Acute Lymphoblastic Leukemia

Gabriella Leggio

Abstract: Leukemia is a cancer of the blood and bone marrow due to increased amounts of abnormal or immature white blood cells. A type of leukemia that occurs in the early forms of lymphocytes is called acute lymphoblastic leukemia (ALL). Diagnosis is made by the confirmation of different tests that are preformed. Once diagnosed, ALL is aggressively treated following an oncologist's treatment plan. There are a few different options for treatment of ALL. However, the prognosis for acute lymphoblastic leukemia is very poor. There is current research being conducted for new treatments and agents in order to cure patients with acute lymphoblastic leukemia (ALL).

Keywords: Leukemia, ALL, leukemia, Once diagnosed, confirmation

I. INTRODUCTION

The human body is a complex structure that is made up of many different systems. If one of these systems is compromised, it has a major effect on the entire body. One agent in specific that can destroy the body is called Leukemia. Leukemia is a cancer of the blood and bone marrow. It is different than most cancers because it is one that develops in the bone marrow where the blood cells are produced. Leukemia is detected by the presence of a high white cell count in the blood and abnormal cells present in the bone marrow. There are two types of classifications in which the type of leukemia is determined by. If the cancer develops quickly then it is classified as acute and if the cancer develops over a period of time it is classified as chronic. The types of blood cells that are affected are also determined. There are two different types of white blood cells that have the potential to turn into leukemia; lymphocytes or myelocytes. The four different types of leukemia, based on the cell types affected, include Acute Lymphoblastic Leukemia (ALL), Chronic Lymphocytic Leukemia (CLL), Acute Myeloid Leukemia (AML), and Chronic Myeloid Leukemia (CML). The diagnosis of the leukemia is determined by many tests, including a complete blood count (CBC), cytogenetic analysis, lumbar puncture, and bone marrow aspiration and biopsy. Treatment for leukemia is very invasive and hard on the patient. Depending on the type of leukemia, treatment plans are specific for each individual. Treatment options include chemotherapy and a stem cell transplant. Another option for treatment is participation in a clinical trial. In order to participate in a clinical trial, there are a certain criteria that the individual must meet. This criterion is based on age, gender, stage of disease, current medications, existing medical conditions, etc. In specific, Acute Lymphoblastic Leukemia (ALL) is one of the cancers that occurs in the early forms of lymphocytes. These lymphocytes turn into lymphoblasts and take over the bone marrow. Since ALL is a type of acute leukemia, it must be aggressively treated proceeding diagnosis.

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Within ALL, there are two main subtypes that are classified as B-cell and T-cell ALL. There are also other subtypes such as precursor B-cell, early T-cell precursor ALL, Burkitt-type, and Philadelphia chromosome positive ALL. These subtypes are a result of the type of lymphocyte affected. Patients who are diagnosed with ALL range from pediatrics to adults. It is seen dominantly in pediatrics but is found among adults as well. There are many different factors that play a role in treatment for the patient and are crucial to surviving with ALL. There are also current studies that are researching new treatments and drugs to hopefully find a cure for ALL.

II. ONCOLOGY

Oncology is a field of medicine that deals with the study and treatment of cancer. If an individual is diagnosed with cancer they are sent to see a special type of doctor. This doctor is called an Oncologist. They are responsible for deciding the patient's treatment, delivering compassionate care, and monitoring the patient's progress. Hematology is a field that focuses on internal medicine, specifically the blood. This type of doctor is called a Hematologist and they deal with individuals who have blood disorders. Typically, some doctors will specialize in both oncology and hematology. For a patient with acute lymphoblastic leukemia (ALL) this is the doctor that the patient would see. Leukemia is a cancer of the blood which develops in the bone marrow, and originates from the uncontrolled growth of an abnormal blood cell. The bone marrow is the soft, spongy center of certain bones that produces the three major types of blood cells: white blood cells (leukocytes) to fight infection; red blood cells (erythrocytes) that carry oxygen; and platelets (thrombocytes) that help with blood clotting and stop bleeding (Texas Children's Hospital, 2016). Bone marrow is made up of blood, fat, and stem cells that are eventually turned into different types of blood cells. Figure 1 shows the lineage of the blood cells from the origin of the stem cell. Starting as a stem cell, it can either become a myeloid or lymphoid cell. Lymphoid lineage cells include T, B, and natural killer (NK) cells, while megakaryocytes and erythrocytes (MegE) as well as granulocytes and macrophages (GM) belong to the myeloid lineage (Kondo, 2010).

