PATHOLOGY OF BLOOD AND LYMPHATIC SYSTEM– 10

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MYELOPROLIFERATIVE NEOPLASMS

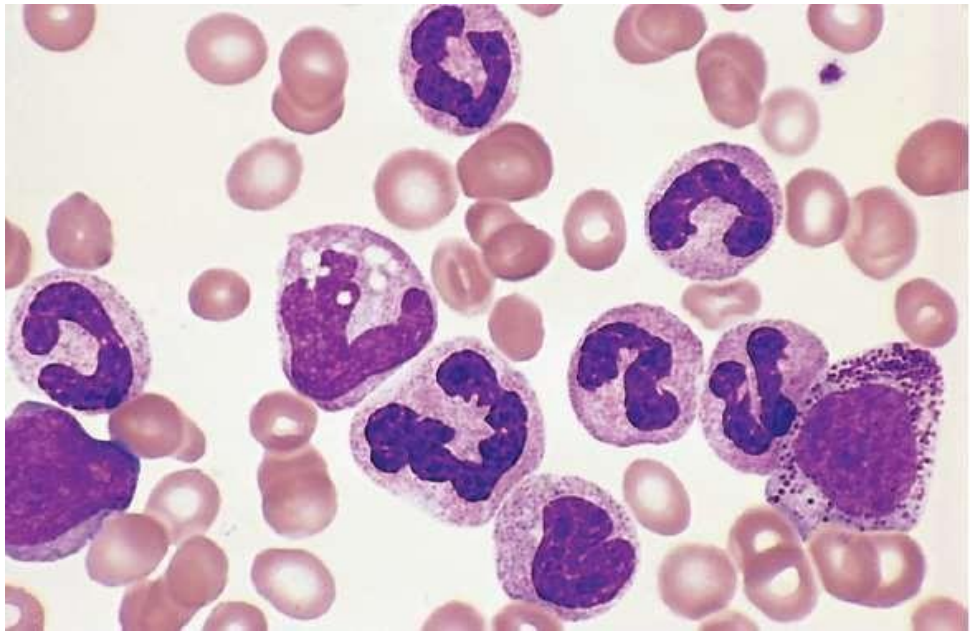
- Maturation is normal, but proliferation is high
- Permanently active tyrosine kinase pathway, independent from growth factors
- BM is hypercellular, peripheral blood shows cytosis
- Neoplastic stem cells in MPN often seeds to spleen, liver and occasionally LNs, causing extramedullary hematopoiesis and thus hepatosplenomegaly
- Tendency to transform to AML

CHRONIC MYELOID LEUKEMIA

- Most common MPN
- Harbor t(9;22) □ Philadelphia chromosome, results in fusion of Bcr/Abl genes and production of a tyrosine kinase that results in prolonged cell survival
- Mutation is present in all BM cells (myeloid, erythroid and megs)
- Affects adults 25-60 years
- Symptoms: non-specific: fatigue, heavy abdomen, weight loss
- Imatinib: tyrosine kinase inhibitor, specific for bcr/abl mutation
- Accelerated phase: worsening of symptoms, higher WBC count, thrombocytopenia, resistance to imatinib
- Blast crisis: transformation to acute leukemia (AML>ALL)

MORPHOLOGY OF CML

- Leukocytosis, can be >100K
- Shift to left
- Basophilia, eosinophilia
- Thrombocytosis
- Anemia
- BM: increased nyeloid and megs
- Spleen: EMH
- Blasts: low
- Leukemoid reaction: high WBC and shift to left, occurs in severe inflammation



POLYCYTHEMIA VERA

- Mutation in tyrosine kinase JAK2, normally acts in the signaling pathway of erythropoietin receptor and other growth factor receptors
- Hematopoietic cells become less dependent on growth factors
- Excessive proliferation of erythroid, megs and myeloid (panmyelosis)
- Erythrocytosis is most prominent, results in polycythemia (low erythropoietin level)
- Insidious onset of symptoms, middle age, plethora, sometimes cyanosis, headache, dizziness, pruritis, peptic ulcer
- Thrombosis and tissue infarction, bleeding is also common (GIT), gout
- Spent phase: occurs after an interval of 10 years of symptoms, BM become fibrotic, hematopoiesis shifts to spleen
- Blast crisis: transformation to AML (rare)
- Treatment: phlebotomy, JAK2 inhibitor

