Leukemia

Dr . Asaad Issa
Dept. of pediatrics, college of Medicine
University of Basra

Learning Objective

1-To figure the type of leukemia

2-What is clinical feature of leukemia.

3-How do you differentiate from other disease.

4-The aim of treatment.

5-How to deal with family and child with cancer

Introduction

- Leukemias are the most common malignant neoplasms in childhood

- The leukemias may be defined as a group of malignant diseases in which genetic abnormalities in a hematopoietic cell give rise to an unregulated clonal proliferation of cells. The progeny of these cells have a growth advantage over normal cellular elements because of their increased rate of proliferation and a decreased rate of spontaneous apoptosis. The result is a disruption of normal marrow function and, ultimately, marrow failure.

- The clinical features, laboratory findings, and responses to therapy vary depending on the type of leukemia.

Leukemia

Types

A. Acute leukemia : :

1. Acute lymphoblastic leukemia 75% .
2. Acute myeloblastic leukemia 20%.

B. Chronic leukemia

— Chronic myeloid leukemia 3%.

1. Philadelphia chromosome +ve
2. Juvenile myelomonocytic leukemia

Acute lymphoblastic leukemia

- The disease is more common in children with certain chromosomal abnormalities, such as Down syndrome, Bloom syndrome, ataxia-telangiectasia, and Fanconi anemia
- The etiology of ALL is unknownalthough several genetic and environmental factors are associated with childhood leukemia

Factors Predisposing to Childhood Leukemia

GENETIC CONDITIONS
Down syndrome
Fanconi anemia
Bloom syndrome
Diamond-Blackfan anemia
Shwachman-Diamond syndrome
Kostmann syndrome
Neurofibromatosis type 1
Ataxia-telangiectasia
Severe combined immune deficiency
Paroxysmal nocturnal hemoglobinuria
Li-Fraumeni syndrome
ENVIRONMENTAL FACTORS
Ionizing radiation
Drugs
Alkylating agents
Epipodophyllotoxin
Benzene exposure

Clinical features of acute lymphoblastic leukemia.

1. **General system effects :** Fever (60%), Lassitude (50%) And Pallor (40%)

2-Hematologic effects arising from marrow invasion

— Anemia , Neutropenia, Thrombocytopenic ,1-2% pancytopenia

3. **Clinical manifestations arising from lymphoid system invasion :**
   1. Lymphadenopatly, sometimes mediastinal lymphadenopatly.
   2. Splenomegaly
   3. Hepatomegaly.

4. Clinical manifestations of extramedullary invasion:

A. Central nervous system involvement

↑ intracranial pressure ,Focal neurologic sign,Hypothalamic syndrome polyphagia with wt gain, Diabetes insipudus.Chloromas of the spinal cord in ALL, CNS haemorrhage (Hg) .

B. Genitouriny tract involvement

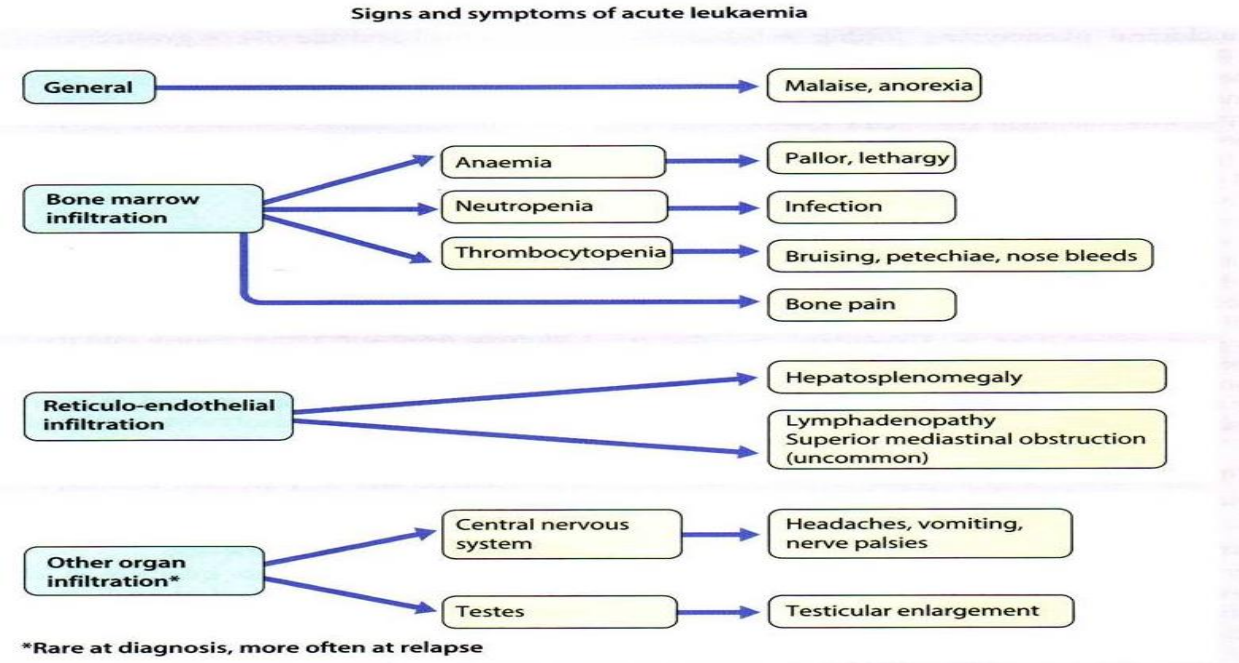
- Testicular involvement
- Renal involvement present with hematuria, hypotension renal failure

