Acute lymphoblastic leukemia
Dr.Hussein Alatabi

- Acute lymphoblastic leukemia (ALL): is amalignant disorder of lymphoblasts occuring as aresult of indefinite clonal proliferation of single lymphoblast that has undergo malignant transformation. This lymphoblastic clonal proliferation leads to overgrowth and the crowding out of normal marrow

- Precursors,invasion of non hematopoietic tissues and suppresion of differentiation of normal cells causing in effective heamatopoiesis ALL is the most common cancer of childhood,and the peak incidence occure between 2 and 5 years old,more common in white and boys

causes

- * unknown,may be associated with
- *Genetic predisposition(identical twins ,down syndrom,ataxia telangectasia , bloom syndrom,wiscott-aldrich syndrom ,congenital hypogamaglobul-

inemia)

*immunodeficiencies(ionizing radiation ,chemical exposure, immunosuppressive therapy.

Complications

- Due to disease:
- Hyperleukocytosis(WBC)>400,000) can lead to stroke.
- Mediastinal mass(usully T-cell lineage) wich can lead to cardiorespi-ratory arrest
- Tumor lysis:leads to renal failure and cardiorespiratory arrest(arrhythmias)
- Sever anemia:can lead to CHF

- Coagulopathy: lead tostroke and hemorrhage
- Hypocalcemia:lead to RF and cardior-espiratory arrest
- Febrile neutropenia:lead to infection, strock,sepsis

Other compiications;Due to therapy:

- Cranial radiation(brian tumors, learnig deficit
- Growth retardation
- Vincristne(vcr):SIADH,hair loss
- L-asparagenase:pancreatitis, cogulo-pathy
- Adriamycin,Doxorubicin,daunorubicin: cardiac toxicity
- Cyclophosphamide:hemorrhagic cystitis, sterility
- Methotraxate(MTX):hepatotoxicity

Prognosis

- Remission induction with present therapy is 95%
- Long term survival approches 80%

Differential Diagnosis

- Non malignant conditions:
  - JRA
  - Infectious mononucleosis
  - ITP
  - Acute infectious lymphocytosis
  - Aplastic anemia
  - Pertusis and parapertusis
- Malignant cnditions:
  - Neuroblastoma
  - Lymphoma
  - Retinoblastoma
  - Rhabdomyosarcoma
  - Acute myeloid leukemia

Clinical features

- History
- Bleeding(cutanous and mucocutanous) due to low platlets count and cogulopathy
- Bone pains, arthalgia, limp due to infiltrative disease of bone
- Fatigue and paller due to anemia
- Stridor, orthopnea, SOB or any respiratory distress due to mediastinal mass, pleural effsion
- Oliguria,anuria(RF due to tumor lysis syndrom)
- Ocular pain,blurred vision, photophbia due to infiltration of leukemia to orbit,optic n.,….
- Headache, vomiting, seizures,..due to leuk. Infiltration of CNS

Physical examination

- Pallor(anemia)
- Lymphodenopathy(infiltration with leuke.)
- HSM(infiltration)
- Bone tenderness(infiltration)
- Petechiae,purpura,subconjunctival and retinal hemorrhage(thrombocytopenia)
- Subcutuneus nodules(leuk. Infiit. To skin)
- Extermity weakness,numbness or tingling (spinal cord compression)

Laboratory aids

- CBC: either increase WBC or neutropenia,thrombocytopenia,low Hb, prepheral smear my show leukemic lymphoblast
- Bone marrow aspirate(BMA): if more than 25% of leukemic lymphoblast is diagnostic
- Immunophenotyping and cytogenic studies onBMA for diagnosis and prognosis
- Biochemical abnormalities(hyperurisemia)
- CXR
- CSF exam. With lymphoblast(CNS involv.)

Prognstic factors

- Patients with following criteria are at high risk for relapse and require more intensive treatment:
- Age < 1 year or >10 years of age
- WBC count > 50,000
- Translocation t (9-22), t (4-11) t (1-19)
- Hypodiploidy (<46 chromosome)

Therapy

Stratified according to risk groups

-risk assesment based on clinical features ,biologic charact. Of lymphoblasts and BM response to initial therapy;(low risk ,stander risk, high and very high risk)

-Over all, there are four phases of therapy :

*Induction *Consolidation *Delayed intensification *Maintenance

Therapy (cont.)

- Induction :to achieve remission (< 5% blast in bone marrow)
  -vcr -steriod -L asparginase -doxyrubicine or daunorubicin -intrathecal methotraxate(MTX)
- Consolidation and CNS prophylaxis: to prevent CNS disease.
  -itrathecal MTX along with oral(6 MP);(6 marcaptopurine) and MTX -itrathecal MTX along with cranial radiation,oral 6 MP and MTX

Therapy (cont.)

- Delayed intensification : to further decrease leukemic burden -vcr -steriod -L asparginase -doxyrubicin – cyclophosphamide -cytosinearabinoside -6 thioguanine(6 TG) -intrathecal MTX
- Maintenance :long treatment for 2.5 years in girls and 3 years in boys -Dialy oral 6MP ,weekly MTX and monthly of vcr and steriods with intrathecal MTX every 3 months **CNS leukemia at diagnosis: cranial radiatin and triple intrathecal(MTX, ARA-c, hydrocortison) in addision to drug above.

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****** End ALL

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Acute myeloid leukemia Dr.Hussein Alatabi

- Acute myloid leukemia (AML) : is block in differentiation and an unregulated proliferation of myeloid progenitor cells.**exact cause unknown, may be aquired risk factors (exposure to benzene, ionizing radiation or therapy induced);it is seventh most common pediatric malignancy.
  ** classified according to FAB to 7 subtypes (M1,M2,M3,M4,M5,M6,M7)

Complications at Diagnosis

- Bleeding
- Disseminated intravascular coagulation (DIC)
- Infection
- Leukstasis
- Tumour lysis syndrom

Prognosis **

- 85% achieve remission with intensive chemotherappy
- 30-40% achieve long term survival

Clinical features

- History :
  *fever *paller *weight loss\anoroxia
  *fatigue *bleeding *bone or joint pain
- Physical examination : *signs of anemia (paller, fatigue, dyspnea, heart murmer,….. *signs of thrombocytopenia (petechiae,brusing,.. *signs of infection (fever,….. *other finding (HM , SM , lymphadenopathy , gingival hyper plasia ,papilledema, cranial nerves or skin manifestation

Laboratory aids

1. CBC : anemia,thrombocytopenia, increase or decrease WBC, *smear:myeloid may be seen
2. BMA : > 30% of myeloblast is diagnostic
3. Others; eloctrolytes, CSF for cells and cytology

Therapy

- Most effective drugs for remission induction in AML are anthracycline as doxorubicin
- Consolidation with ARA-C and L-asp.
- Intrathecal ARA-c for CNS prophylaxs
- Duration of treatment 6-9 months
- Allogenic BMT may be the best treatment of AML in first remission

Therapy (supportive care)

- Hydration
- Alkalization
- Blood products support
- Broad spectrum antiboitic and antifungul,..
- Prophylaxis;as trimethoprim\sulfmethoxazole for pneumocystis ca.

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********END AML**********