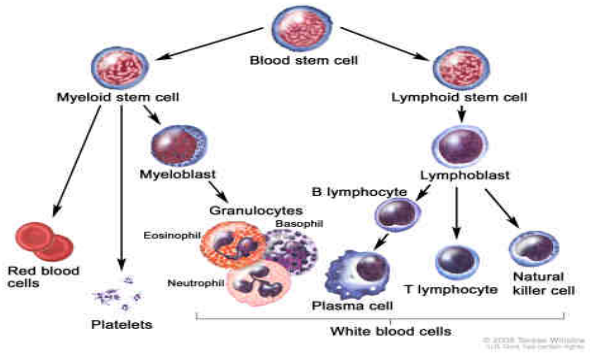

Figure 1: Complete Lineage of Blood Cells

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http://www.seattlecca.org/diseases/leukemia-facts.cfm

Figure 1: Lineage of different types of blood cells originating from the blood stem cell. The cells split into either myeloid or lymphoid stem cell. The cells split again trickling down to what we know as red blood cells, platelets, and white blood cells.

Acute lymphoblastic leukemia (ALL) is a heterogeneous group of disorders caused by clonal expansion of immature lymphoid cells (Gastier-Foster, 2010). With ALL, the lymphoblast cells start off as blasts and produce lymphocytes, which are a type of white blood cell. The types of lymphocytes are B-lymphocytes, T-lymphocytes, and natural killer (NK) cells. The job of the B-lymphocyte is to produce antibodies to fight infections. T-lymphocytes are responsible for cellular immunity and aid B-lymphocytes in producing antibodies. The role of natural killer (NK) cells is to defend the body's immune system by attacking virus-infected or tumor cells.

III. DIAGNOSIS OF ALL

The two main subtypes of ALL are B-cell and T-cell ALL. ALL develops from early-stage lymphocytes in various stages of development (Leukemia & Lymphoma Society, 2016). Precursor-B ALL, characterized by a malignant proliferation of immature B-lineage lymphoid cells, comprises the majority of all leukemias in both adults and children (Gastier-Foster, 2010). According to the Leukemia & Lymphoma Society, 85% of ALL cases affect B-lymphocytes, and about 15% affect T-lymphocytes. ALL rarely affects the natural killer (NK) cells.

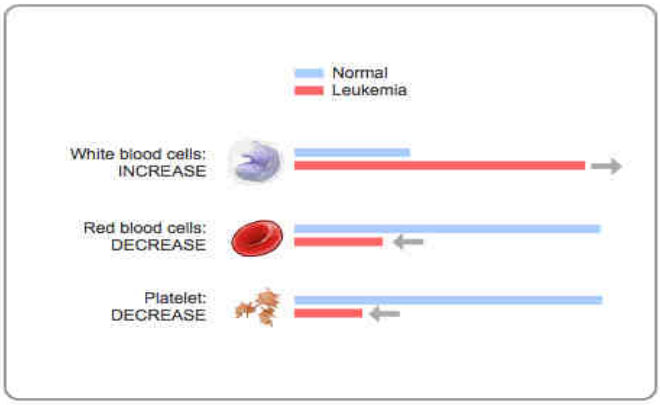
The diagnosis of ALL is determined by various factors. The first indication would be to assess the type of symptoms the individual is having. It is seen that individuals with acute leukemia are more susceptible to experience many symptoms. The individual will present with fevers, fatigue, swollen lymph nodes, bone pain, etc. Other symptoms may include easy bruising and bleeding or purple looking patches on the skin. In order for the doctor to confirm diagnosis, they would have the patient undergo many different tests. The first tests would be a complete blood test (CBC) and a peripheral blood smear. A CBC is done in order to check the patient's white blood cells, red blood cells, and platelet counts. Table 1 shows the normal values for the CBC in adults.

