AML affects which age ?

Occur at all age groups, but more common in elderly

Heterogenous

All patients of AML appears the same or there is variables between them?

The Diagnosis of AML is made by ?

1- morphologic
2- immunophenotypic
3-karyotype (type of mutation)

The prognosis of AML depends most importantly on .....

type of mutations (molecular and cytogenetic studies

The symptoms of AML are (slow or accelerated )

accelerated, become significant within few weeks

The symptoms of AML are related to .....

1-anemia
2-thrombocytopenia
3-neutropenia

AML cells (loves or rarely) leaves the blood stream and go to LN, spleen and solid organs

Rarely

If AML cells leaves the blood stream and go to LN, spleen and solid organs , what we call this ?

myeloid sarcoma (acute monoblastic leukemia)

The mutations that lead to AML affect which genes?

Mutations in genes of transcription factors required for maturation and differentiation of myeloblasts .
(The cells stay in the blast stage) (maturation arrest)

What are all the mutations that happens in AML ?

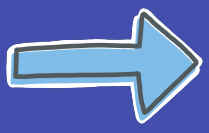
1-Mutations in genes of transcription factors required for
maturation and differentiation of myeloblasts

2- Additional mutations in tyrosine kinase pathways (RAS)

3- Epigenetic mutation is common (20%); mutation is isocitrate
dehydrogenase (IDH) produces an oncometabolite that blocks enzyme of epigenome and interferes with myeloblast differentiation

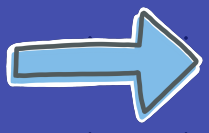
(RAS , IDH)

In AML , the mutation of isocitrate dehydrogenase (IDH) produces what ?



an oncometabolite that :
1-blocks enzyme of epigenome
2-interferes with myeloblast differentiation

What is the WHO-classification of AML ?



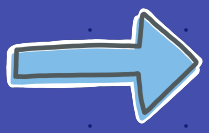
1-Therapy related AML: occurs after treatment with chemo or radiotherapy

2- AML with recurrent cytogenetic mutation (common translocations)

3- AML with myelodysplasia: occurs de novo or complicates MDS

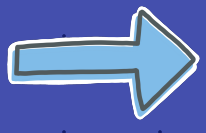
4-AML-Not otherwise specified

When can we say that this patient has AML ? (Diagnosis)



20% blasts in peripheral blood or bone marrow (of nucleated cells)

What is the morphology of AML ?



1- large cells
2-high N/C ration (large pale nucleus with nucleolos)
3-fine granules in the cytoplasm (two shapes : rods , granules)
4-fine chromatin
5-prominent nucleoli

What is the special name of the appearance of peroxidase enzyme in AML ?

Auer rods: small pink rods present in cytoplasm, represent peroxidase enzyme

What are the markers of Myeloblasts ? Express some special proteins what are they?

1-CD34 (appears in myelo and lympho plasts)
2-myeloperoxidase (MPO) (only in the myeloblast)
3-CD13
4-CD33

Describe the outcome of AML

Generally poor, <30% responds to chemotherapy

Which one is the worst between this two (AML or ALL)

AML

The outcome will be worse

If there is a P53 mutation in AML this will tell us what ?

What is the treatment of AML ?

1-<30% responds to chemotherapy
2-IDH inhibitors are new promising drugs

What is the other name of acute promyelocytic leukemia?

AML-M3

In acute promyelocytic leukemia , the Maturation is arrested at which stage ?

promyelocyte

Describe the morphology of acute promyelocytic leukemia

1-heavy cytoplasmic granules
2-numerous Auer rods
3-negative for CD34 (remember only with blasts)
4-The nuclei are commonly cleaved.

What is the mutation of acute promyelocytic leukemia ? And what is the result of this mutation?

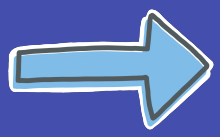
t(15;17) fusion between PML gene
(chrom 15) with alpha retinoic acid receptor (RARA) on chrom 17.

