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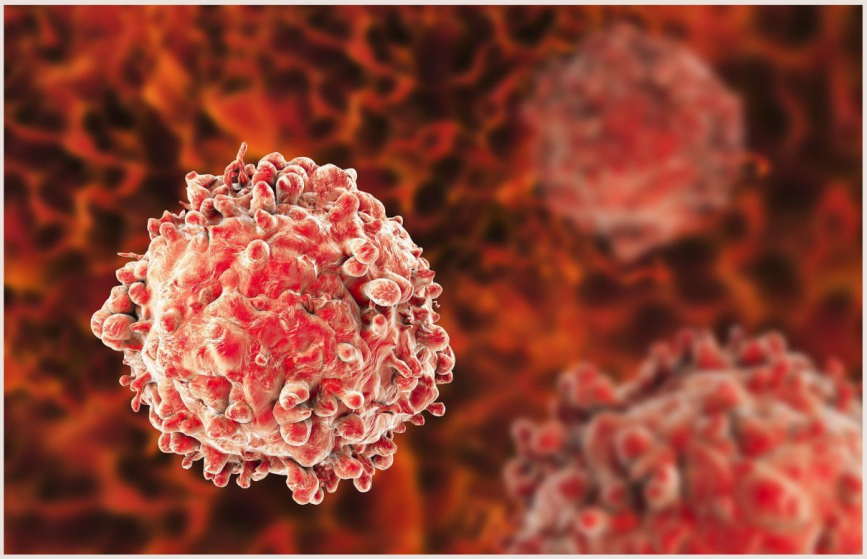
LEUKEMIA



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Introduction

Leukemia is a group of cancer diseases that originates from the bone marrow leading to the formation of large number of white blood cells. The developed white blood cells are not developed fully and are biologically referred to as leukemia or blast cells. Major symptoms of leukemia are bruising, bleeding, tiredness, increased risks to infections and fever. The symptoms arise from lack of effective blood cells. Diagnosis of leukemia involves bone marrow biopsy and blood tests.

The exact cause of leukemia has never been established but is believed to come from multiple causes. In particular, leukemia is inherited or may be predisposed by the environment factors. Predisposing factors involves ionizing radiations, smoking, and exposure to some form of chemicals such as benzene, Down syndrome and prior chemotherapy. Largely, leukemia is genetic and Individuals from families with history of leukemia have higher risks.

Leukemia exist in four different types; Chronic lymphocytic (CLL), acute myeloid (AML), acute lymphoblastic leukemia (ALL) and Chronic myeloid leukemia (CML). Lymphomas and leukemias fall under the group of tumors that affect human blood, the lymphoid system and the bone marrow (Egawa, 2004). Treatments of leukemia involve various combinations o f radiation, targeted, chemotherapy, and transplant of bone marrow (Masihi, 2001). In addition, there are supportive care treatments and palliative care.

Other less adverse types of leukemia are managed through watchful waiting method. Although there are different approaches in treating leukemia, the success of any treatment method depends on the type of leukemia and the age of the patient. Treatment of leukemia are more advanced in developed worlds with an average survival rates been 57% in U.S. Children, under fifteen years of age has a survival rate chance of 60% to 80% based on the type of

leukemia suffered. Patients treated from acute leukemia and have over five years of cancer free are likely to be fully healed.

According to recent statistics in 2012, Leukemia increased to 352, 000 leading to over 265,000 deaths. Leukemia is identified as the most common type of cancer among small children with many children suffering from ALL type of leukemia. However, over 90 percent of leukemia cases have been diagnosed from adults with most adults suffering from AML and CLL. Further studies indicate that, leukemia occurs mostly in developed world.

Genetics of leukemia

The human body has 46 Chromosomes in each cell which exist as 23 pairs (U.S National Library of Medicine. 2014). These chromosomes exist in two copies; chromosome 16 is inherited from each parent and form a pair. Chromosomes 16 exists in over 90 million DNA representing 3 percent of DNA in human cells (U.S National Library of Medicine. 2014). Several types of genetic related conditions are attributed to changes in Chromosome 16. These changes involve structural or number of copies of chromosomes in the DNA. As a result of these changes on chromosome 16, genetic problems such as 16p11.2 deletion syndrome, alveolar capilar dysplasia and cancer diseases arise (U.S National Library of Medicine. 2014).