C. Gastrointestinal involvement :leukemia infiltrate in the GIT-silent until terminal stages most common site is the cecum.

D.Bone and joint involvement : Bone pain (Direct leukemic infiltration of the periosteium, Bone infarction , Expansion of marrow cavity by leukemic cells)

E.Skin involvement occurs in neonatal leukemia.

F. Cardiac involvement due to leukemia infiltration .
G. Lung involvement



Diagnosis of Acute lymphoblastic leukemia

1. **CBC and Blood film morphology**(Hb low or normal, W.B.C high or low, Plt low. Blood film show normochromic, normocytic and presence of blast cells)
2. **Bone marrow .**
    - ***Histochemistry*** by special stain(periodic acid Schiff,
    - ***Immunphentypes*** :by immunophenotyping of blast cell by flow *cytometric analysis* to detect intracellular antigens.
    - **Cytogentic.**
    - **Flocytometry**
3. **Chest radiograph**
4. **Blood chemistry** (Bu ,Uric acid ,Ca , PH, LDH,K,SGOT,SGPT.
5. **CSF for the diagnosis of CNS leukemia**.
- CNS 1: < 5 WBC/mm^3 No. blast , CNS 2: <5 WBC / mm^3 blast
- CNS 3: > 5WBC /mm^3 blast.

WHO classification of ALL : Depend on surface markers

- 85% of cases of ALL *B-lymphoblastic leukemia* (previously termed precursor B-ALL or pre–B-ALL)
- 15% are *T-lymphoblastic leukemia*,

- 1% are derived from mature B cells. The rare leukemia of mature . Mature B cells is termed *Burkitt leukemia*

Classification of ALL according to risk group

1-Slandered risk : (good prognostic factor)

- Age 1-10 yr
- Leukocyte count <50,000/µL
- Rapid response to therapy < 14 during induction
- Hyperdiploidy
- Trisomy of specific chromosomes (4, 10, and 17),

2-High risk. (poor prognostic factor)

- Age younger than 1 yr or older than 10 yr
- Initial leukocyte count of >50,000/µL
- Immunophenotype T-cell , mature B- cell
- Slow response to initial therapy > 28days
- Chromosomal abnormalities: hypodiploidy, Philadelphia chromosome + (9.22) or infantile leukemia(4.11).
- Gene mutations
- CNS disease at diagnosis CNS 2 or 3.
- mediastanial mass

Classification of bone marrow remission :

M1 → blast in B.M : < 5% , M2 → blast in B.M : 5- ≤ 25% , M3 → blast in B.M : > 25%

Treatment of acute lymphoblastic leukemia

The aim of treatment:

- Induce a clinical and hematologic remission.
- To maintain remission by chemotherapy and prophylactic CNS therapy
- To treat the complications of therapy and of the disease.
- To prevent relapse (B.M,CNS,Testicular).

Treatment includes

1. General care
2. Hydration and xyloric.
3. Platelets and blood transfution.
4. Antibiotic for infection .
5. Chemotherapy according to protocol
6. Stem cell transplantation

Phases of treatment of ALL:

1) Remission induction phase : (4 wk) and consists of vincristine weekly, a corticosteroid such as dexamethasone or prednisone, and usually a single dose of a long-acting, pegylated asparginase preparation. Patients at higher risk also receive daunomycin at weekly intervals. With this approach, 98% of patients develos *remission*, as defined by <5% blasts in the marrow and a return of neutrophil and platelet counts to near-normal levels after 4-5 wk of treatment.

Intrathecal chemotherapy is always given at the start of treatment and at least once more during induction.

2) Consolidation phase focuses on intensive CNS therapy in combination with continued intensive systemic therapy in an effort to prevent later CNS relapses. Intrathecal chemotherapy is given repeatedly by LP.

3) Intensification 14-28 wk

4) M**aintenance Phase :** lasts for 2-3y :daily mercaptopurine and weekly oral methotrexate, usually with intermittent doses of vincristine and a corticosteroid

Outcome of ALL :Improvements in therapy and risk stratification have resulted in significant increases in survival rates, with current data showing overall 5 yr survival of approximately 90%