Result :
Chimeric fusion gene produces a protein that blocks promyelocyte maturation by inhibiting the action of retinoic acid (Vit A)

What is the treatment of acute promyelocytic leukemia ?

1- All trans-retinoic acid (ATRA) a vitamin A analogue, overcomes this block.
2-Effect is synergistic with arsenic trioxide (degrades oncoprotein)

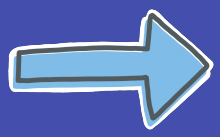
What is the cause of death in acute promyelocytic leukemia ?



(Bleeding)

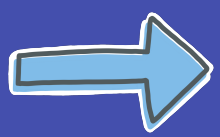
Malignant promyelocyte secrete tissue factor, causing DIC

Lymphoblastic lymphoma when occurs in solid tissue (Type B or T ) is more common



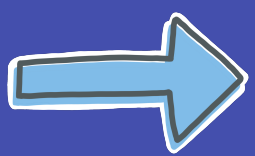
T

Acute lymphoblastic leukemia when circulates peripheral blood and involve bone marrow (Type B or T ) is more common



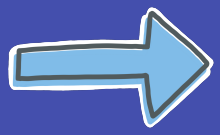
Type B

What is the most common childhood malignancy ?



B-ALL

What are the type of cells that appear in ALL ? (Which stage )



Neoplastic cells are lymphoblasts, the most immature lymphoid cell.

| | | |
|---|---|---|
| ALL is an (Aggressive or benign) neoplasms | → | Aggressive |
| ALL cells express which proteins? | → | 1-CD34<br>2-TDT |
| In general Which one is more common (T or B) ALL ? | → | B |
| T ALL present in (adolescents or boys ) ? | → | In Both but in boys more common |
| T ALL involves thymus (Yes or No) | → | Yes |
| B-ALL tends to disseminate to which solid organs ? | → | (brain, testis,spleen)<br>But remember that it appears more commonly in the peripheral blood and the Bone Marrow |

The mutations that lead to ALL affect which genes?

Mutations in transcription factors for genes responsible for maturation of blasts

In B-LL, mutation in ..... gene

PAX5

Most childhood B-ALL have which mutations?

hyperdiploidy (>50 chromosomes) and t(12;21), involving ETV6 and TUNX1 genes, creating new transcription factor.

Adult B-ALL have which mutations ?

Adult B-ALL exhibits t(9;22) between ABL and BCR genes, similar to chronic myeloid leukemia, creating a new tyrosine kinase protein (imatinib)

What is the name of the drug that targets the new tyrosine kinase protein that results from the t(9;22) between ABL and BCR genes?

imatinib

t(9;22) between ABL and BCR genes appears in which type of leukemia?

1- Adult B-ALL
2-chronic myeloid leukemia

T-ALL shows mutation in .....

NOTCH1 gene (70%of cases), PTEN gene (tumor suppressor) and CDKN2A (promotes cell cycle)

What are the clinical features of ALL ?

1- Anemia, thrombocytopenia and neutropenia
(Bone pain , Lymphadenopathy and hepatosplenomegaly , Testicular enlargement , Mediastinal mass (T-ALL) and CNS involvement )

2-Damage to solid organs secondary to leukemic infiltration

In terms of prognosis, there are two classifications for B-ALL what are they?

Favorable prognosis

Poor prognosis

What are the Favorable prognostic factors in B-ALL ?

1-hyperdiploidy
2-low WBC count
3- age between 2-10 years

What are the Poor prognostic factors in B-ALL?

1-age < 2 years
2- age in adolescents or adults
3-WBC count >100k

Describe the morphology of ALL :

1-Blasts are large, high N/C
ration
2-Chromatin is open (pale)
انتبه لكلمة open
3- Nucleolus
sometimes present
4-Cytoplasm is
not granular

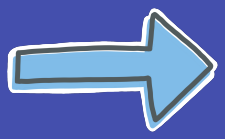
What are the B cell markers ?

CD 22
CD19

What are the T cell markers?