Change in chromosome 16 structure lead to several types of cancer. In particular, this is due to such aspects as translocations and rearrangement of chromosomes. Myelodysplastic syndrome leukemia and chronic myeloid leukemia are associated with these chromosome changes (U.S National Library of Medicine. 2014). Acute myeloid leukemia is associated with chromosomal rearrangement of chromosome 16. Chromosome 21 is another copy of chromosome that is inherited from each parent and is the smallest (U.S National Library of Medicine. 2014).

Chromosome 21 exists in over 48 million blocks of DNA forming 2 percent of DNA in human cells. In the same way, the structure and quantity of chromosome 16 results in different genetic problems, changes in chromosome 21 leads to various genetic heath problems. In particular, some type of acute myeloid leukemia is associated with chromosome 21; changes and rearrangement of chromosome 21 leads to 7 percent of acute myeloid leukemia.

Other conditions involve the Down syndrome that is associated with intellectual disability, facial appearance and weak muscles among the infants. Biologically, Down syndrome results when extra copies of chromosomes 21 in some body cells (U.S National Library of Medicine. 2014). Medical studies reveal that having extra copies of chromosome 21 leads to disrupting in the normal development of cells leading to increase health problems (Egawa, 2004). Similarly, structural and translocation problems of chromosome 21 lead to other several types of cancer such as acute lymphoblastic leukemia that is diagnosed at child hood.

Types of leukemia

The classification of leukemia is done based on the degree of acuteness and chronic condition. Acute leukemia is conspicuous for increased number of immature blood cells (U.S National Library of Medicine. 2014). The increased production of immature blood cells leads to crowding in the bone marrow and hence inhibiting production of healthy blood cells (Penn Medicine. 2014). Immediate treatment is required for acute case of leukemia to tone down the rapid accumulation and progression of the malignant cells. When the acute leukemia condition sets in it spreads to other organs through the blood stream. Acute leukemia is the most common condition among children (Hutter, 2010).

Chronic leukemia is known for excessive build up of fairly mature but abnormal white blood cells. The chronic condition may take months or several years before progressing to other

areas. In the case of chronic leukemia, cells production is at a higher rate than the normal rate. This results in several abnormal white blood cells. Unlike the acute leukemia that requires immediate treatment, chronic leukemia requires monitoring before treatment is done for optimal efficiency of therapy used (Hutter, 2010). Chronic leukemia is found among older people but not limited to age.

A. Acute lymphoblastic leukemia (ALL)

Acute lymphoblastic leukemia (ALL) is an acute type of cancerous leukemia. The ALL leukemia is conspicuous due to overproduction of cancerous immature white blood cells referred to as lymphoblast (Seiter, 2014). Patients with ALL leukemia develop lymphoblast overproduction condition in the bone marrow (U.S National Library of Medicine. 2014). The multiplication of abnormal white blood cells progresses at alarming rate and lead to adverse damage and eventual death of the patient (Penn Medicine. 2014). In particular, the overproduction of immature white blood cells inhibits the production of red blood cells, white blood cells and the platelets. This condition infiltrates to other parts of the body **(**Inaba, Greaves and Mullighan, 2013).

ALL leukemia is prevalent among young children at age 2-5 years while in other cases it peaks at old age (Hutter, 2010). Reliable data indicates that over six thousand cases of ALL are reported in the U.S each year (Seiter, 2014). Other unverified data indicate that ALL leukemia is common in U.S, Costa Rica and Italy. Treatment and cure of ALL stands at 80% among young children while 40% among the adults **(**Inaba, Greaves and Mullighan, 2013). ALL was the first leukemia type to respond positively to chemotherapeutic treatment such as amniptein, methotrexate and antifolates developed in the 40s (U.S National Library of Medicine. 2014).

