Acute Lymphoblastic Leukemia

I. Introduction:

The leukemias are a group of disorders characterized by accumulation of malignant white blood cells in bone marrow and cells. Each year in the United State, more than 40,000 adult and 3,5000 children learn they have this disease.

II. Classification of Leukemia:

The types of leukemia can be grouped based on how quickly the disease developes and get wores . Leukemia is either chronic (which usually gets wores slowly) or Acute (which usually gets wores quickly).

. *Chronic leukemia :* Early in the disease. The leukemia cells can still do some of the work of normal white blood cells. It is also subdivided into myleoid and lymphoid goups.

-Chronic lymphocytic leukemia (CLL); it accounts for more than 15,000 new cases of leukemia each years. Most often, people diagnosed with disease are over age 55. It almost never affected children.

-Chronic myeloid leukemia (CML); it account for nearly 5,000 new cases of leukemia each years. It mainly affected adult.

. *Acute leukemia :*The leukemia cells can not do any of the work of normal white blood cells. The number of leukemia cells increases rapidly. Acute leukemia usually worsens quickly.It defined as the presence of over 30% of blast cells in the bone marrow at clinical presentstion. It is further subdivided according of weather the blasts are shown to be myeloblasts or lymphoblast.

-Acute lymphocytic (lymphoblastic)leukemia(ALL); it is the most common type of leukemia in children.

-Acute myeloid leukemia(AML); it account for more than 13,000 new cases each years . It occours in both adult and children.(1,2,3)

III. Acute lymphoblastic Leukemia:

It is rapidly form of leukemia or cancer of the white blood cells characterized by excess unusually immature white blood cells destined to become lymphocytes. Acute lymphoblastic leukemia is also called acute lymphocytic leukemia and is abbreviated ALL. Acute refer to the undifferentiated, immature state of the circulating lymphocytes "blast", and to the rapid progression of disease, which can be fatal in weeks to months if left untreated. ALL is the most common cancer occurring in children , representing almost 25% of cancer among children. For unexplained reason, the incidence of ALL is substantially high for white children than for black children , Factor associated with an increased risk of ALL have been identigied. The main environmental factor is radiation , namely prenatal exposure to x-rays or postnatal exposure to high doses of radiation.(1,4)

IV. Classification of ALL:

ALL classificate on the basis of morphology:

•*French_American_British (FAB) group.*

1.ALL-L1 :small uniform blast cell.

2.ALL-L2 : larger varied blastic cell with more heterogeneity.

3.ALL-L3 : larger varied blastic cell with vacuoles "mature".

•*On the basis of immunological marker:*

B-cell ALL

early pre-B ALL (also called pro-B ALL) -- about 10% of cases

common ALL - about 50% of cases

pre-B ALL - about 10% of cases

mature B-cell ALL (Burkitt leukemia) -- about 4% of cases

T-cell ALL

pre-T ALL - about 5% to 10% of cases

mature T-cell ALL - about 15% to 20% of cases

The subtypes of ALL carry slightly different outlooks, but other factors (like gene changes in the leukemia cells) may also have an impact. Some of these prognostic factors are listed in the next section.

V. Symptoms:

Initial symptoms are not specific to ALL. But worsen to the point that medical help is sought. The symptoms are :

-Anemia.

-Bone pain,joint pain.

-Breathlessness.

-Pitting.

-Thrombocytopenia.

-Enlarged lymph nodes , liver and/or spleen.

The signs and symptoms of ALL result from the lack of normal and healthy blood cells.(4)

VI. Causes of ALL:

ALL occurs when a bone marrow cell develops errors in its DNA . The error tell the cellto continue growing and dividing , when a healthy cell would normally die. The bone marrow produces immature cells that developed into leukemia white blood cells called lymphoblasts . These abnormal cells are unable to function crowd out healthy cells. Although a few cases are associated with inherited genetic Syndromes, for example ; Down Syndrome, Bloom Syndrome, Fanconi Syndrome, Anemia.

