - Post-Polycythemic Myelofibrosis and Myeloid Metaplasia

- Red cell mass decreases
- BM cellularity decreases
- BM fibrosis (reticulin and collagen increased)
- Splenomegaly – with extramedullary hematopoiesis
Spent Phase - Post-Polycythemic Myelofibrosis and Myeloid Metaplasia

- Leukoerythroblastic blood smear with dacryocytes (tear-drop cells)
- Megakaryocytes still prominent and clustered
Genetics

- Specific defects in only 20%
- +8, +9, del 20q, del 13q, del 1p
- No Philadelphia chromosome or BCR/ABL fusion gene
- Genetic defects increase during progression to MDS or AML
Diagnostic Aids

JAK-2 mutation (V617F) for:

- polycythemia vera (sensitivity 65-97%),
- essential thrombocythemia (sensitivity 30-57%), and
- chronic idiopathic myelofibrosis (sensitivity 35-95%),
Prognosis

- Without therapy -> survival a few months
- With therapy survival -> survival >10 years
- Death due to thrombosis or hemorrhage
- MDS or AML in only 2% treated with non-cytotoxic agents
- MDS or AML in 10-20% treated with cytotoxic agents
Essential Thrombocythemia

Synonyms

- Primary thrombocytosis
- Idiopathic thrombocytosis
- Hemorrhagic thrombocytemia
Essential Thrombocytemia

- Incidence 1-2.5 per 100,000 annually
- Age: 50-60 years, equally in men and women
- Minor peak at 30 years, mostly women
- Rarely in children
Essential Thrombocythemia

Sites of involvement

Bone marrow

Peripheral blood

Spleen (platelet sequestration site - minimal extramedullary hematopoiesis)
Clinical Features

- More than one-half asymptomatic, incidental finding
- The rest presenting with thrombosis or hemorrhage
- Modest splenomegaly in 50%
- Significant hepatomegaly in 15-20%
Diagnostic criteria

Positive criteria

- Platelets $>600 \times 10^9/L$
- BM Bx proliferation of enlarged, mature megakaryocytes
Diagnostic criteria

Exclusion criteria

1. No evidence of Polycythemia vera
   - Hb <18.5 g/dL in men and <16.5 g/dL in women
   - Stainable iron in BM
   - Normal ferritin levels
Diagnostic criteria

Exclusion criteria (cont’d)

2. No CML (Ph negative)
3. No chronic idiopathic myelofibrosis
4. No MDS
5. No reactive thrombocytosis (a/w tumor, infection, splenectomy)
Diagnostic Aids

JAK-2 mutation (V617F) for:

- polycythemia vera (sensitivity 65-97%),
- essential thrombocythemia (sensitivity 30-57%),
- and chronic idiopathic myelofibrosis (sensitivity 35-95%),
Peripheral Blood Morphology

- Thrombocytosis
- Platelets: small to large
- WBCs normal
- Basophilia absent
- RBCs normal
Morphology Bone Marrow

► Normocellular or mildly hypercellular

► Giant megakaryocytes, clustered or scattered, with abundant mature cytoplasm, hyperlobulated nuclei

► Reticulin not increased
Genetics

- Only 5-10% with abnormal karyotype
- del (13q22), +8, +9
Prognosis and Predictive Factors

- 10-15 year survival common
- Splenectomy worsens survival (sequestration reservoir is eliminated and Plts increase)
- Transformation to MDS and AML in <5% and usually therapy-related
- Fibrosis may increase (DDX: CIMF)