LEUKEMIA

Debanjali Adhikary

Student of bsc biotechnology hons with research

Amity university

Amity institute of biotechnology department

ABSTRACT

Leukemia is an amalgam of cancers and its also called blood cancer. Many people have lost their life due to this cancer.Abnormal growth of cells is called cancer. In simple language we can say that they are actually the abnormal WBC cells which are not fully developed is called leukemia cells. Leukemia cells grow rapidly than as compared to normal cells. The abnormal cells survive longer, build up in larger numbers and enter the bloodstream. In 1811, Peter Cullen defined a case of splenitis acutus with unexplainable milky blood. Alfred Velpeau defined the leukemia associated symptoms and observed pus in blood vessels 1825.In 2012, 3,52,000 people were affected by leukemia and 2,65,000 deaths occurred. AML is the most common type of acute leukemia in adults. CLL the most common chronic adult leukemia.Chronic leukemias are rare in children.

KEYWORDS

Leukemia, lymphocytes

INTRODUCTION

ALL –acute lymphoblastic leukemia is also called acute lymphocytic leukemia. The term ‘’acute’’ means that leukemia can spread and progress easily , and if no treatment is done it can be fatal with the passage of time. It develops from lymphocytes. Leukemia cells usually invade the blood quickly and fairly. It spreads to other parts of the body like liver, lymph nodes, spleen , brain and spinal cord etc. This is different from the AML acute myeloid leukemia which is present in other blood cell types in the bone marrow. It is the most common type of cancer in children.

Other types of cancer that start in lymphocytes are called lymphomas { either non Hodgkin lymphoma or Hodgkin lymphoma}. The bone marrow is mainly affected on the other hand the lymph nodes are affected by lymphomas. If 20 % of the bone marrow is made up of lymphoblast the disease is called and is considered leukemia.

The size of the lymph node is also important.

CAUSES OF LEUKEMIA

Leukemia is caused by many risk factors but the root causes are unknown. But these root factors only lead into a fatal disease stage.

Some causes are mentioned below

. Exposure to UV rays

. Prior chemotheraphy

. Smoking

. Family history

. Ionizing radiation

. Work involving chemicals

. Human T—cell leukemia virus—I [HTLV-I]

. Myelodyplastic syndrome

. Inherited syndromes

EXPOSURE TO UV RAYS

UV radiation is the form of electromagnetic radiation that comes from the sun and man made sources like tanning beds and welded torches .

SUNLIGHT

It's the main source of UV radiation, even though UV rays make up small portion of sun's rays. Different types of UV rays from the sun that reach the ground in different amounts.

The strength of UV rays reaching the ground depends on a number of factors_

1. Time of day: UV rays are the strongest between 10 am and 4 pm.
2. Season of the year: UV rays are stronger between spring and summer months.
3. Distance from the equator: UV rays exposure goes down as you get farther from the equator.
4. Altitude : more UV rays reach the ground at higher elevations.

   Higher –energy UV rays are a form of ionizing radiation. This means they have enough energy to remove electron from an atom or molecule. The ionizing radiation can damage the DNA in cells, which leads to cancer.

PRIOR CHEMOTHERAPY

Chemotherapy is the use of drugs to treat cancer. Chemo drugs travel through the bloodstream to reach carcinogenic cells all over the body. This method has made chemo useful for cancers such as Leukemia that has spread in the body.

A subset acute myeloid leukemia known as '' secondary AML'' develops following treatment with chemotherapy.

Some chemo drugs are used to often treat AML

1. Cytarabine [cytosine arabinoside or ara—C]
2. An anthracycline drug, such as daunorubicin [daunomycin] or idarubicin

Other chemo drugs that may be used to treat AML include;

1. Cladribine
2. Fludarabine
3. Mitoxantrone
4. Etoposide
5. 6—thioguanine
6. Hydroxyurea
7. Corticosteroid drugs
8. Methotrexate
9. 6—mercaptopurine
10. Azacytidine
11. Decitabine

SMOKING

Smoking causes blood cancer as the cigarette is made up of nicotine which is harmful for our health. The poison in cigarette smoke weakens the body's immune system, making it harder to kill the carcinogenic cells.

Smoke of tobacco has poison which damages cell;s DNA.