Table 1: Complete Blood Count (CBC) Ranges for Both Male/Female

Parameter	Normal Range (Male)	Normal Range (Female)
WBC	5,000-10,000/mL	5,000-10,000/mL
RBC	4.6-6.0x10^6/mL	4.2-5.0x10^6/mL
Platelet	150,000 - 400,000/mL	150,000 - 400,000/mL

Table 1: Values of a complete blood count (CBC), which includes the white blood cell (WBC), red blood cell (RBC), and platelet counts in both males and females.

An individual who is suspected to have leukemia will show different results on their CBC than a healthy person. Their CBC may show an abnormal increase of the white cell count and would also show an abnormal decrease in the red blood cells and platelets.

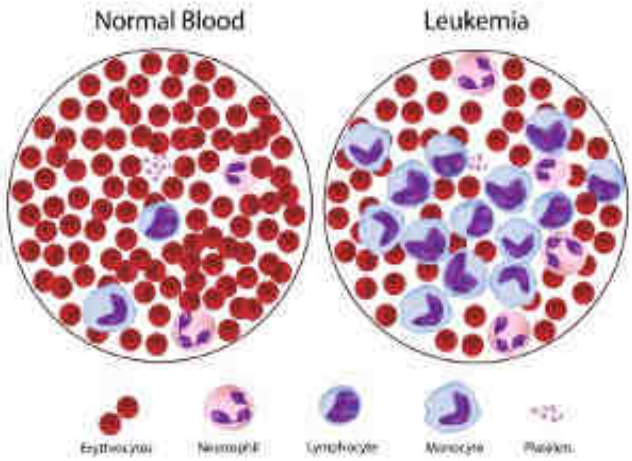


http://www.hematology.org/Patients/Cancers/Leukemia.aspx

Figure 2: Comparison of Normal and Leukemic Blood Counts

Figure 2: Comparison of complete blood count (CBC) components between normal and leukemic counts. Shows the increase or decrease of white blood cell, red blood cell, or platelets.

A peripheral blood smear is preformed in order to show if there are any abnormal blood cells present in the patient's blood. This test also shows the quantity, size, and shape of cells, which gives valuable information in diagnosing the leukemia. Figure 3 shows two types of peripheral blood smears. One of which is normal and the other that possess leukemia. As shown, there is an excess of cells and many abnormal looking white cells. In the normal blood smear, there is a proportionate amount of erythrocytes (RBC) and white cells.



http://www.geneticdisorders.info/article/8553143612/leukemia-blood-cancer

Figure 3: Normal and Leukemic Peripheral Blood Smears

Figure 3: Peripheral blood smears of normal and leukemic blood. In the normal blood, there is an adequate amount of WBC. In the leukemic blood, there is an excessive amount of lymphoblast's (WBC).

In addition, the patient would also undergo cytogenetic analysis. Cytogenetics is the study of the quantity and structure of chromosomes. A sample of blood or bone marrow is studied in order to see if there are any chromosomal changes in the DNA due to the leukemia.