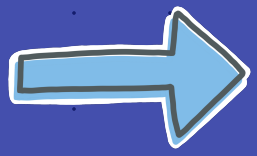
CD3, CD4, CD8

Langerhans cell histiocytosis is a neoplasm of which cell ?



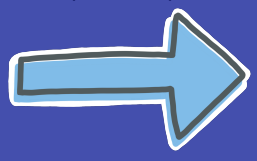
dendritic cells (Langerhans cell)

Langerhans cells express which cell markers ?



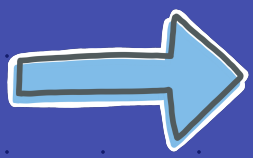
CD1a , Langerin

What is Langerin ?



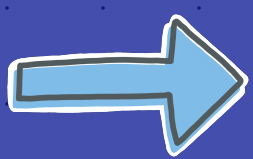
transmembrane protein, attached to Birbeck granules (tennis ricket shape under electron microscope)

Describe the morphology of the Proliferating Langerhans cells :



large and vacuolated, similar to macrophages

What is the mutation in Langerhans cell histiocytosis ?



acquired mutation in serin/threonine kinase BRAF, leads to hyperactivity of this kinase

We have two types of LCH what are they?

1- Multi systemic LCH
2-UNInsystem LCH

Multi systemic LCH Occurs mostly in ..... (مين اكثر اشخاص بصيبهم)

children less than 2 years

What we can see in patent that have Multi systemic LCH ?

1-Multiple cutaneous lesion, composed of LCs (most)
2-Hepatosplenomegaly and lymphadenopathy
3-Pulmonary lesions
4-Osteolytic lesions
5-Extensive bone marrow infiltration leads to pancytopenia

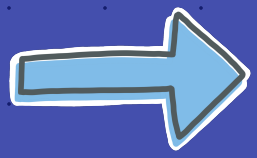
Multi systemic LCH Treated with .....

chemotherapy

What is the other name of UNInsystem LCH ?

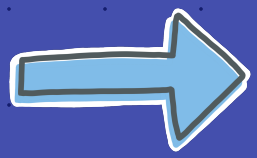
eosinophilic granuloma

UNInsystem LCH affects a single organ, most commonly .....



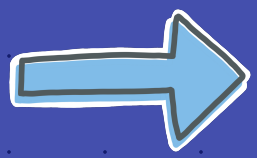
1-bone (most common)
2-skin
3- lung
4-stomach

There are two types of unisystem LCH what are they?



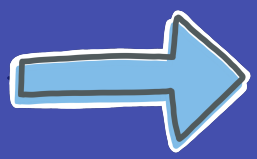
1-unifocal
2-multifocal

Unifocal unisystem LCH is commonly ( symptomatic or asymptomatic)
And it is (painful or painless)



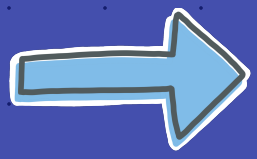
asymptomatic , painful

Multifocal unisystem disease presents in .....



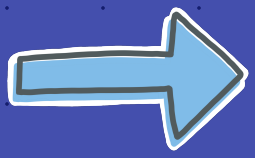
Children

Mulfocal unisystem disease commonly affects .....



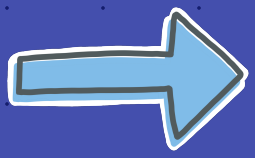
calvaria bone, extends to pituitary gland causing diabetes insipidus, exophthalmous (Hand-Schuller-Christian triad).

What is Hand- Schuller-Christian triad and appears in which disease?



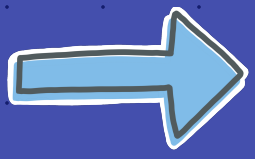
Mulfocal unisystem disease presents in children, commonly affects calvaria bone, extends to pituitary gland causing diabetes insipidus, exophthalmous

Proliferating LCs are admixed with ..... (Unisystem LCH)



numerous eosinophils, lymphocytes, plasma cells and neutrophils

What is the treatment of unisystem LHC ?



1-unifocal:
surgical excision
2-multifocal:
chemotherapy, sometimes spontaneous regression