Signs and symptoms

Initially, ALL symptoms are not easily visible but become despicable as the condition worsens. In particular, symptoms are evident after malignant and immature white blood cells crowd the bone marrows (Penn Medicine. 2014). People with ALL leukemia experience malfunctioning of red blood cells, platelets and leukocytes. Abnormalities signs are detected through blood tests, renal function tests, electrolyte tests and liver tests **(**Inaba, Greaves and Mullighan, 2013).

General symptoms and signs are; anemia, general feeling of fatigue, dizziness, unexplained fever, weight loss, unexplained bruising bone pain (U.S National Library of Medicine. 2014). Others include; breathlessness, enlarged lymph nodes, spleen and liver, swelling of the lower abdomen and appearance of red lines on skin due to low levels of platelets in the blood. Addition symptoms involve chest pains, cough, vomiting (Seiter, 2014).

Causes and predisposing factors

ALL results from damaged DNA leading to unregulated production of immature white blood cells. ALL leukemia is associated with excessive exposure to radiation and chemicals presence in animal and human bodies **(**Inaba, Greaves and Mullighan, 2013). Excessive radiation exposure is the leading risk factor in ALL leukemia. Progressive studies indicate that prolonged exposure to certain chemical lead to ALL condition (Penn Medicine. 2014).

Unconfirmed studies indicate that ALL condition also affects individuals who have been treated from other cases of cancer using chemotherapy and radiation (Kimura, Ashihara and Maekawa, 2006). ALL leukemia is diagnosed through bone marrow biopsy, physical examination and blood tests. ALL type of leukemia is common in males than females. For

instance, according to data collected in 2010 U.S, more incidences of ALL were recorded from boys than girls (Seiter, 2014).

Treatment of ALL

Effective treatment of ALL leukemia depends on the urgency of detection. Early detection of ALL leukemia leads to effective treatment. Lasting remission where no cancerous cell can be detected (Hutter, 2010). However, the main treatment methods of ALL are through Chemotherapy, immunotherapy, radiation and steroid therapy (Inaba, Greaves and Mullighan, 2013). Other advanced treatment methods are integrated treatment involving bone marrow and stem cell transplants (Motohashi, 2009).

B. Acute myeloid leukemia (AML)

Acute myeloid leukemia (AML) is also referred to as acute non-lymphocytic leukemia (ANLL). AML is a type of cancer characterized by rapid and abnormal growth of leucocytes cells (Weinblatt, 2013). The abnormal white blood cells overcrowd in the bone marrow inhibiting normal production of blood cells (Cancer org. 2014). AML is a common leukemia that affects adults and incidences of the conditions increases with age. However, AML leukemia is rare and results in roughly 1 % deaths reported in U.S (Cancer org. 2014). AML condition worsens with age. There are other several subtypes of AML condition, prognosis and treatment depending on the subtype (Cancer org. 2014).

Signs and symptoms

The most prevalent sign is the replacement of normal blood cells with abnormal cells. Lack of normal blood cells make the patient vulnerable to several infections; individuals' immune system is low since most white blood cells are abnormal and cannot serve the role of fighting pathogens (Kimura, Ashihara and Maekawa, 2006). Anemic condition results and

patients experience fatigue, shortness of breath and paleness (Weinblatt, 2013). AML patients experiences bleeding and bruising due to lack of enough platelets in the blood. In the same way, ALL has no specific signs; AML condition has no specific sign. However, patients may have influenza like signs (Cancer org. 2014).

General symptoms are; fatigue, fever, loss of appetite, breath shortness, petechie spots on the skin, joint and bone pains and chronic infections. In some cases, enlargement of spleen is seen. However, unlike ALL condition, lymph node swelling is not common in AML. At other times, AML patients may experience gum swelling (Weinblatt, 2013). Although in rare cases, the development of leukemic mass outside the bone marrow occurs or a tumor grows outside the bone marrow (U.S National Library of Medicine. 2014).

Causes of AML leukemia

Major causes of AML leukemia include a number of risk factors such as exposure to hazardous chemicals, radiation ionizers and heredity factors (Seiter, 2014). Preleukemia which is a blood disorder condition may lead to AML leukemia (Cancer org. 2014). Chemical exposures that increase the risk of AML condition include; organic solvents, benzene and other carcinogenetic substances (Cancer org. 2014). Radiations such as X-rays, nuclear and other radiation rich elements accelerate risks of AML condition (Colvin and Elfenbein, 2003). Families with a history of AML leukemia lead to several congenital conditions of AML (Weinblatt, 2013).