FAMILY HISTORY

Family history plays a key role in leukemia . the family members can pass on genetic mutations that increases a person's risk of leukemia. All cancers are result of mutation and some mutations are hereditary that is passed down from parent to child , making them develop cancer

INHERITED SYNDROME

Leukemia too depends on some inherited syndromes. There is a 20% chance of developing leukemia in children patients who have Down;s syndrome. The 10 % chances are for transient leukemia that resolves within months of birth.

Other syndromes are

Ataxia telangiectasia

Bloom syndrome

Klinefelter syndrome

Neurofibromatosis

IONIZING RADIATION

There are many radiations present over the atmosphere of the earth. There are many rays like X – rays , gamma rays etc. specially people who are survivors of nuclear point explosions and atomic explosions can develop leukemia. Even usage of radiotherapy can be a big risk.

HTLV—I HUMAN T CELL LEUKEMIA VIRUS –I

Its also known as acronym HTLV—I, or as human T—cell leukemia virus type 1.This is transmitted primarily through infected body fluids including blood, breast milk and semen. Risk factors include unprotected sex, injected drug use and transplantation of tissue.. this was the first oncogenic virus to be discovered in 1977. The virus can cause adult T cell leukemia. Mothers can pass the virus to children through breastfeeding and there is limited evidence of transmission rate has ranged from 3.9% to 27%. HTLV—I has been detected in cervical secretions and semen. several studies have reported that transmission rates of up to 63% from transfusions of blood from a donor with HTLV—1. One study reported transmission rate of 87% from tissue transplants. HTLV—1 is widespread in certain regions of the world such as Caribbean basin, Japan, south America and Africa .

MYELODYSPLASTIC SYNDROME

They are a group of disorders caused by the blood cells that are poorly formed or don't work properly. They arise from the material present inside your spongy bones or tissues.

SYMPTOMS

1. Fatigue
2. Shortness of breath
3. Easy or unusual bleeding, due to low blood platelet count
4. Frequent infections

TYPES OF LEUKEMIA

Based on characteristics

. acute leukemia

. chronic leukemia

Based on type of WBC affected

. lymphocytic leukemia

. myelogenous leukemia

ACUTE LEUKEMIA

It's a type of cancer of the blood and bone marrow—the spongy tissue inside bones where blood cells are made. The disease progresses rapidly and creates immature blood cells, rather than mature ones. Its also called acute lymphoblastic leukemia.

SYMPTOMS

Signs and symptoms of acute lymphocytic leukemia may include

. bleeding from the gums

. bone pain

. fever

.pale skin

. weakness

CAUSES

It occurs when a bone marrow cell develops changes in its genetic material or DNA. A cell's DNA contains the instructions that tell a cell what to do. Normally the DNA tells the cell to grow at a set rate and to die at a set time. When this happens, blood cell production becomes out of control. The bone marrow produces immature cells that develop into leukemic WBC called lymphoblasts.

CHRONIC LEUKEMIA

It is a type of cancer of the blood and bone marrow—the spongy tissue inside bones where blood cells are made. The term chronic comes from the fact that this leukemia typically progresses more slowly than other types of leukemia.it most commonly affects older adults. The term lymphocytic in chronic lymphocytic leukemia comes from the cells affected by the disease.

SYMPTOMS

. enlarged painless lymph nodes

. fatigue

. fever

. pain in the upper portion of abdomen

. night sweats

. weight loss

CAUSES

Something happens to cause changes that is mutations in the DNA of blood producing cells. A cell's DNA contains instructions that tells the blood cells to produce abnormal, ineffective lymphocytes.

These abnormal lymphocytes continue to live and multiply when healthy lymphocytes would die . the abnormal lymphocytes accumulate in the blood and certain organs, where they cause complications. They may crowd healthy cells out of the bone marrow and interfere with blood cell production. Monoclonal B cell lymphocytosis causes an increased number of one type of lymphocyte in the blood.

CHRONIC MYELOMONOCYTIC LEUKEMIA [CMML]

By world health organization [WHO] has been redefined as a myelodysplastic/myeloproliferative neoplasm. It originates from a clonal hematopoietic malignancy , in which it starts in the blood forming cells of the bone marrow and invadesthe blood. It affects mainly older adults. There are about 1100 cases each year. Hematologists and oncologist are specialists who treat people who have CMML or other types of blood cancer. There is also sometimes an increase of immature cells called blast cells. These abnormal blood cells either stay in the bone marrow or are destroyed before they get into the bloodstream. As the CMML develops, the bone marrow becomes full of the abnormal monocytes. These abnormal blood cells then spill out into the bloodstream.