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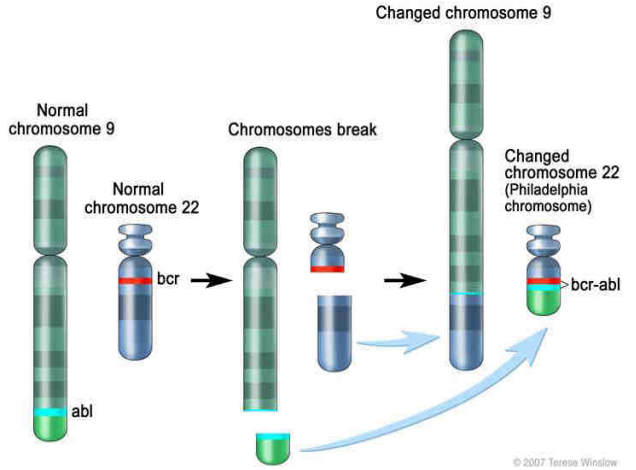
Patients with ALL are shown to have a translocation event occur between two chromosomes. In genetics, a chromosome *translocation* is a chromosome abnormality caused by rearrangement of parts between nonhomologous chromosomes (U.S. National Library of Medicine, 2016). The two most common chromosomes that translocate in ALL patients are chromosomes 9 and 22. The chromosome then becomes shortened and is classified as the Philadelphia chromosome. Figure 4, shows the formation of the Philadelphia chromosome on a genetics level. It demonstrates the translocation event between chromosome 9 and 22 and shows the fusion of the bcr-abl gene on chromosome 22. The Philadelphia (Ph) chromosome, resulting in a BCR-ABL fusion protein with deregulated tyrosine kinase activity, is the most common cytogenetic abnormality found in adult patients diagnosed with acute lymphoblastic leukemia (ALL) (Soverini et al, 2014).

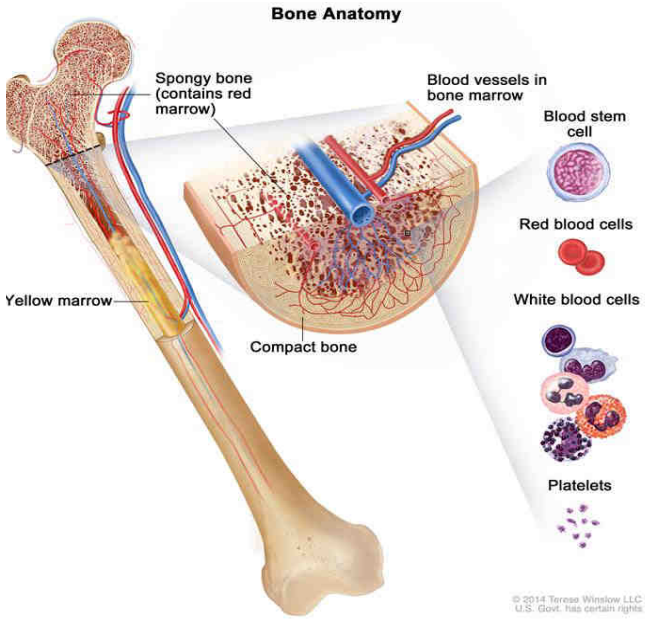


http://www.cancer.gov/publications/dictionaries/cancer-terms?cdrid=44179

Figure 4: Formation of the Philadelphia Chromosome

Figure 4: During the formation of the Philadelphia chromosome, translocation occurs with chromosome 9 and 22. Those pieces fuse together to form the bcr-abl gene on the new chromosome 22 (Philadelphia chromosome).

Patients that are suspected to have ALL also undergo a bone marrow aspiration and biopsy. The bone marrow biopsy and aspiration (BMBA) is an essential diagnostic approach to the diagnosis of hematological disorders (Talamo et al, 2010). This test provides information about the type of cells/cell structure within the bone marrow. Blood cells are formed specifically in the bone marrow and this is where the blood stem cells produce myeloid and lymphoid stem cells. The two different types of bone marrow are red or yellow. The red marrow consists of red blood cells, white blood cells, and platelets. Within the yellow marrow, there is a higher amount of fat cells present which causes the color of the marrow to be yellow. Spongy bone contains the red bone marrow and is found in flat bones such as the vertebrae, ribs, sternum, and pelvis. Yellow bone marrow is found in the shaft of a long bone. Yellow marrow stores adipocytes (fat cells), which provides a source of energy for the body. Figure 5, shows the anatomy of a bone and the location where the different bone marrows are found.



http://www.cancer.gov/types/leukemia/patient/adult-aml-treatment-pdq

Figure 5: Anatomy of the Human Bone

Figure 5: Anatomy of a bone. Shows the makeup of compact and spongy bone each containing a type of bone marrow. Spongy bone is found at the ends of bones where as compact bone is found along the shaft of bone. Red bone marrow is found in the spongy bone containing RBC, WBC, and platelets. Yellow bone marrow is found inside the shaft of the bone containing fat cells.