Diagnosis of AML infection

Complete blood count tests helps in assessing the existence of AML condition. In this case, excess number of white blood cells may infer leukemic blasts (Seiter, 2014). Blood tests

also may also show decreased red blood cells and platelets which signify likelihood of AML condition. Other tests include; bone marrow biopsy tests (Weinblatt, 2013).

Treatment

Chemotherapy is the first treatment adopted in AML conditions. This chemotherapy treatment is done in two phases; induction and post remission (consolidation). Acute myeloid leukemia is curable but effective treatment and cure for patients with AML depends on number of factors such as the subtype of AML (Colvin and Elfenbein, 2003). Epidemiologically, AML is a relatively rare leukemic cancer occurring in 1% of reported cases of blood cancer (Seiter, 2014).

Chronic lymphocytic leukemia (CLL)

Chronic lymphocytic leukemia (CLL) mostly affects the adults (Byrd, 2014). The CLL affects the B-cell lymphocytes present in the bone marrow leading to the development of lymph nodes. B cells production increase in the bone marrow and blood inhibiting the development and growth of healthy blood cells (Janssen, 2011). Ideally, chronic lymphocytic leukemia (CLL) occurs as a stage in the development of small lymphoma (SLL) present in the lymph nodes. CLL is considered adult leukemia affecting individuals at age 50 and majority of the patients being men (U.S National Library of Medicine. 2014). In rare cases, the diseases also affect children and teenagers (Byrd, 2014). Research and DNA analysis has led to the identification of two CLL conditions that have different survival rates; CLL positive and CLL negative.

Symptoms and Signs

Blood tests are the most commonly used method of assessing the symptoms of CLL. Blood tests indicate the level of white blood cells in the blood (Janssens, 2011). Enlarged lymph

nodes with few white blood cells and no disease pathogens in the blood may signify the presence of CLL. The diagnosis of CLL involves assessing the level of white blood cells. This is ascertained after consecutive visit to the physician. Presence of increased lymphocytosis among the old people may be likely sign of CLL (Byrd, 2014). In addition, diagnosis may involve ascertaining the presence of B cells in the blood or the bone marrow. Among the routine methods use to assess the condition of CLL in the body is the clinical staging and chromosomal abnormalities prognosis among other methods (Janssens, 2011).

Treatment

The main methods used in CLL treatment involve controlling the condition rather than cure (Zhukov and Tjulandin, 2008). The most commonly used treatment methods are; immunotherapy, chemotherapy, radiation therapy, bone marrow transplant and biological therapy (Masihi, 2001). In some cases, treatment of symptoms is done surgically in the case of enlarged spleen or through radiation therapy (Byrd, 2014). However, the initial method adopted for treating CLL condition depends on exact diagnosis and disease progression (Gribben, 2008). In addition, the method used may depend on clinical experience of the medical officer. Several types of agents are used in CLL therapy (Motohashi, 2009).

Chronic myeloid leukemia (CML)

Chronic myeloid leukemia (CML) is also referred to as chronic granulocytic leukemia (CGL) (Provan and Gribben, 2010). CML is white blood cells cancer despicable for high number of unregulated growth of myeloid cells. In CML leukemia, mature granulocytes cells overcrowd the bone marrow. CML condition is attributed to chromosomal translocation. Improved research has enabled the production of targeting drugs that improve survival rates of CML patients.

Patients are able to have quality life using the targeting drugs (tyrosine kinase inhibitors (TKIs) than traditional chemotherapy drugs (Besa, Buehler, Markman and Sacher, 2013).

Signs and symptoms

The symptoms of CML depend on the stage of disease and diagnosis. CML condition does not follow systematic stages and hence not easily detected (Provan and Gribben, 2010). However, most patients diagnosed with CML are asymptomatic. The most prevalent symptom is increased number of white blood cells. Other symptoms may be through enlarged spleen and liver in the upper quadrant leading to pain. Enlarged spleen may lead to increased pressure on the stomach leading to loss of appetite and weight loss. Mild fever is also experience and night sweats (U.S National Library of Medicine. 2014).

