PATHOLOGY OF BLOOD AND LYMPHATIC SYSTEM-9

Dr. Tariq Al-Adaily, MD د. طارق العديلي
Associate Professor
Department of Pathology
The University of Jordan
Email: TNALADILY@ju.edu.jo

School of Medicine

MYELOID NEOPLASMS

- Arises from hematopoietic progenitor stem cells
- Neoplastic cells proliferate and efface normal hematopoietic cells
- Divided into:
- Acute myeloid leukemia: impaired maturation, increased proliferation (myeloblast)
- Myeloproliferative neoplasms: normal maturation, increased proliferation
- Myelodysplastic syndrome: abnormal maturation, normal proliferation
- MPN and MDS can transform to AML
- BM is hypercellular in all myeloid neoplasms
- Clonal hematopoiesis of indeterminant prognosis (CHIP): represents a precursor for AML and MDS, patient has normal cell count despite the presence of a clone with a mutation

ACUTE MYELOID LEUKEMIA

- Occur at all age groups, but more common in elderly
- Heterogenous, diagnosis is made by morphologic, immunophenotypic and karyotype studies
- Prognosis depends most importantly on type of mutations (molecular and cytogenetic studies
- Symptoms are accelerated, become significant within few weeks
- Symptoms are related to anemia, thrombocytopenia and neutropenia
- Involvement of LN, spleen and solid organs is rare. When occurs, it is called myeloid sarcoma (acute monoblastic leukemia)

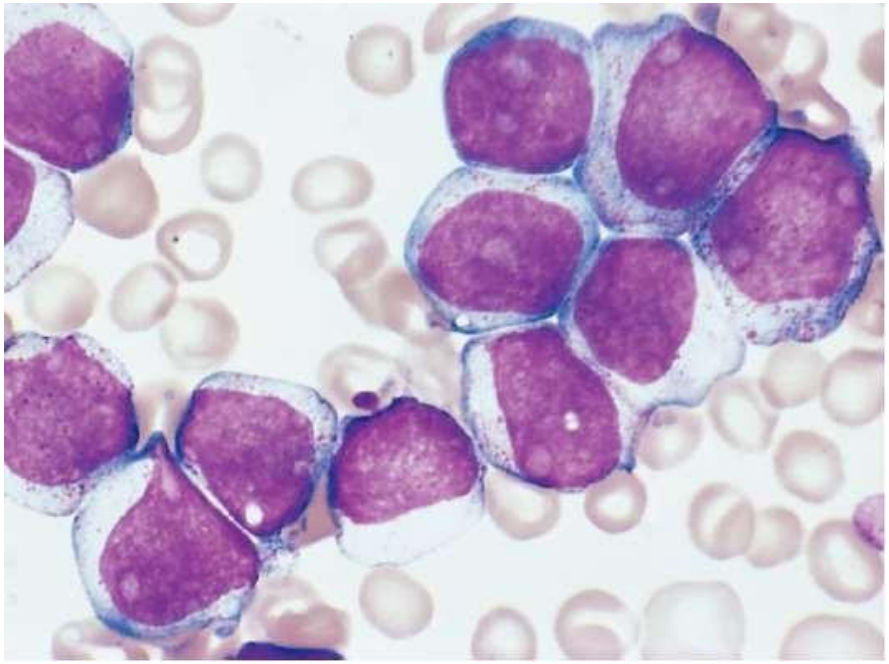
PATHOGENESIS

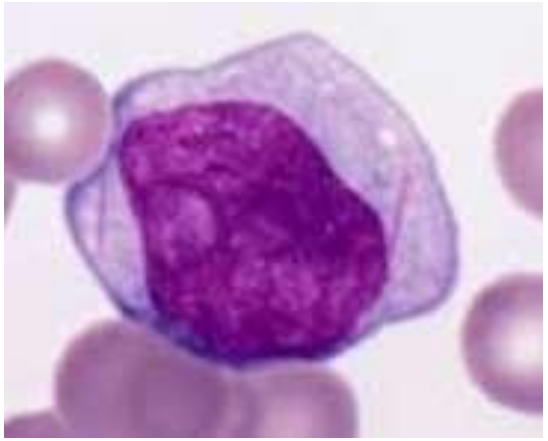
- Mutations in genes of transcription factors required for maturation and differentiation of myeloblasts
- Additional mutations in tyrosine kinase pathways (RAS)
- Epigenetic mutation is common (20%); mutation is isocitrate dehydrogenase (IDH) produces an oncometabolite that blocks enzyme of epigenome and interferes with myeloblast differentiation

WHO-CLASSIFICATION

- Therapy related AML: occurs after treatment with chemo or radiotherapy
- AML with recurrent cytogenetic mutation
- AML with myelodysplasia: occurs de novo or complicates MDS
- AML-Not otherwise specified

- Diagnosis of AML: 20% blasts in peripheral blood or bone marrow (of nucleated cells)