When undergoing a bone marrow aspiration and biopsy procedure, the aspiration is usually done first. This procedure is preformed in order to check the status of the disease and to observe the progression of treatment. A bone marrow aspiration is a procedure in which a sample of the soft tissue inside the bone is obtained for testing. This will also provide information about the red blood cells, white blood cells, and platelets. A bone marrow biopsy is the second part of the procedure where a sample of solid bone marrow is obtained. This marrow is also sent off to the lab for further testing.

A bone marrow aspiration and biopsy is usually preformed outpatient or inpatient at the patient's bedside. In order to preform a bone marrow biopsy and aspiration the patient must be in on their side or stomach depending on the bone that is used. Usually the superior iliac crest is used as the biopsy site. Before the biopsy, a local anesthetic is injected into the subcutaneous tissue to numb the area and reduce pain (Hjortholm et al, 2013). The biopsy needle is then inserted into the bone through the bony cortex. A syringe is attached and used to draw up bone marrow aspirate. Obtaining the biopsy is the second part of the procedure. If the biopsy is performed in the posterior or anterior iliac crest, the larger trephine biopsy (TB) needle is used to collect a cylindrical sample of solid bone marrow (Hjortholm et al, 2013). Once the sample is obtained, the needle is removed and pressure is applied to stop the bleeding. When both the aspirate and biopsy is collected it is smeared on microscope slides for further testing. Figure 6 shows the bone marrow biopsy and aspiration and the correct position of the patient during the procedure. It also includes the anatomy of the hipbone, as well as instruments

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used and microscopic images of the bone marrow specimen. As shown, the bone marrow with leukemic cells is packed with blasts. Compared to the normal bone marrow, there is a difference between the cells and isn't as packed.

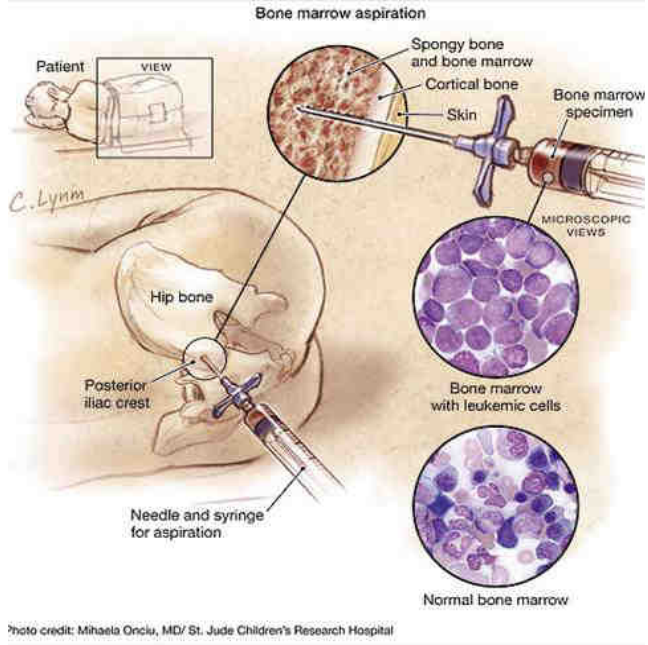
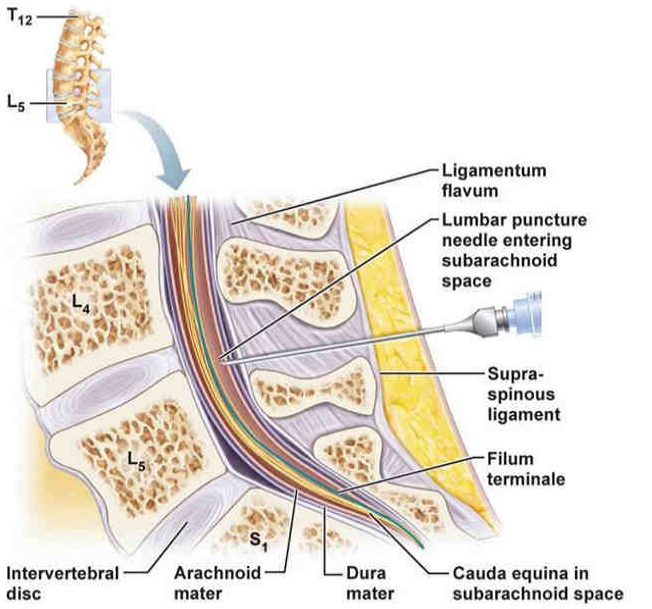