There is no known cause for CML. However, CML is common among males than females. Excessive radiations may lead to CML over time. CML is diagnosed through blood tests to assess the level of granulocyte cells. Bone marrow biopsy is also performed. Cytogenetic is another diagnostic method that is used to assess the chromosomal abnormality (U.S National Library of Medicine. 2014). CML was the first leukemia condition that was found to have strong links with genetic factors. CML condition arises from chromosomal translocation and is classified into three phases; chronic phase, accelerated phase and the blast crisis (Provan and Gribben, 2010).

Drug treatment helps to stop the progression if detection is made early. The blast crises stage exhibit similar predisposition as acute leukemia. CML has limited symptoms and most patients realize the condition during the accelerated and blast crisis. Research indicates that over

85% of patients get diagnosis at chronic phase. The chronic phase is asymptomatic but mild symptoms such as fatigue, hip pain and abdominal fullness may be experienced (Provan and Gribben, 2010).

Treatment

The only known curative treatment for CML is bone marrow or stem transplant. Other treatments involve the use of Tyrosine Kinase inhibitors and leukopheresis (Kufe, Pollack, Weichselbau et al., 2003). Verifiable data indicate that survival rates for CML patients using Tyrosine kinase inhibitors is high while reported deaths are minimal (Besa, Buehler, Markman and Sacher, 2013).

Improving treatment methods of Leukemia

Chemotherapy

Chemotherapy is a cancer treatment method that uses special chemical substances known as anti-cancer drugs. These drugs are prescribed for curative intent, to prolong the patient's life or to reduce symptoms (palliative chemotherapy). Chemotherapy is one of the major pharmacotherapy for cancer conditions along with targeted and hormonal therapy (Zhukov and Tjulandin, 2008). Chemotherapy drugs help in killing abnormal cells that is the main aspect in cancer diseases. One notable aspect of chemotherapy is decreased production of blood cells (immunosuppressant), loss of hair and inflammation on digestive tract lining (U.S National Library of Medicine. 2014).

Chemotherapy regimens are used in the treatment acute lymphoblastic leukemia (ALL). This involves a combination of different treatments such as multiple ant leukemic drugs. Chemotherapy is also effective in treating acute myeloid leukemia (AML). In these treatments,

Chemotherapy is done in phases; remission induction, intensification and maintenance therapy. The aim of remission induction is to kill rapid cancerous cells from the blood.

Remission induction chemotherapy is followed by intensification chemotherapy that involves the use of high doses of intravenous multidrug. Maintenance chemotherapy is done to eliminate any residue cells that were not killed in remission as intensification regimens. In all acute case of leukemia, maintenance chemotherapy is effective in inhibiting relapse of cancerous cells.

Treating acute promyelocytic leukemia (APL)

Acute Promyelocytic leukemia (APL) is a version of acute myelogenous leukemia (AML) where abnormal accumulation of immature white blood cells is prevalent (Tefferi, 2006). Acute Promyelocytic leukemia (APL) is one of the most treatable forms of leukemia with higher survival rates. Patients experiences anemia, fatigue, weakness, dyspnea, low platelets, bruising and nose bleeding (Bishop, 1997). APL results from chromosomal translocation of chromosome 17 (RARA), APL is distinguishable from other aspects of AML through bone marrow biopsy examination.

APL treatment is unique due to its sensitivity to all-trans retinoic acid (ATRA; tretinoin). ATRA does not kill malignant cells directly but is effective with time after administration (Tefferi, 2006). In 2013, Arsenic trioxide became the standard remission treatment for APL in chemotherapy (Lacroix, 2014). Another treatment method for APL is through consolidation chemotherapy. Consolidation chemotherapy is used to prevent relapse and enhance the survival rates of patients (Bishop, 1997).

Stem cell transplants

Stem cell transplants refer to the transportation from the bone marrow or peripheral blood cells in the treatment of leukemic cancers (Kane, 2008). In this case, the patient's immune system is destroyed through radiation or chemotherapy before cell transportation. Stem cell transplant is a dangerous procedure and only done when the patient life is threatened. Stem cell transplant is notably used in most type of leukemia (U.S National Library of Medicine. 2014).