Laboratory findings

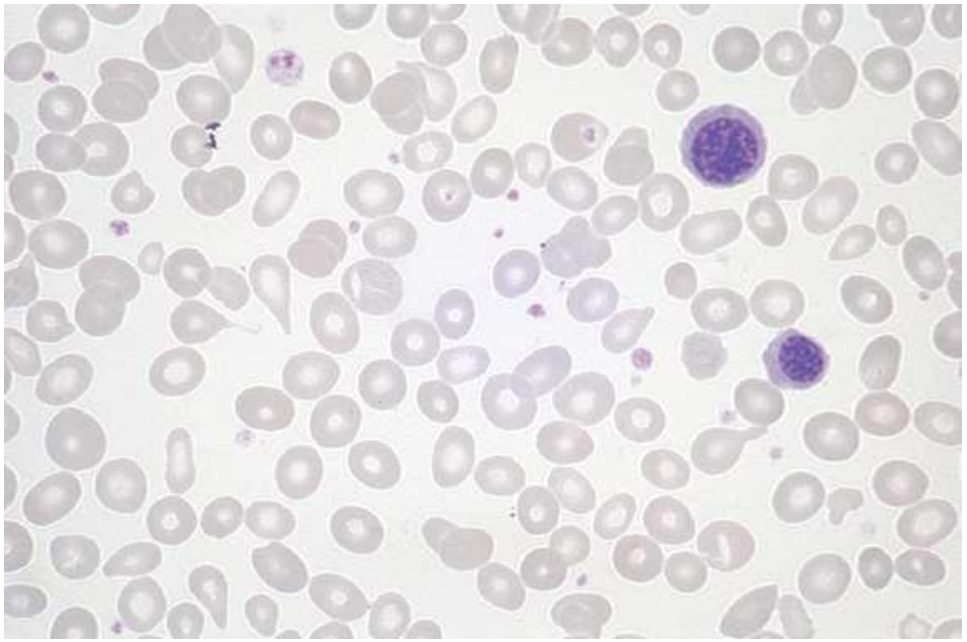
- High RBC count
- Hematocrit 60% of more
- Leukocytosis is common
- Basophilia
- Thrombocytosis is common

PRIMARY MYELOFIBROSIS

- Over BM fibrosis, reducing capacity for hematopoiesis, leads eventually to cytopenia and massive EMH
- JAK-STAT signaling pathway is active in all cases
- 50% have mutation in JAK2, 5% in MPL gene (thrombopoietin receptor)
- Neoplastic megakaryocytes secrete TGF-B, which activates fibroblasts in BM to deposit reticulin and collagen fibers, also causes angiogenesis
- RBC production is impaired, RBCs appear as tear-drop, patients have anemia

MORPHOLOGY

- Peripheral blood: tear-drop cells, nucleated RBCs, shift to left (leucoerythroblastic anemia)
- WBC: can be normal of increased
- Plt: high, then low
- BM: early: hypercellular and focal fibrosis, late: hypocellular and extensive fibrosis. Megakaryocytes are increased and form clusters



CLINICAL FEATURES

- Non-specific symptoms, weight loss, anemia, massive splenomegaly, gout, bleeding, infection
- Worse outcome than CML and P Vera. 4-5 years survival
- Frequent transformation to AML (5-20%)
- JAK2 inhibitor: decreases splenomegaly and symptoms

ESSENTIAL THROMBOCYTHEMIA

- Predominantly thrombocytosis (occasional leukocytosis)
- JAK2 mutation is sometimes positive, but NO bone marrow fibrosis
- Splenomegaly is positive in 50%
- Good outcome

LANGERHANS CELL HISTIOCYTOSIS

- Neoplasm of dendritic cells
- Langerhans cells express CD1a and Langerin
- Langerin is a transmembrane protein, attached to Birbeck granules (tennis ricket shape under electron microscope)
- Proliferating Langerhans cells appear large and vacuolated, similar to macrophages
- Pathogenesis: acquired mutation in serin/threonine kinase BRAF, leads to hyperactivity of this kinase

MULTISYSTEMIC LCH

- Occurs mostly in children less than 2 years
- Multiple cutaneous lesion, composed of LCs
- Hepatosplenomegaly and lymphadenopathy
- Pulmonary lesions
- Osteolytic lesions
- Extensive bone marrow infiltration leads to pancytopenia
- Treated with chemotherapy

UNISYSTEM LCH

- AKA eosinophilic granuloma
- Affects a single organ, most commonly bone, then skin, lung, stomach
- Can be unifocal or multifocal
- Unifocal is commonly asymptomatic, can cause pain
- Mulfocal unisystem disease presents in children, commonly affects calvaria bone, extends to pituitary gland causing diabetes insipidus, exophthalmous (Hand-Schuller-Christian triad).
- Proliferating LCs are admixed with numerous eosinophils, lymphocytes, plasma cells and neutrophils
- Treatment: unifocal: surgical excision, multifocal: chemotherapy, sometimes spontaneous regression