Acute Leukemia

Acute Myeloid Leukemia (AML)

- at all ages groups (more common in elderly)
- Heterogenous

Diagnosis
- Morphologic
- cytochemical / immunophenotypic
- cytogenetic / Karyotype

* prognosis Depend Most importantly on Types of Mutations
- Molecular
- cytogenetic studies

-> Symptoms: accelerated (within weeks)
- Anemia
- Thrombocytopenia
- Neutropenia (& Monocytosis)

(rare)
* involvement of => Acute Monoblastic Leukemia
- LN
- spleen
- Solid organs
- Name became (Myeloid Sarcoma)

* Maturation & Differentiation of Myeloblasts is common 20% & requires Mutations
- Mutations in tyrosine kinase pathway (RAS)
- Mutations in genes of transcription factors
- Epigenetic Mutation => isocitrate dehydrogenase (IDH) => produce oncometabolite => block Enzyme of Epigenome

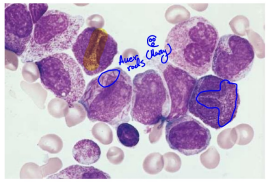
interferes with Myeloblast differentiation (Must will)

We can use this information for New promising Drug

Acute promyelocytic Leukemia (AML-M3)

- Malignant promyelocyte secrete Tissue factor causing => DIC
* Maturation arrested at promyelocytic stage
- Leukemic cells appear similar to promyelocytes (Morphology)
- Heavy cytoplasmic granules
- Numerous Auer rods
- -ve for CD34

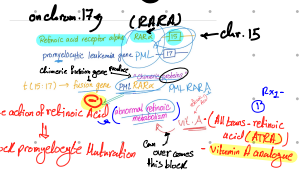
while (AML) is (+)



* APL: malignant promyelocytes show numerous cytoplasmic granules and Auer rods. The nuclei are commonly cleaved. *

* Carry recurrent Mutation:

t(15;17) fusion between PML gene on chromosome 17 (RARA) chr. 15



Precursor B & T cell Neoplasms

* lymphoblastic lymphoma when occurs in solid tissue T > B

Lymphoblastic
- Lymphoma (LL) => when occures in solid tissue
- Acute Leukemia (ALL) => when circulates peripheral blood & involve BM

T > B
- B-LL
  - Mutation in PAX5 gene
  - * Mutation in proteins
    - RAS Signaling
    - & tyrosine Kinase
    - => promoting cell survival

B > T
- B-ALL
  - * The Most common childhood Malignancy
  - tend to disseminate to solid organs
    - Brain
    - testis
    - spleen
  - => * Neoplastic cells are => lymphoblasts & the Most immature lymphoid cell
  - => Aggressive Neoplasms Express CD34, TDT
  - => * Most childhood B-ALL have hyperdiploidy (>50 chromosomes) & t(12;21) involving ETV6 & TUNX1 genes creating New transcription factor
  - => Adult B-ALL Exhibits
    - t(9;22) between (ABL & BCR) genes creating New Tyrosine Kinase protein
    - * similar to chronic Myeloid Leukemia
    - Rx: imatinib

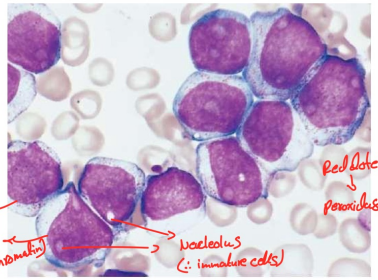
- T-ALL
  - less common
  - presents in adolescents
  - involving Thymus
  - (More common in boys)
  - * Mutation in
    - NOTCH1 gene (70% of cases)
    - PTEN gene => tumor Suppressor
    - CDKN2A => promotes Cell cycle

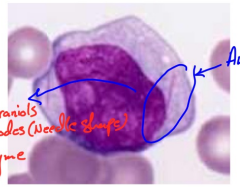
* Mutations in transcription factors for genes responsible for Maturation of Blasts

