WBC Disorders

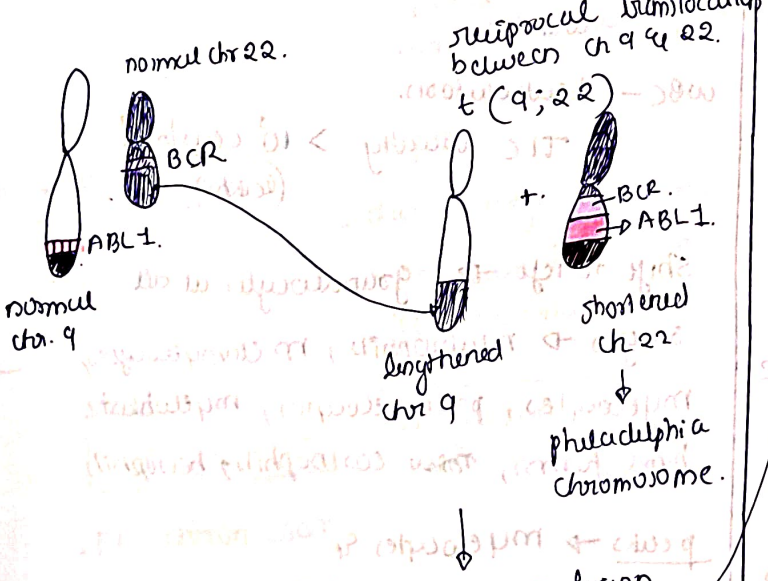
Chronic Myeloid Leukemia (CML)

- chronic myeloid leukemia is a (MPN) myeloproliferative neoplasm characterized by overproduction of cells of myeloid series with prominent granulocytes in blood and bone marrow.
- It harbors BCR::ABL 1 gene associated with marked splenomegaly.

ETIO-pathogenesis

CML is distinguished from other MPN by the presence of

Chimeric BCR-ABL1 gene.



new BCR-ABL fusion gene.

BCR-ABL gene is formed by a balanced (9;22) translocation that moves ABL from long arm of chr 9 to a position on long arm of chr 22 adjacent to BCR.

- this increase length of ch 9 & shortens chr 22.
- this shortened chromosome 22 is known as philadelphia chromosome.

95% → by cytogenic rearrangements.

5% → by cytogenic rearrangements involving more than 2 chr.

new BCR-ABL1 fusion gene → BCR-ABL1 oncoproteins (P210) → tyrosine kinase → activation of growth factor signalling pathways.

- ABL kinase phosphorylate protein that induce signaling through same pro-growth & pro-survival pathways that are turned on by hematopoietic growth factors, including the RAS JAK/STAT pathways.

→ there is excessive production of neutrophils and megakaryocyte progenitors.

Clinical feature

- 30-60 years.
- weakness, fatigue, weight loss etc.
- fullness of abdomen, dragging sensation → splenomegaly.
- hepatomegaly.

DD → Leukemoid reaction.

BCR ABL → Karyotyping.
FISH
PCR assay.

STAGES OF CML

(1) Chronic phase.

- most are diagnosed in this phase.
- Leukemia cells retain capacity for differentiation and maturation
- disease is responsive to chemotherapy.
- duration : 3 - 5 years.
- If not treated can go to accelerated / blastic phase.

(2) Accelerated phase

- more aggresive.
- 70% Chronic p ——→ accelerated phase.
- Leukemic cells shows increasing loss of differentiation & maturation.
- Increased proliferation & resistance to chemotherapy.
- span - few months.
- myeloblast - 10-19% in blood or bone marrow.
- Staining Basophilia. (>20%)
- persistent thrombocytopenia
- megakaryocyte proliferation in sheets / clusters. + fibrosis
- persistent / ↑ splenomegaly unresponsive to therapy.

Blast phase.

- Blood picture resembles acute Leukemia & has poor prognosis
- Extremely resistant to chemotherapy.
- median survival.
  2 - 6 months.
- blasts 20% or more. myeloblast (no auer rod) / lymphoblast.

LAB Diagnosis

peripheral Blood smear findings

RBC - normocytic normochromic anemia

WBC - Leukocytosis.
TLC usually > 10^5 cells/mm^3 (1 lakh).

Shift to left → granulocyte at all stages → neutrophils, metamyelocytes, myelocytes, promyelocytes, myeloblasts, band forms, eosinophils, basophils

peaks → myelocytes & segmented neutrophils.

Basophilia - Imp for diagnosis since it is rare in other ds.

- Blasts < 10% of circulating WBC.
- decreased NAP/LAP score.
  < 20 (N - 40 - 100).
  Helps to diff btw CML & Leukemoid rxn.
- platelets → Increased.
  (50%) thrombocytosis.
- spleen is enlarged due to Extramedullary hematopoiesis.

Diagram ✱.

Marrow findings

Cellularity : marked hypercellularity due to myeloid hyperplasia.

- M:E ratio : Exceeds 20:1
- Erythropoiesis : diminished as disease progresses
- Myelopoiesis : marked hyperplasia.
  Blast cells < 10%.
  Basophils, eosinophils & precursors are usually found.
- Megakaryopoiesis : N/↑
  - dwarf megakaryocytes.
  - Sea blue histiocytes.
    Granulomatous cells?

Cytogenetics - confirmatory.

- Ph chromosome
- karyotyping
- FISH
- PCR assay.