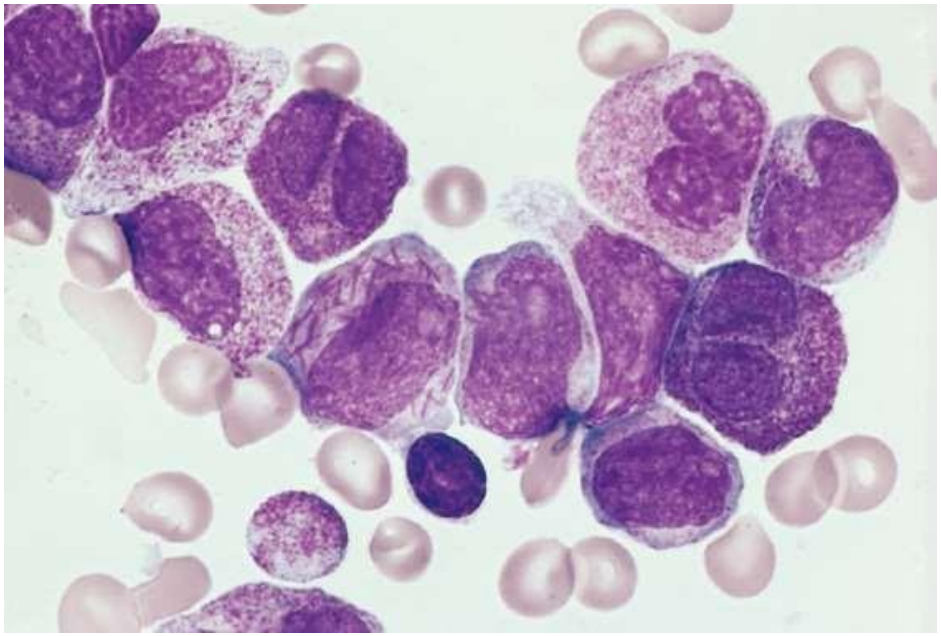
- Morphology: large cells, high N/C ration, fine granules in cytoplasm, fine chromatin, prominent nucleoli
- Auer rods: small pink rods present in cytoplasm, represent peroxidase enzyme
- Myeloblasts express CD34, myeloperoxidase (MPO), CD13, CD33
- Sometimes: monoblast, erythroblast, megakaryoblast

OUTCOME

- Generally poor, <30% responds to chemotherapy
- Worse than ALL
- P53 mutation: worse outcome
- IDH inhibitors are new promising drugs
-

ACUTE PROMYELOCYTIC LEUKEMIA

- Also called AML-M3
- Maturation is arrested at promyelocyte stage
- Leukemic cells appear similar to promyelocytes (heavy cytoplasmic granules, numerous Auer rods, negative for CD34)
- Carry recurrent mutation: t(15;17) fusion between PML gene (chrom 15) with alpha retinoic acid receptor (RARA) on chrom 17. Chimeric fusion gene produces a protein that blocks promyelocyte maturation by inhibiting the action of retinoic acid.
- All trans-retinoic acid (ATRA), a vitamin A analogue, overcomes this block. Effect is synergistic with arsenic trioxide (degrades oncoprotein)
- Malignant promyelocyte secrete tissue factor, causing DIC



- APL: malignant promyelocytes show numerous cytoplasmic granules and Auer rods. The nuclei are commonly cleaved.

MYELODYSPLASTIC SYNDROME

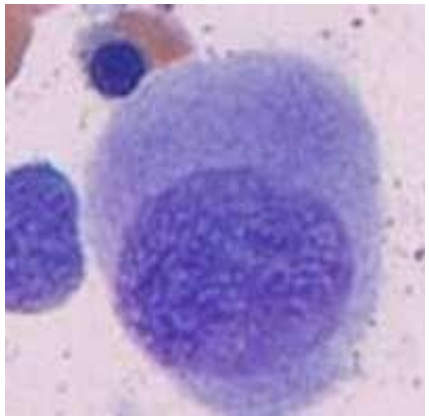
- Main feature is defective maturation, ineffective hematopoiesis, high risk for transformation to AML
- BM is replaced by a clonal progeny of transformed stem cell that has an capacity to differentiate into 3 cell lines but with abnormal morphology and function
- Hallmark of MDS: hypercellular BM, peripheral cytopenia and morphologic dysplasia
- Tendency for accumulating more mutations and transform to AML
- Most cases are idiopathic, rarely follows chemo or radiotherapy (therapy related)
- Most patients are old

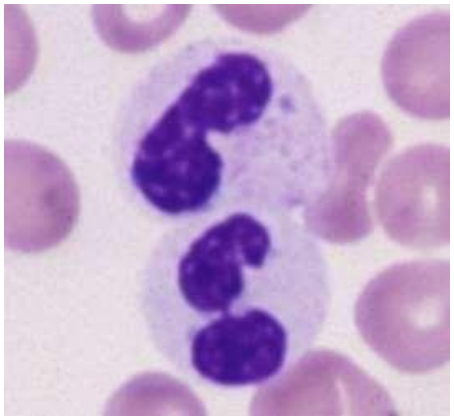
PATHOGENESIS

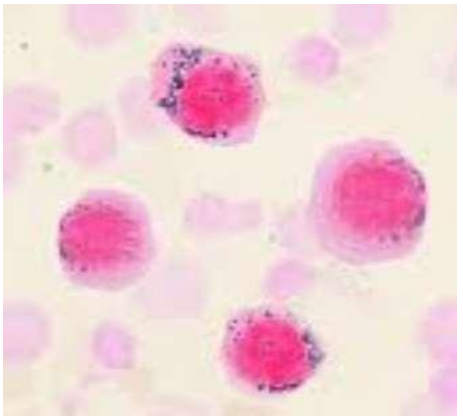
- Chromosomal aberration in 50% of cases: monosomy 5, monosomy 7, deletions of 5q, 7q, 20q, trisomy 8
- Mutations in epigenetic factors that regulate DNA methylation and histone modifications
- RNA splicing factors: abnormal RNA processing → ring sideroblasts
- Transcription factors
- 10% have P53 mutation

MORPHOLOGY

- Erythroid: macrocytic anemia, megaloblastoid nuclei, ring sideroblasts (iron accumulation inside mitochondria)
- Myeloid: decreased granulation, hyposegmented nuclei of neutrophils
- Megkaryocytes: small, hypolobated nuclei
- Myeloblasts: can be increased, but <20% of nucleated cells







SYMPTOMS

- Refractory anemia, thrombocytopenia, neutropenia
- Survival 9-29 months