AML could be according to WHO classification

1. Therapy related AML
   - occurs after treatment with (chemo or radiotherapy)
2. AML with recurrent cytogenic Mutation
3. AML with Myelodysplasia (occurs) De Novo or complicates MDS
4. AML - Not otherwise specified (if -ve for all the before)

* Diagnosis of AML => 20% blasts in peripheral blood or BM (of nucleated cells)





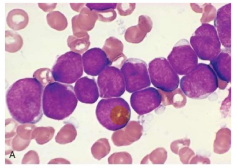
- Morphology: large cells, high N/C ration, fine granules in cytoplasm, fine chromatin, prominent nucleoli (large Nucleus)
- Auer rods: small pink rods present in cytoplasm, represent peroxidase enzyme
- Myeloblasts express CD34, myeloperoxidase (MPO), CD13, CD33 (Markers)
- Sometimes: monoblast, erythroblast, megakaryoblast (No in Myelocyte)

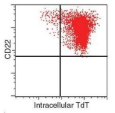
* outcome

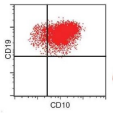
- Generally poor 😔
  - <30% responds to chemotherapy
- P53 Mutation ⇓ Worse outcome
- IDH inhibitors are New promising drugs

MORPHOLOGY OF ALL

- Blasts are large, high N/C ration
- Chromatin is open (pale)
- Nucleolus sometimes present
- Cytoplasm is not granular (agranular)
  - ∴ Very Minimal







+ B-acute

CLINICAL FEATURES

- Anemia, thrombocytopenia
- Bone pain
- Lymphadenopathy and hepatosplenomegaly
- Testicular enlargement
- Mediastinal mass (T-ALL)
- CNS involvement
- Damage to solid organs secondary to leukemic infiltration
- Favorable prognostic factors in B-ALL: hyperdiploidy, low WBC count, age between 2-10 years ← children
- Poor prognostic factors in B-ALL: age < 2 years, age in adolescents or adults, WBC count >100k

WBC < 50K

Dendritic cell

(APC) Antigen presenting cell

Langerhans cell Histiocytosis

(LCH)

* Neoplasm of Dendritic cells
* Langerhans cells express CD1a & Langerin
  - Langerin ⇓ transmembrane protein ⇓ attached to Birbeck granules (tennis racket shape under electron Microscope)
* proliferating Langerhans cells ⇓ Appear large & vacuolated (similar to Macrophages)
* Pathogenesis
  - Aquired Mutation in Serin/Threonine Kinase BRAF ⇒ lead to its Hyperactivity

LCA

Multisystemic LCA

*** Mostly in children < 2 years**

* symptoms *

- Multiple cutaneous lesion composed of LCs (Langerhans cells)
- Hepatosplenomegaly & lymphadenopathy
- pulmonary lesions
- osteolytic lesions
- Extension BM infiltration ⇓ leads to **pancytopenia**
  ⇓ Multi ـ بعكس الكل

*** Treated with chemotherapy ***

UNI systemic LCH

أكثر شغلة وحدة → *** ARA eosinophilic granuloma**

(Most commonly) * Affect a single organ * (less common)

1. Bone
2. Skin
3. lung
4. stomach

* can be *

unifocal

- commonly Asymptomatic
- Can cause pain

Rx ⇒ - Surgical Excision

Multifocal unisystem Disease

1 بـ ← uniLCH ← أمابع Multifocal

* Hand-schuller-christian triad *

- present in children
- Commonly affect Calvaria bone
  - * Parts of frontal Bone *
- Extends to pituitary gland ⇓ causing Diabetes insipidus
- Exophthalmous (بروز العين.)

Rx ⇒ - chemotherapy

* sometimes spontaneous regression

(Microscopy)

* proliferating LCs admixed with * Numerous

- Eosinophils
- lymphocytes
- plasma cells
- Neutrophils

← هاد ال uni لحاله بسايرهم وبزيدو