DIAGNOSTICS

MOLECULAR BIOLOGY AND LEUKEMIA DIAGNOSIS

The diagnosis and classification of leukemia started with simple morphological examination and now embraces use of special stains, cytochemistry and immunophenotyping . genetic studies have shown and progressed from karyotyping to detection of genetic changes with genes. The methods described by scientists are still of early age of development and so far have provided relatively little in the way of an extension of available diagnostic information. Sometimes the methods provide extensions to existing techniques, for example by the detection of bcr rearrangements in patients who have CML or ALL but do not have a detectable Philadelphia chromosome. Another example is retrospective diagnosis of gene rearrangements using DNA from slide preparations. However , it should be noted that it has only very recently been shown that there is a causal relationship between Ph chromosome and leukemia

TREATMENT FOR ALL

ACUTE LYMPHOBLASTIC LEUKEMIA

It needs rapid treatment

COMBINING LESS TOXIC THERAPIES the intensive chemotherapy treatments used for ALL have serious side effects that many older patients cannot tolerate .targeted therapies may have fewer side effects than chemotherapy.

USING CAR T—cell therapy--this is a type of treatment of some children and adults with ALL. They are now being explored and used in adults with B cell ALL

TARGETED THERAPIES

certain gene changes include the below

. Enasidenib

.Ivosidenib

.Venetoclax

.Midostaurin

.Glasdegib

TREATMENT OF CHRONIC LYMPHOCYTIC LEUKEMIA

CLL is slow growing and it worsens with time. Here the bone marrow makes too many lymphocytes.

Clinical trials have shown that the targeted therapy ibrutinib benefits both younger and older patients with CLL.

Ibrutinib was the first non—chemotherapy drug approved to treat CLL. It shuts down a signalling pathway called B—cell receptor signalling pathway, which is commonly overactive in CLL cells.

Depending on people's age ibrutinib may be given in combination with another drug rituximab is given.

FLOW CYTOMETRY AND CYTOCHEMISTRY

This method is where dyes, chemicals or tests are applied to leukemia cells in the laboratory. These chemicals and dyes provide information about leukemia and its sub type. The CLL cells have distinctive markers, called cell surface proteins, on the outside of the cell. The pattern of these markers is called the immunophenotype. These tests are used to differentiate CLL from other kinds of leukemia, which can involve lymphocytes. Both tests can be done from a blood sample.

GENOMIC AND MOLECULAR TESTING

The doctors may recommend testing the leukemia cells for specific genes, proteins, chromosome changes. Because CLL cells divide very slowly looking at the chromosomes is often less useful than using test to find genetic mutations. Fluorescence in situ hybridization assays and other genetic tests such as PCR are used to find genetic changes.

Some changes are—

1. Deletion of the long arm of chromosome 13[del[13q]], which is found in half of the patients.
2. An extra copy of chromosome 12 [trisomy]
3. Del[11q]
4. Del[17q]
5. NOTCH1 mutation

These results determine how quickly disease will progress and help determine your treatment options.

DIAGNOSTICS OF ACUTE MYELOGENOUS LEUKEMIA

AML

MAY GRUNWALD—GIEMSA STAIN

Blood and bone marrow smears are morphologically examined using a May Grundwald Giemsa stain. Its recommended with 500 nucleated cells and 200 leukocytes on blood smears that can be counted with latter spicules. A blood blast count of 20% or more is required, except for AML with t[15;17],t[8;21], or inv[16] and some cases of erythroleukemia. countries still rely more on cytochemistry to identify lineage movement rather than on immunophenotyping.

CYTOGENETICS

Conventional cytogenetics analysis is a mandatory component in the diagnostic evaluation of patients with acute leukemia. Chromosomal abnormalities are detected in 55% of adult AML

About 7 recurrent balanced translocations and inversions, and variants are recognized in WHO category AML with myelodysplasia related features when 20% or more blasts are present.

BIOBANKING

Its strongly recommended within the clinical trials to store patients' pretreatment leukemic narrow and blood within a biobank. A prerequisite for biobanking is the patient informed consent that ideally should allow a broad spectrum of correlative laboratory studies that should include analysis of germline DNA. The samples should include nucleic acid and viable cells.

CONCLUSION

Flow cytometry is the standard option for CLL the most common leukemia in adults. Even scientists are working to find more cures for leukemia by using molecular biology techniques.

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