AML (Acute Myeloid Leukemia)

→ Accumulation of immature myeloid blasts in marrow

→ Adults

Classification:-

FAB classification ⇒

AML - M_0 → AML undifferentiated

AML - M_1 → AML w/o maturation

AML - M_2 → AML ε maturation

AML - M_3 → Acute promyelocytic leukemia (APML)

AML - M_4 → Acute myelomonocytic leukemia

AML - M_5 → Acute monocytic leukemia

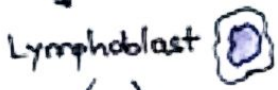
AML - M_6 → Acute erythro leukemia

AML - M_7 → Acute megakaryoblastic leukemia

Normal Hematopoiesis

Adults,

Blood cells start their life in Bone marrow as HSC



GRANULOCYTES

plasma cell

LYMPHOCYTES

WBC (Leucocytes)

WHO classification ⇒

(I) AML c genetic abbretions ⇒

(i) AML c t(8;21)(q22;q22) → RUNX1/RUNX1T1 fusion gene

(ii) AML c inv(16)(p13;q22) → CBFB/MYH11 fusion gene

(iii) AML c t(15;17)(q22;11-12) → RARA/PML fusion gene

(iv) AML c t(11q23:v) → KMT2A fusion gene

(v) AML c normal cytogenics & mutated NPM1

(II) AML c MDS like features ⇒

(i) with prior MDS → Dx based on clinical history

(ii) AML c multilineage dysplasia → Dysplastic cell typical of MDS

(iii) AML c MDS like cytogenic abbretions → 5q, 7q, 20q abbretions

Pathogenesis :-

→ Mutation involving normal myeloid differentiation.

① t (8; 21) :→ RUNX1 / RUNX1T1 fusion gene
⇊
Blocks maturation of myeloid cells

② inv (16) :→ CBFB / MYH11 fusion gene

③ t(15; 17) :→ RARA / PML fusion gene
↳ Retinoic Acid Receptor α

→ Mutation → constitutive activation of progrowth signalling pathway.

① Activating mutation in (FLT3)
↳ Receptor tyrosine kinase

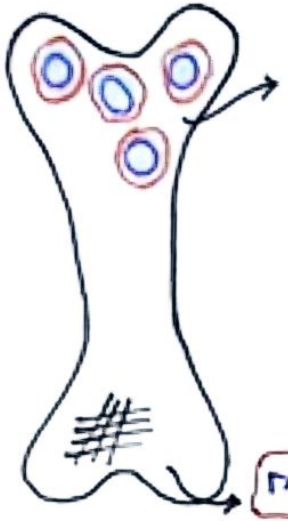
→ Mutation that maintain/regulate epigenome

① Mutation leading to abnormal DNA methylation

② IDH mutated AML

→ Mutation of Tp53

Morphology :-



> 20% myeloblasts in bone marrow
- → delicate chromatin
- → 2-4 nucleoli
- → more voluminous cytoplasm than Lymphoblast
- → Azurophilic granules

↓

Sometimes take form of **Auer rods** (mostly in APML)

Marrow fibrosis

{ AML & megakaryocytic differentiation → Fibrogenic cytokines → Fibrosis }

- Sometimes, in blood → (Blasts = 0)

↓

Aleukemic leukemia

(∴ BM examination is necessary)

	Lymphoblast	Myeloblast
• Size	Small	Large
• Amnt of cytoplasm	↓	↑
• Granules in cytoplasm	⊖	⊕
• Auer rods	⊖	⊕
• Chromatin	condensed	opened up/delicate
• Nucleoli	1 (inconspicuous)	2-5 (prominent)
• Stains	PAS +	MPO +

Immunophenotyping :-

- $CD34^+$ → marker of immature myeloid blasts
- $CD64^-$ → marker of mature myeloid cells
- $CD33^+$

Clinical features :-

1) Anemia → Pallor, fatigue
2) Neutropenia → ↑ risk of infection
3) Thrombocytopenia → ↑ bleeding tendency
4) Fever
5) Tumor ē monocytic differentiation
   ↓
   infiltrate → Skin (Leukemia cutis)
   infiltrate → Gingiva
6) Localised soft tissue mass
   K/a - myeloblastoma/myeloid sarcoma/chloroma