Figure 6: Illustration of a Bone Marrow Biopsy and Aspiration.

Figure 6: Illustration of the position of the patient during the bone marrow biopsy and aspiration. Includes the anatomy of the hipbone, instruments used and microscopic images of the bone marrow specimen.

Another viable test that would be preformed is a lumbar puncture, also known as a spinal tap. This is a procedure that is preformed in order to obtain and examine the cerebrospinal fluid (CSF) that is located surrounding the brain and spinal cord. The internal fluid of the system, or cerebrospinal fluid (CSF), is maintained as a protein-poor product of the plasma and is an ideal milieu for the proper functioning of nerve cells (Wood, 2013). This procedure is preformed either outpatient or inpatient at the patients bedside. During this procedure, the patient hovers over in order to get a curvature in the spine. The site of the tap is between the widest spaces of the lumbar vertebras L2-L5. Once the site is found, the area is numbed with lidocane. A small needle called a stylist is then inserted into the subarachnoid space in the lower back area. Immediately, the CSF fluid drains out and is caught by a test tube that will be sent off for testing. After the extraction of fluid, it is replaced by an injection of chemotherapy that goes straight into the spinal canal. This is done in order to target the spine and brain cells more direct than intravenously and to also give back the amount of fluid that was taken out. CSF offers a valuable, although indirect, vehicle for defining brain malfunctions. Inferences from CSF data, however, require a clear understanding of the relationship between the CSF and brain (Wood, 2013). Figure 7, shows the anatomy of the spine and the lumbar vertebrae involved in the procedure, including an illustration of the stylist being inserted into the subarachnoid space.



http://www.oxfordmedicaleducation.com/clinical-skills/procedures/lumbar-puncture

Figure 7: Anatomy of the Spine and Lumbar Puncture Location

Figure 7: Illustration of the stylist being inserted into the subarachnoid space of the spine during a lumbar puncture procedure.

IV. SUBTYPES OF ALL

Acute lymphoblastic leukemia (ALL) is divided into subtypes in order for better classification. These subtypes provide doctors with the ability to make a specific treatment plan rather than a broad one. Subtypes of ALL are an indication for which lymphocytes are affected in the body. The two main subtypes are B-cell and T-cell ALL. Subtypes also include precursor B-cell ALL, early T-cell precursor ALL, Burkitt-type ALL, and Philadelphia chromosome positive ALL. Immunophenotype of the leukemia is determined by weather the B-cell or T-cell lymphocyte the leukemic cells originate from. It is also determined by the maturity of the cells present.

Flow cytometry-based immunophenotyping (FC-MRD), differentiates leukemic cells from normal cells based on aberrant antigen expression (leukemia-associated immunophenotype, LAIP) (Øbro, 2012). Flow cytometry is a type of test that is preformed on patients with ALL to examine the cells to distinguish what type of markers are present. This test will determine which cells are involved such as B-cells or T-cells. Therefore, its known that B-ALL involves B-cells and T-ALL involves T-cells. Graph 1, shows flow cytometry being performed on leukemic cells. The two slides at the top show normal patterns of antigen expression and the two slides at the bottom show increased amounts of leukemic cells (green dots). CD45 is a common lymphocyte antigen that is responsible for the function of the cell. CD10 is called CALLA (common acute lymphocytic leukemia antigen), which is a marker for ALL. The graph also shows an increase in CD10 and would be an indication that the sample contains CALLA. Therefore, this patient would be diagnosed with ALL.

