LEC 13: Introduction to Leukemia

What is Leukemia؟

- Leukemia is a malignant disorder of the hematopoietic system characterized by the uncontrolled proliferation of abnormal white blood cells in the bone marrow and peripheral blood.
- These malignant cells interfere with normal hematopoiesis, leading to bone marrow failure and systemic complications.

Epidemiology

• Leukemia accounts for about 3% of all cancers worldwide.

• It is the most common childhood malignancy, particularly acute lymphoblastic leukemia (ALL).

• Acute myeloid leukemia (AML) is more common in adults, especially the elderly.

• Chronic leukemias (chronic lymphocytic leukemia [CLL] and chronic myeloid leukemia [CML]) are more prevalent in middle-aged and older adults.

Etiology and Risk Factors

Several genetic and environmental factors contribute to leukemia development, including:

A. Genetic abnormalities (e.g., Philadelphia chromosome in CML, RUNX1 mutations in AML).
B. Ionizing radiation exposure (e.g., nuclear accidents, radiation therapy).
C. Chemical exposure (e.g., benzene, chemotherapy drugs).
D. Viral infections (e.g., HTLV-1 in adult T-cell leukemia/lymphoma).
E. Inherited syndromes (e.g., Down syndrome increases ALL and AML risk).

Pathophysiology: Leukemia arises from genetic mutations in hematopoietic stem or progenitor cells, leading to:

A.Uncontrolled proliferation of malignant leukocytes.

A. Failure of differentiation, causing immature (blast) accumulation.
B. Suppression of normal hematopoiesis, leading to anemia, neutropenia, and thrombocytopenia.
C. Tissue infiltration, affecting the liver, spleen, lymph nodes, and CNS.

Classification of Leukemia

Leukemia is broadly classified into two major categories based on the cell lineage and progression rate:

1. Acute Leukemia (Rapid Progression)

A. Acute Lymphoblastic Leukemia (ALL): Affects lymphoid progenitor cells, most common in children.
B. Acute Myeloid Leukemia (AML): Involves myeloid precursor cells, commonly seen in adults.

2. Chronic Leukemia (Slow Progression)

A. Chronic Lymphocytic Leukemia (CLL): Affects mature lymphocytes, mainly in older adults.
B. Chronic Myeloid Leukemia (CML): Characterized by the Philadelphia chromosome (BCR-ABL fusion gene), leading to increased granulocytic proliferation.

Clinical Significance

Leukemia presents with a wide range of symptoms, including:

- Bone marrow failure (anemia, recurrent infections, bleeding tendencies).
- Organ infiltration (hepatosplenomegaly, lymphadenopathy).
- Constitutional symptoms (fatigue, fever, weight loss, night sweats).

Acute Leukemia: Classification & Diagnosis

Definition: Acute leukemia is a malignant disorder of hematopoietic stem cells, characterized by the rapid proliferation of immature white blood cells (blasts) in the bone marrow, peripheral blood, and other tissues. It leads to bone marrow failure, resulting in anemia, infections, and bleeding.

Classification of Acute Leukemia

Acute leukemia is classified based on the lineage of malignant cells:

A. Acute Lymphoblastic Leukemia (ALL)

- Origin: Lymphoid progenitor cells.

• Common in: Children (most common childhood leukemia.(

• Subtypes:

• B-cell ALL (B-ALL) – Most common, affects bone marrow and lymphoid organs.

• T-cell ALL (T-ALL) – Less common, often presents with a mediastinal mass.

• Immunophenotyping Markers:

• B-ALL: CD19+, CD10+, TdT.+

• T-ALL: CD3+, CD7+, TdT.+

B. Acute Myeloid Leukemia (AML)

• Origin: Myeloid progenitor cells.

• Common in: Adults (median age ~60 years..

• Subtypes: (Based on morphology and differentiation

• AML with minimal differentiation.

• AML without maturation.

• AML with maturation.

• Acute promyelocytic leukemia (APL) – Associated with DIC.

• AML with monocytic differentiation – Gingival hyperplasia is common.

• Immunophenotyping Markers: CD13+, CD33+, MPO+ (Myeloperoxidase positive.(

Clinical Features of Acute Leukemia

Acute leukemia presents with a rapid onset of symptoms due to bone marrow failure and leukemic cell infiltration. Key features include:

A. Bone Marrow Failure Symptoms:

a. Anemia: Fatigue, pallor, shortness of breath.
b. Thrombocytopenia: Easy bruising, petechiae, mucosal bleeding.
c. Neutropenia: Recurrent infections, fever.

B. .Leukemic Cell Infiltration:

• Lymphadenopathy: Enlarged lymph nodes (common in ALL).

• Hepatosplenomegaly: Abdominal discomfort and early satiety.

• Bone pain: Due to marrow expansion.

• Gingival hyperplasia: Common in AML with monocytic differentiation.

• Mediastinal mass: Seen in T-cell ALL (causing cough and breathing difficulties.(

C. Disseminated Intravascular Coagulation (DIC):

• Seen in Acute Promyelocytic Leukemia (APL), causing bleeding and clotting issues.

D .CNS Involvement (mainly in ALL): Headaches, vomiting, cranial nerve palsies.

Diagnosis of Acute Leukemia:

A. Complete Blood Count (CBC): Leukocytosis or leukopenia, anemia, thrombocytopenia.

B. Peripheral Blood Smear

• Blast cells >20% in peripheral blood or bone marrow (WHO criteria).

• AML: Large blasts with Auer rods (needle-like inclusions).

• ALL: Small blasts, condensed chromatin, no Auer rods.

C. Bone Marrow Aspiration & Biopsy

• Confirms diagnosis and determines blast percentage (>20% confirms acute leukemia.(

D. Coagulation Studies

DIC panel in suspected Acute Promyelocytic Leukemia (APL)

E. Lumbar Puncture: To assess CNS involvement, especially in ALL.

F. Immunophenotyping (Flow Cytometry)

• Differentiates AML from ALL based on cell markers:

• AML: CD13, CD33, MPO.+

• ALL: CD19/CD10 (B-ALL), CD3/CD7 (T-ALL), TdT.+

Summary Table – Acute Leukemia Classification & Diagnosis

Features	ALL	AML
Cell of origin	Lymphoid progenitors	Myeloid progenitors
Common age group	Children	Adults
Peripheral smear	Small blasts , condensed chromatin	Large blasts , auer rods
Keys markers	CD19, CD10 (B.ALL),CD3(T.ALL)	CD13, CD33, MPO+
Bone marrow	>20% lymphoblasts	>20% myeloblasts
Clinical features	LAD, HSM, CNS involvement	Gingival hyperplasia (monocytic AML, DIC (APL)
Diagnosis	FCM, BMB	FCM, BMB

FCM:flowcytometry, BMB:bone marrow biopsy,LAP: lymphoadenopathy, HSM:hepatosplenomegaly

Dr- Raghda Hameed Jasim
Path/ Heamatology/ M.B.Ch .B-F.I.B.M.S

DR-Thabat Rayes Ashkah
Pediatrics / M.B.Ch .B- MSc