AML Acute Myeloid Leukemia — Infiltration of malignant myeloid cells into blood, bone marrow and other tissues.

Age 15 → 40

Pathogenesis: Difference from CML is that mutation occur only in myeloblast in case of AML while in CML it occur in all precursor cells.

mutation

- t(8;21) → M2
- t(15;17) → M3
- inv(16) → M4

School uniform appearance

8 types of ~~Class~~ AML based on FAB classification.

(M0 → M7)

- M0 → AML ~~without~~ with minimal differentiation
- M1 → AML without maturation
- M2 → AML with maturation
- M3 → Acute PM L (promyelocytic) → DIC
- M4 → Acute MM L (myelomonocytic)
- M5 → Acute M L (monocytic)
- M6 → Acute E L (erythrocytic)
- M7 → Acute Meg L (megakaryocytic)

NOTE: → myeloperoxidase.

→ All are MPO negative positive except M_0 which is negative.

M_0 – MPO (-Ve)

M_1 –

most common ← (M_2) – t (8; 21) present; max. chances of chloroma

M_3 – t (15; 17) present; max faggot cells; DIC

M_4 – inv(16); PR of both myeloblast & monoblast

M_5 – t (9; 11); highest incidence of tissue infiltration, organomegaly & lymphadenopathy

M_6 – Abnormal erythroid precursor seen.

least common ← (M_7) → Least common type

→ Common in Down's syndrome

→ Megakaryocytes are seen

→ Release of platelet derived growth factors (PDGF) cause myelofibrosis

Clinical features

A. Due to bone marrow failure – same as that of CML

Lymphoma feature of (AML) not CML

B) Due to organ infiltration by leukaemic cells →

a) Bones - pain & tenderness ✓
b) Lymphadenopathy ✓
c) Splenomegaly ✓
d) Hepatomegaly ✓
e) Kidney → Leukemia infiltrations ✓
f) Gum hypertrophy → Common in AML M4 & AML M5
g) Chloroma or granulocytic sarcoma → localized tumor forming mass occuring in skin of orbit (proptosis) → common in AML M2.

Lab diagnosis

I Blood picture:

→ RBC ↓
→ Platelet ↓
→ WBC - Only one type cells - MYELOBLAST ↑
- presence of auer rods (max in M3)

Myeloblast (auer rods)
↓
Faggot cell.

II Bone marrow examination

1) hypercellular
2) myeloblasts > 20% ; auer rods +.
3) Erythropoiesis — reduced
4) Megakaryocytes — reduced

III Cytogenetic $M_2 - t(8;21)$
$M_3 - t(15;17)$
$M_4 - inv(16)$

APML → patient immediately goes to DIC.

IV Cytochemistry.

	AML	ALL
a) MPO	+	−
b) Sudan Black	+	−
c) NSE	+ (M_3, M_4, M_5)	−
d) PAS	− (+) in M_6	+
e) Acid phosphatase	−	+

V Treatment → 1) Treatment of Anaemia & Haemorrhage

2) Cytotoxic Drug Therapy a) Cytosine arabinoside
b) Anthracyclines (
c) 6-Thioguanine

PM leukemia (M_3) – Tretinoin (Lectinoic acid) ATRA

3) Allogenic bone marrow transplantation

Prognostic factors.

Good
- Age < 40 yrs
- M_2, M_3, M_4 form of AML
- Blast cell with auer rods
- TLC < 25×10^9/L
- t(15;17), t(8;21), inv16
- Leukemia without preceding MDS

Bad.
- Age < 2 yr or > 55 yrs.
- M_0, M_6, M_7 forms of AML
- complete karyotypes
- TLC > 100×10^9/L
- Deletions 5q, 7q
- AML with preceding MDS or anticancer drug exposure

ALL → All composed of immature, precursor B (pre-B) or T (pre-T) lymphocytes → lymphoblast.

Age
1) Pre B-cell ALL → 3-5 yrs
2) Pre T-cell ALL → Adolescent male

Pathogenesis → Pre B cell ALL → Hyperdiploidy
(190 KD)
→ Hypodiploidy
→ loss of fn mutations → PAX5, E2A, EBF gene
→ t(9;22) translocation (BCR & ABL)

→ Pre T cell ALL → Gain of function mutation (NOTCH 1 gene)
(210 KD)

CML (9;22) 210 KD
ALL (9;22) 190 KD

ALL
→ L1 (→ commonest) Best
→ L2
→ L3 (rare) worse prognosis

Clinical features:-

A) Due to BM failure → ; same.
B) Organ filtration
a) Bone pain Tenderness
b) LymphA
c) Splenomy
d) Hepatomy
e) compression of mediastinal vessels or airway - by pre-T ALL

ALL {
f) Meningeal involvement / CNS
g) testicular involvement
}

Lab diagnosis

I Blood picture → RBC ↓
→ platelet ↓
→ WBC — same type (lymphoblast)

II BM → high cellularity ✓
→ 30 % blast cells in BM (lymphoblast)
→ EP ↓ ✓
→ MK → ↓ ✓

III Cytogenicity
IV Cytochemistry → NSE - Non-specific esterase (-)
→ Periodic acid Schiff (+)
→ Acid phosphatase (+)

(Children only on ALL)

Treatment

BM transplant → major option

Prognostic factors

Criteria	Good	Bad
Age	2 - 10 yrs	< 2 yrs & > 10 yrs
Gender	♀	♂
Race	White	Black
CNS mediastinum, testicular involvement	Ab	Pr
blood count	$< 10 \times 10^4$	$> 10 \times 10^4$
cytogenetics	Hyperdiploidy	Hypodiploidy t(9;22)

CLL / SLL → Small Lymphocytic Lymphoma
Chronic lymphocytic leukemia.

→ Neoplasms arise due to an abnormal neoplastic proliferation of B cells

→ Age → median age of 60yrs

→ mature mutated lymphocytes come in the blood.

Pathogenesis → Deletion of 13q (most common), 11q, 17q
→ Trisomy of 12q

Clinical features

A) ✓ same

B) enlarged superficial lymph nodes

C) Hepatosplenomegaly

lab diagnosis — Blood

Smudge / basket cells
↳ ruptured lymphocytes

Blood picture
90% lymphocytes

Immunophenotyping
CD 19 (B-cells) markers
CD 20
CD 23
CD 5
surface IgM & IgD

Lymph node biopsy → Diffuse Proliferation pseudofollicles