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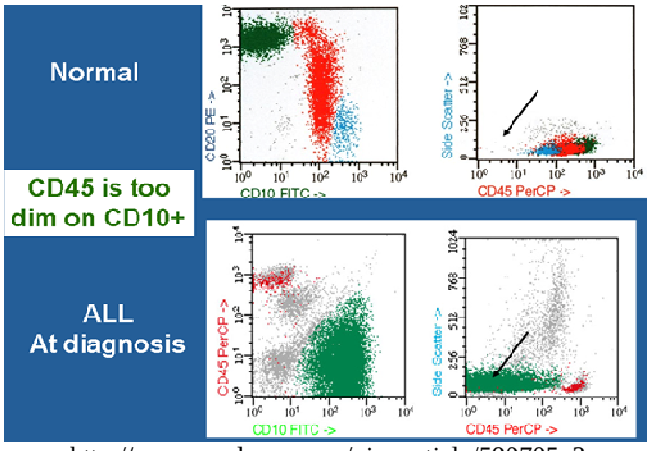

http://www.medscape.org/viewarticle/590705_3

Graph 1: Flow Cytometry Results of Normal and Leukemic cells

Graph 1: Example of flow cytometry preformed on normal and ALL cells. The two slides at the top show normal patterns of antigen expression and the two slides at the bottom show leukemic cells (green dots) have increased. Shows an increase in CD10 and therefore indicates a diagnosis of ALL.

Precursor B-ALL is characterized by a proliferation of lymphoblast's arrested at an early stage of B-cell maturation (Tang, 2012). Precursor B-ALL is the result of too many white blood cells produced and interrupted during development leaving the B-cells immature. Early T-cell precursor (ETP) acute lymphoblastic leukemia (ALL) is a recently recognized high-risk T lymphoblastic leukemia (T-ALL) subgroup (Jain, 2016). ETP ALL is characterized by lack of expression of the T-lineage cell surface markers CD1a and CD8, weak or absent expression of CD5, aberrant expression of myeloid and hematopoietic stem cell markers (for example, CD13, CD33, CD34 and CD117), and a gene expression profile reminiscent of the murine early T-cell precursor (Zhang, 2011).

Another subtype of ALL is Burkitt Leukemia. Burkitt-type ALL is a result of an excess production of white blood cells. These WBC are called B-lymphocytes and form in the blood and bone marrow. Burkitt's leukemia is separated by its typical morphologic features (blasts with typical French-American-British [FAB] L-3 morphology compared to FAB L-1/L-2 morphology in pre-B ALL) and a classic immunophenotype (blast positivity for CD45 [bright], CD20 [bright], CD10, CD19, surface immunoglobulin [SIg], Ig light chain restriction, and negative terminal deoxynucleotidyl transferase [TdT]) compared to pre-B ALL blasts (which are positive for CD45 [dim], CD10, CD19, and TdT and negative for CD20 and SIg) (Rawlinson, 2011). Burkitt-type ALL is a type of disease of the mature B-cells and is found to be very curable. Lastly, another subtype is Philadelphia chromosome-positive ALL. Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL) is initiated and driven by the oncogenic fusion protein BCR-ABL, a constitutively active tyrosine kinase (Appelmenn, 2015). In patients with ALL, a translocation event occurs at chromosome 9 and 22. This then results in the fusion of the BCR-ABL protein.

V. TREATMENT

Immediately following diagnosis, the oncologist will communicate treatment options with the patient. Treatment options for leukemia are very invasive but these measures need to be taken in order to fight the cancer. The main options to treat acute lymphoblastic leukemia (ALL) are chemotherapy and stem cell transplant. There is also the possibility of participating in a clinical trial as a last resort.

