Leukemias

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

-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).

5-How to deal with family and child with cancer

-Understanding of the importance of sensitive early diagnostic counseling.

-Understanding of the psychological impact of cancer on children and their families.

Type of Leukemia

1-Acute leukemias represent a colonel expansion and arrest at a specific stage of normal myeloid or lymphoid hematopiesis, types of acute leukemia:

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

2-Chronic leukemia

Chronic myeloid leukemias 3%.

1. Philadelphia chromosome +ve
2. Juvenile myelomonocytic leukemia

Acute lymphoblastic leukemia

Incidence

- Peak incidence between 2 and 5 years of age.
- Account for 25-30% of all childhood cancer.

Etiology :

1- Ionizing radiation.
2- Chemicals.
3- Drugs .
4- Genetic:
   -Identical twins.
   -Chromosomal abnormalities (down syndrome , Bloom, fanconie anemia).
5- Increase incidence:
   -Ataxia telenegiectasia .
   -Diamond blackfan

6-Breast feeding of more than (6) months duration-decreasing risk of leukaemia to (11%).

7-conjugate Hb vaccination at the ages of (3)month and (2)years-(28%)lower incidence of leukaemia

Clinical features of Acute lymphoblastic leukemia.

1. General system effects.
    1. Fever (60%)
    2. Lassitude (50%)
    3. Pallor (40%)
2. Hematologic effects arising from Marrow invasion
    1- Anemia
    2- Neutropenia
    3- Thrombocytopenic
    4- One -2% pancytopenia
3. Clinical manifestations arising from lymphoid system invasion.
    1- Lymphadenopathy → sometimes mediastinal lymphadenopathy.
    2- Splenomegaly
    3- Hepatomegaly.
4. Clinical manifestations of extramedullary invasion:

- Central nervous system involvement.
- ↑ intracrania pressure.
- Focal neurological sighs .
- Hypothalamic syndrome (polyphagia with excissive wt gain) .
- Diabetes insipadus.
- Chloromas of the spinal cord in ALL) .
- CNS-Hg.

5. Genitourinary system involvement .

- Testicular involvement

- Renal involvement present with hematuria hypotension renal failure

6. Gastrointestinal involvement. leukemia infiltrate in the GI--silent until terminal stages most common site is the ceccum.
7. Bone and joint involvement :

- Bone pain is one of the initial symptoms in 25%.
- Direct leukemic infiltration of the periosteim
- Bone infarction
- Expansion of marrow cavity by leukemic cells.

8. Skin involvement occurs in neonatal leukemia.
9. Cardiac involvement due to leukemia infiltration .
10. Lung involvement

Diagnosis

1- C.B.P(Hb may be low or normal, W.B.C high or low, Plt low. Blood film show normochromic, normocytic and blast)

2- Bone marrow send for:

- Histochemistry : by special stain(periodic acid Schiff,
- Immunophentypes :by immunophenotyping of blast cell by flow cytometric analysis to detect intracellular antigens.
- Cytogentic:by cytogenetic analysis of leukemia blasts and there are two major classes of cytogenetic aberration (visible loss or gain chromosomal,a balanced exchange without apparent loss or gain of DNA)

3- Chest radiograph for mediastanial mass

4- Blood chemistry (Bu ,Uric acid ,Ca , PH, LDH,K,SGOT,SGPT.

5- CSF for the diagnosis of CNS leukemia.

-Present of more than 5WBC/mm^3

-Identification of blast cells on cytocentrifuge examination.

CNS involvement in leukemia

-CNS 1 : < 5 WBC/mm^3 No. blast

-CNS 2: <5 WBC / mm^3 blast

-CNS 3: > 5WBC /mm^3 blast.

D.D

1-Aplastic anemia

2-AML

3-Mylofibrosis

4-Ivolvement of bone marrow by other malignancy like lymphoma, neuroblatoma.

Poor Prognosis

1) Age under one year and greater than 10 years, poor prognosis .
2) WBC ≥ 50.000. plt. <20.000.
3) Immunophenotype T-cell, mature B- cell .
4) DNA index <1.16 hypodiploidy(no of chromosomal less than 45).
5) Cytogenetics philadelphic chromosome + (9.22) or infantile leukemia(4.11).
6) CNS disease at diagnosis CNS 2 or 3.
7) mediastanial mass

8) Early response to induction therapy patients: who are not in remission at the end of induction therapy(M2 or M3) this because the blast cell contain ACTH receptor if increase in receptor more response to steroid and no. of blast cell in 8 days less than one 1000 in CBP .

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

- General care
- Hydration and hydoxyurea
- Plt. and blood transfusions.
- Antibiotics
- Chemotherpy

Aim of treatment:

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

Tumor lysis syndrome

Risk factor (TLS)

1. Presence of bulky disease.
2. Adenopathy, hepatosplenomegaly and high leukocyte count.
3. ↑ lactate dehydrogenease, uric acid creatinine, and decreased urine output.
4. TLS is highest at 12-72 hr after initiating chemotherapy.
5. Symptom can also precede the therapy or occur as long as 7 days later.
6. The main principle of TLS prevention and treatment.

Diagnosis

1. 25% increase over pretreatment values in serum phosphate, potassium, uric acid or urea nitrogen.
2. Or -25% decline in serum calcium.
3. (Any two of the above metabolic changes must occur within 4 days of treatment).
4. Rise in serum creatinine > 2-5mg /dL.
5. Serum K level > 6.0mmol /L.
6. Decline is serum calcium to < 6mg/dL.

7. Development of life threatening arrhythmia or renal insufficient, cardiac arrhythmias, sudden death and seizures.
8. (TLS is defined as the presence of laboratory tumor lysis syndrome and any one of the above criteria) .

Clinical manifestations and treatment

1. Nausea, anorexia.
2. Cardiac arrhythmia .
3. Seizures .
4. Muscle cramps, tetany.
5. Oliguria or anuria.
6. Alterations in consciousness

Management of TLS

Fluids and Alkalinization :-

1-Aggressive hydration 3000ml/m2/day (1/2 G.S).

2-Urine output should be maintained more than 100ml/m2/hr urine s.q ≤ 1.010.

3-Diuretics may be used (mannitol 0.5g/a) furosemide 0.5-1 mg//g.

4- Urine alkalinization (urine PH ≥ 6.5-7.5 / sod. Bica.40 mg/m2.

5- Allopurinol oral or iv…. 100mg/m2 every 8hr, 200-400 mg/m2/day

6-Recombinant form of urate oxidase (rasburicase 0.15-0.20mg/kg IV for 5-7 days. ↓ uric acid level by 4 hours after treatment.

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