CML

Normal Count

- RBC: 4.5-5.5 millions/dL
- Platelet: ~~1.5-4~~ 4-5 lakhs/dL
- WBC: 4000-11000/dL

TLC ↑↑↑.

Characterised by – 1) Leucocytosis with granulocytic immaturities (10,000 – 2 lakhs).

2) Basophilia

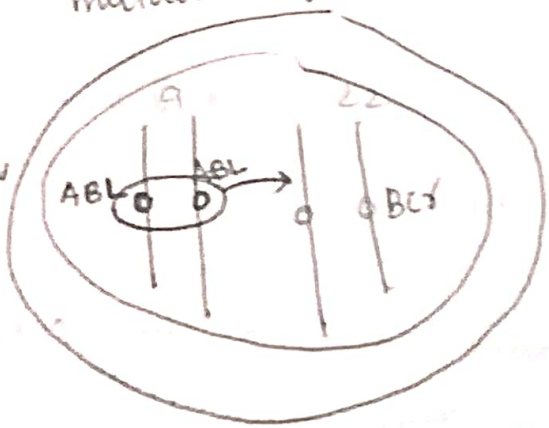
3) Splenomegaly (massive).

4) Distinct chromosomal abnormality – Philadelphia chromosome

Age: > 50 yrs

Pathogenesis:-

mutation of (9 & 22)



It can be in any of the precursors (MB, PM, M, MM, BI)

Due to physical, chemical, biological agent

↓

Translocation (abl gene in 9th chromosome move to 22nd chromosome it reaches and fuse with bcr gene) → known as

fusion gene → leads to uncontrolled mitosis

(enzy tyrosine kinase)

22nd chromosome is giving a portion of it which doesn't contain any gene

→ It is known as philadelphia chromosome.

ABL - BCR fusion gene

Treatment:-

Targeted therapy - Imitinib (oral tablet)

↓

apoptosis of all cells having fusion gene. ; also inhibit abnormal tyrosine kinase.

t(9; 22)

↓ ↓

(abl-bcr)

Pathogenesis as flow chart.

ABL gene (normal on chromosome 9)

↓

translocated to chromosome 22

↓

Fuse with BCR gene

↓

ABL-BCR hybrid gene → philadelphia chromosome

↓

210 KD fusion protein

↓

Abnormal (tyrosine kinase) → signal transduction even without growth factors

↓

Uncontrolled mitosis

↓

CML

Based on the blast there are 3 phases (Leukemia)

Chronic phase	Accelerated phase	Blast crisis
C	A	B
Blast cells <10%	Blast cells 10-19%	>20%.

Clinical features:

A. Due to bone marrow failure
- a) Anemia — pallor, lethargy, dyspnoea
- b) Bleeding manifestations → spontaneous bruises, petechiae, bleeding from gums
- c) Infections

B. Hypermetabolism
- ↳ weight loss
- ↳ lassitude
- ↳ anorexia
- ↳ night sweats

C. Splenomegaly → massive

Lab diagnosis

Blood
- a) Hb ↓
- b) Platelet ↓
- c) WBC ↑↑

Bone marrow
- a) Cellularity
- b) Myeloid cells ↑
- c) Erythropoiesis ↓
- d) Megakaryopoiesis ↓

Cytogenetics
- Cytogenetics
- Karyotyping
- t(9;22)

Cytochemistry
- NAP scores ↓

Others
- S. uric acid ↑

Blood picture
- Normocytic normochromic (anemia)
- Thrombocytopenia
- Marked leucocytosis (> 200,000/μl or more)

Garden party appearance
- Immature neutrophils (BF, MM, M, PM)
- Basinophilia; Eosinophilia.

II Bone marrow → a) Hypercellularity (proliferating myeloid cells)
b) Myeloid cells → predominate in bone marrow with ↑ myeloid erythroid ratio
c) Erythropoiesis → Reduced
d) Megakaryocytes → Reduced

III Cytogenetics - show characteristic chromosomal abnormality → philadelphia (Ph) chromosome → t(9;22) → BCR/ABL fusion gene.
- Conformatory (very expensive)
- ~~special stain~~

IV Cytochemistry - special stain : NAP (Neutrophil alkaline phosphatase)
→ high lights granules
→ [NAP/LAP score will be less in CML]
→ Leukaemoid rx → NAP score ~~reduced~~ elevated.

Leukemoid Reaction

→ WBC count - 50,000 - 1,00,000.
→ WBC is reactive in response to exogenous agents like infection.

Defn: reactive excessive leucocytosis in peripheral blood resembling that of leukaemia in a subject who doesn't have leukaemia.

- Blood picture confusing with CML.
- Clinical features of CML is absent

Causes — Infections
Intoxications
Malignant diseases
Severe hemorrhage and severe hemolysis

Lab findings

1) Leucocytosis - never exceeds 1 lakh

2) Proportion of immature cells less than 5%.

3) Infective cases show → toxic granulation & Dohle bodies

4) NAP score elevated

5) Cytogenetic studies → negative.

Treatment of CML.

1) Treatment of anaemia & haemorrhage
   a) blood transfusions
   b) platelet transfusions.

2) Imatinib oral therapy
   a) Inhibits signal transduction BCR/ABL fusion protein
   b) Induces apoptosis in BCR/ABL +ve cells & eliminates them

3) Allogenic bone marrow transplantation

Differences b/w LR & CML

Feature	Leukemoid Rn	CML
TLC ✓	25,000 - 100,000/ml	> 1 lakh.
DLC	→ Dominant cells PMN's ✓ → normal basophils ✓	→ All maturation stages → Basophilia pr.
NAP score	elevated ✓	Reduced ↓
Philadelphia Chromosome	Absent	Present ✓
ABL - BCR fusion gene	Absent	Present
Major etiology	Infections Intoxication	Genetic factors radiations. chemicals, drugs
Organ infiltration	Ab	P (rare)
Massive splenomegaly	Ab ✗	P ✓