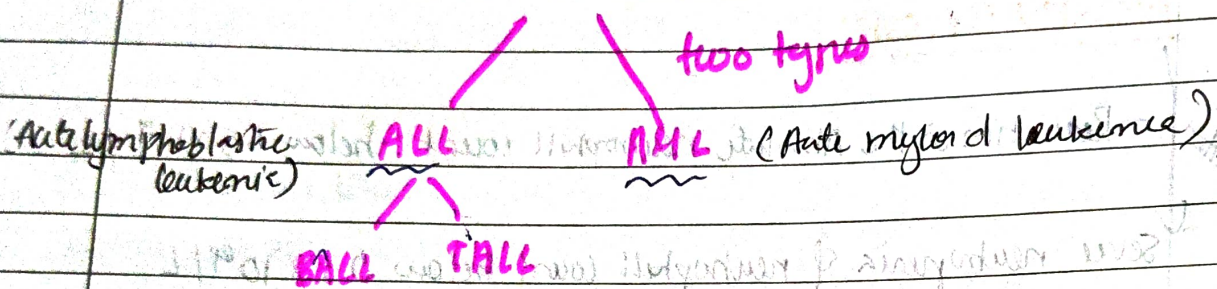


ACUTE LEUKEMIA:

Acute leukemia are a diverse group of malignant tumors characterized by neoplastic proliferation of immature hematopoietic cells.

- The immature cell $\rightarrow$ Blast cells.

$\downarrow$
constitute more than 20% of the nucleated cell in peripheral blood smears.



ETIOLOGY: maybe due to protooncogenes & tumor suppressor gene factors

Environmental factors:

• Ionizing Radiation

• Drugs

- Alkylating Agents - nitrogen mustard, chlorambucil
- Chemotherapy drugs.

• Genetic disorders - Down syndrome, Fanconi's Anemia (AML)

• Acquired Disorders

• PNH & Aplastic Anemia may transform into Acute leukemia.

PATHOGENESIS:

Driver mutation $\rightarrow$ gene Rearrangement & point substitution.

Transcription factor Mutations:

abnormalities of transcription factors
 → X-by driver mutation
 ↓
 normal stem cell differentiation.

Eg: B-ALL contains mutation affecting PAX5.

Complementary Recurrent driver mutations: These mutations affect signalling molecules like tyrosine kinase + of RAS.

Epigenetic Alterations:

Eg: BCR-ABL in ALL (driver mutation)
 PML-RARA in APL
 IDH1 & IDH2 in ALL
 JIA → ALL, AML
 → CML/LL

CLASSIFICATION:

FAB (French, American, British)

↓
 based on morphological & cytochemical changes of blood cells
 ② Immunophenotyping

Cytochemistry

→ study of chemical present in cytoplasm of cell.

⇒ Myeloperoxidase (MPO): present in granules of mature or immature Myeloid cell. (ALL M1, 2, 3, 4) & Acute Rods give +ve colour.
 So Able to differentiate b/w ALL & ALL.

⇒ Sudan Black B (SBB) → stain Myeloid cell (glycosphospholipids in the cell) → Black colour

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VIVA

leukemia $\rightarrow$ Malignant cell in blood
 lymphoma $\rightarrow$ Malignant cell in lymph nodes

$\Rightarrow$ PAS $\rightarrow$ diagnosing ALL

This oxidizes glycogen, mucoproteins, to Aldehydes.

Aldehyde react with PAS $\rightarrow$ pink color.

Myeloblasts are -ve & Lymphoblasts are +ve.

Neutrophil Alkaline Phosphatase (NAP) enzyme localized on granules

present in cytoplasm of neutrophils

NAP/LAP $\rightarrow$ is leucemia or polycythemia.

ALL:

- Neoplasm of lymphoblasts

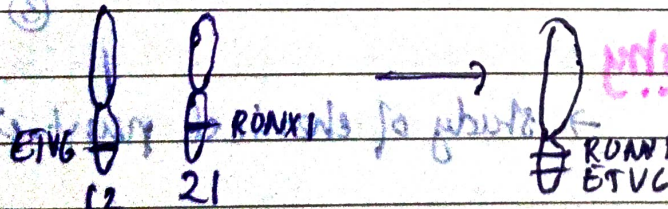
JNA, JJA & B-ALL $>$ B-ALL

most common cancer in children.

PATHOGENESIS:

B-ALL

1) $\rightarrow$ A (12, 21) translocation involving ETV6 & RUNX1 genes in B-ALL



chromosome

2) Mutation in $\rightarrow$ PAX5 gene

$\rightarrow$ TCF3 gene

3) A (9, 22) translocation involving ABL & BCR genes $\rightarrow$ Philadelphia chromosome

TALL

- Mutation in NOTCH1 gene
- mutation that activates tumor suppressor gene PSEN1, APP2A

CLINICAL FEATURES:

- Age - common b/w 1st 5 years of 30-40 years
- Sex - > males
- Onset - Acute with abrupt onset

MOLECULAR

of lymphoma:

BONE MARROW FINDINGS:

- Anemia - fatigue
- neutropenia
- Hypercellular - (packed with lymphoblasts)
- Thrombocytopenia
- First pair of riberal tenderness → Dysplastic expression of architecture of intermediate lymphoid cells

BLOOD:

- Total WBC count ↑
- overall > 20% lymphoblast
- small amount of cytoplasm
- Lack granules
- Therapeutic nuclei
- condensed chromatin
- POX⁺, HPO⁺, SBES

ORGANS

- Mediastinal thymic mass - (common in TALL)
- Lymphadenopathy
- Hepatosplenomegaly
- Testicular enlargement
- CNS involvement

(1421)

Tdt → DNA polymerase
only parent is lymphoblast
X lymphocyte
X myeloblast

IMMUNOPHENOTYPE

(1) common staining

Pre-B of Pre-T lymphoblast → TdT ⊕

(Mamirid deoxynucleotide / precursor)

CLINICAL FEATURES

B cell markers → CD19, CD10, CD20

T cell markers → CD1, CD2, CD3, CD4, CD5 = 8

LAB FINDINGS:

- Hacked ↑ in WBC
- Platelet count ↓
- Hb ↓

- prognostic factors
- 1) Age at diagnosis
 - 2) Initial WBC count
 - 3) Cytogenetics
 - 4) Response to therapy

Peripheral smear

- Normoblastic Normochromic
- WBC ↑ - lymphoblastic

- High N:C Ratio
- condensed nucleus, finely stippled chromatin
- cytoplasm scant to moderate

→ Platelets ↓

Bone Marrow

Cytochemistry

- PAS +ve
- MPO +ve
- SBB ⊕

- Hypercellular
- Erythropo & Myeloid reduced
- Blast 20-100% of marrow cells

Terminal deoxy nucleotid transferase

Biochemical findings

- Serum uric Acid ↑

- LDH ↑

Favorable Prognosis b/w 2-10%

→ Allow cell count

→ Hyperuricemia