Many environmental factor , for example; exposure to ionizing radiation and electromagnetic field , parental use of alcohol and tobacco, smoking, atomic bomb explosion , radiation , benzene, infection of virus.(5)

Cytogenitic: ALL result from somatic mutation in the DNA which activate oncogen and inactivate tumor suppressor genes, disrupt the regulation of cell death , differentiation division. These mutation may be occur spontaneously or as a result of exposure to risk factor. There are different kinds of mutation happen in the DNA (deletion, translocation, inversion). The mutation which occur in ALL is translocation .The poor–risk abnormalities; t(9;22)(q34;q11), giving rise to the BCR/ABL gene fusion and rearrangement of the MLL gene[called Philadelphia chromosome, it is the most common translocation mutation in ALL]. A abnormalities t(1;19)(q23;p13), producing the E2A/PBX1 and rearrangement of MYC with the immunoglobulin genes. And probable good risk translocation t(12;21)(p13;q22) which results in the ETV6/AML1 fusion . These abnormalities occur most frequently in B-lineage , while rearrangements of the T cell receptor genes are associated with T-lineage ALL.(6)

Immunophenotype: The CD19 was the most commonly expressed of B-lineage antigens detected with the positive rate being 100%. In T-ALL, the positive expression rate of CD5 and CD7 was the highest , being 90%. Both B-ALL and T-ALL overlapped in expression of lineage antigens. There was no significant different in the complete remission rate between T-ALL and B-ALL. (7)

VII. Diagnosis:

There are some tests will done to ensure the patient has ALL .

•*(VII.1) Physical exam may reveal the following ;*

-Bruising .

-Enlarged liver and spleen .

-Signs of bleeding (petechiae, purpura).

•**(**VII.2)B*lood tests may show the following;*

-Abnormal white blood cell (WBC) count [increase upto 200×10^9/l].

-Low red blood cells (anemia).

-Low platelet count (thrombocytopenia).

-A bone marrow aspiration will show abnormal levels of certain cells. ALL may also chang the results of the following test:

-B-cell leukemia/lymphoma panel.

-T-lymphocyte count.

-WBC differential.

The diagnosis of ALL by genetic test is very useful to determine the type of ALL . There are some techniques in lab. Are useful to diagnosis;

-(VII.3)*Karyotype analysi;* involves direct morphological analysis of chromosomes from tumor cells under the microscope. This requires tumour cells to be in metaphase and so cells are cultured to encourage cell division prior to chromosomal preparation.

-(VII.4)Fluorescent *in situ hybridization analysis (FISH;* involves the use of fluorescent-labelled genetic probes which hybridize to specific parts of the genome. It is possible to label each chromosome with a different combination of fluorescent labels . This is a sensitive technique that can pick up extra copies of genetic material in both metaphase and intraphase(non-dividing)cells..

-(VII.5)Southern *blot analysis;* involves the extraction of cell DNA followed by restriction enzymes digestion , gel electrophoresis and transfer by"blotting" to a suitable membrane . The DNA is then hybridized to aprobe complementary to the gene of interst.when the probe recognizes

a segment within the boundaries of a single restriction fragment one band is identified but if the gene has been translocated to a new area in the genome a novel band of different electrophoretic mobility is seen..

-(VII.6)Polymerase *chine reaction (PCR)*;can be performed on blood or bone marrow for a number of specific translocationsuch as t(9;22) and t(15;17) It can also be used to detect 'clonal' cells of B- or T-cell lineage by immunoglobulin or T- cell receptor (TCR) gene rearrangement analysis.

-(VII.7)DNA *microarray platforms;*allow a rapid and comprehensive analysis of cellular mRNA to DNA probes which are immobilized on a solid support **.**

-(VII.8)*Immunofluorescence staining;*can be performed for a few chromosomal abnormalities . An example is expression of the promyelocytic leukemia (PML) protein which normally has a punctuate distribution but is diffusely scattered in acute promyelocytic leukemia with the t(15;17)translocation . In addition abnormal fusion proteins can sometimes be detected by specific monoclocal antibodies**.**

-(VII.9)Flow *cytometry;* It is a technique for counting and examinating microscopic particles such as cell and chromosomes . Modren flow cytometers are able to analyze several thousand particles every second***.(2,8,9)***

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VIII. Treatment:

The aim of treatment is to get the blood counts and the bone marrow back to normal . If this occurs, the cancer is said to be in remission (absence of detectable cancer cells in the body, usually less than 5% blast cells on the bone marrow). The earlier ALL is detecteted , the more effective to treatment. Treatment typically takes place in 3 phases ;

-Remission induction.

-Consolidation(intensification)

-Maintenance.

The total treatment usually takes about 2 years , with the maintenance phase taking up most of this tim. Treatment may be more or less intense , depending on the subtype of ALL and other prognostic factors. An important part of treatment of ALL is central nervous system (CNS) prophylaxis – treatment that is meant to ensure the leukemia does not spread to the brain or spinal cord.(9)

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