Stem cell transplant involves the extraction of hematopoietic stem cells (HSC) which may be replaced after the harmful cells have been destroyed (Gribben, 2008). There are two types of stem cells grafts; allogenic and autologous. Autologous involves the use of patient's stored stem cells while allogeneic may be donated from other people (U.S National Library of Medicine. 2014). Autologous is mostly preferred for less complications involving the immune system (Gribben, 2008).

Targeted therapies

Targeted therapies are a form of chemotherapy for cancer conditions. Targeted therapies apply the principle of targeted cells to destroy cancerous cells (Zhukov and Tjulandin, 2008). Targeted therapy focuses on reducing the spread of malignant cells through pharmacotherapy. Targeted therapies may combine different treatments to kill harmful cells (Lacroix, 2014). There are different forms of targeted therapies such as cytotoxic therapy, biologic therapy and immunotherapy (U.S National Library of Medicine. 2014). Targeted therapies are effective in breast cancer, prostate cancer and leukemic cancers. The main categories of targeted therapy are monoclonal antibodies and small molecules. Examples include; Tyrosine kinase inhibitors (Zhukov and Tjulandin, 2008). Targeted therapies do not work like the standard chemotherapy but 'targets' the inner workings if harmful cells.

Immunotherapy

Immunotherapy is a treatment method that involves inducing, suppressing and enhancing immune response (Masihi, 2001). Immunotherapy may activate or suppress the immune response system depending n the condition and effect intended. In cancer cases, immunotherapy is used to activate the immune system in response to harmful cells. Immunotherapy involves the administration of cytokines (Motohashi, 2009). The cytokines lead to the development of antigens that in turn fight the cancerous cells (Kimura, Ashihara and Maekawa, 2006). Although immunotherapy is effective, it results in significant side effects such as allergies and immune tolerance.

Recent studies on leukemia

Recent studies reveal that research on treatment therapies is still on course. In a recent study by a Pennsylvanian University on investigative therapy made from patients' own cells, revealed that over 90% of patient with acute lymphoblastic leukemia (ALL) relapsed and failed to respond to standard therapies. The Pennsylvanian study is part of the modern immunotherapy methods used to treat acute cases of leukemia where other options have failed (Penn Medicine, 2014).

A recent study from San Francisco University found that some subtypes of childhood leukemia (ALL) are treatable with new target drugs. The new treatment drugs are *ibrutinib* and *idelalisib* that target the B-cells thereby reducing the mutation process. These target drugs are effective when used in high doses for young children during chemotherapy (Huimin, Christian, Kyle, Zhengshan, Dirk, Thompson, Natalya, Wei-Yi Chen, et al. 2015). In another study, physicians warned against the use of inbrutinib therapy in CLL leukemia because of higher relapse rates (Kami, Amy, Gerard, Nyla, Weiqiang, Lynne, Arletta, Melanie et al, 2015).

As technological advancement takes place scientists are making great progress in understanding the DNA and leukemia. In particular, recent studies have focused on chromosomal translocations in order to assess how the abnormalities could be corrected. Since each case of leukemia is different from the other, recent research is focused on understanding the gene behavioral changes as part of study on improved target therapies. In addition, further studies are conducted on traditional treatment methods as part of improving their effectiveness when treating leukemia condition (Cancer Org. 2014). For instance, currently researchers are studying new form of chemotherapy drugs such as Sapacitabine, Laromustine and Tipifarnib for treating AML leukemia (Cancer org. 2014).

In another case, Studies on treatment methods of Acute Promyelocytic leukemia (APL) have found that, a combination of ATRA and arsenic trioxide chemotherapies leads to improved cure. In addition, researchers are still studying the effectiveness of autologous and allogeneic methods of stem transplants. In immunotherapy, more studies have been focused on the development of new vaccine therapy such as immune checkpoint inhibitors and other antibodies. These new vaccines would improve the responsiveness of the immune system against various types of leukemia (Jabbour, Cortes, Giles, O'Brien and Kantarjian, 2007).

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