Chemotherapy is a drug that is used in order to treat cancer. Although it may cause many side effects, it is crucial for treating cancer. Chemotherapy drugs are injected into a vein or taken by mouth. A peripherally inserted central catheter (PICC) is used in order to deliver the chemotherapy drugs and is most commonly used because it is intravenous access that is accessible for a prolonged period of time. When the chemo is delivered directly into the bloodstream it automatically targets the cancerous cells around the body. However, some chemo drugs don't have the access to reach some parts of the brain and spinal cord. This is due to the presence of the blood-brain barrier (BBB). This barrier filters the substances that are trying to access the brain and spinal cord. It either blocks or allows substances to pass the barrier. The BBB is formed by the endothelial cells lining the brain micro vessels, under the inductive influence of neighboring cell types within the 'neurovascular unit' (NVU) including astrocytes and pericytes (Abbott, 2013). To overcome this barrier, chemo is injected into the cerebrospinal fluid to kill cancer cells in that area. This injection is called intrathecal chemo and is delivered during a lumbar puncture procedure (spinal tap).

Chemotherapy is given to patients in cycles. After each cycle of treatment there is a rest period in which the body has time to recover. Chemo for acute lymphocytic leukemia (ALL) uses a combination of anti-cancer drugs and is given in 3 phases. These phases include induction, consolidation and maintenance. The first phase of inductions is when intense chemo is given for about a month. The chemo drugs that are given during this phase are dexamethasone, doxorubicin, and vincristine. Prednisone (or prednisolone) has traditionally been used in ALL treatment, but dexamethasone is increasingly considered (Inaba, 2013). Patients who possess Philadelphia chromosome-positive ALL will be given the chemo drug called imatinib. This is a tyrosine kinase inhibitor (TKI) drug that inhibits tyrosine kinases.

If the patient has a successful induction phase and goes into remission, they are then able to move on to the consolidation phase. During this phase, the patient receives the same chemo drugs but in higher doses. This phase commonly uses high-dose (ie, 1–8g/m^2) methotrexate (MTX) with mercaptopurine, frequent pulses of vincristine and glucocorticoid, uninterrupted asparaginase for 20–30 weeks, and reinduction therapy with agents similar to those used during remission-induction (Inaba, 2013). This is done so that the treatment keeps working and the leukemia does not make its way back. If the leukemia stays in remission, the final phase is maintenance. Continuation therapy typically lasts 2 years or longer and comprises mainly daily mercaptopurine and weekly methotrexate with or without pulses of vincristine and dexamethasone (Inaba, 2013). It is

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found that about 80-90% of adults will be in complete remission at some point during the duration of these phases.

Another type of treatment that would be used to treat ALL is a stem cells transplant (SCT). A stem cell transplant is when stem cells from a donor are transferred into the patient with leukemia after receiving high-intensity chemotherapy. The stem cells come from the donor's blood or the bone marrow. They can also come from the umbilical cord of a newborn baby. Stem cell transplants are preformed to treat a patient who isn't responding to treatments, or has relapsed after successful treatment. These high-risk patients require additional therapeutic approaches after achieving remission (Peters, 2015). The high doses of chemotherapy are supposed to wipe out the cancerous cells, but during this they also destroy normal cells of the bone marrow and immune system.

Once the chemotherapy is completed, the new cells are given intravenously. The stem cells for transplantation can be either autologous or allogeneic. Autologous transplantation allows the administration of high-dose chemotherapy without prolonged bone marrow aplasia. In allogeneic transplantation, donor-derived stem cells provide alloimmunity that enables a graft-versus-tumor effect to eradicate residual disease and prevent relapse (Henig, 2014). Hematopoietic stem cell transplantation (HCT) using hematopoietic progenitor cells from the patient (autologous HCT) or a donor (allogeneic HCT) is a potentially curative therapy for many life-threatening cancers and nonmalignant disorders (Majhail, 2015). It is seen that patients with hematologic disorders who have had no success with other treatments respond well to hematopoietic stem cell transplants. Over the past four decades, allogeneic hematopoietic cell transplantation (alloHCT) has evolved as a curative modality for patients with hematologic diseases (Hahn, 2013). AlloHCT as treatment for acute lymphoblastic (ALL) and myeloid leukemias (AML), myelodysplastic syndrome (MDS), and Hodgkin and non-Hodgkin lymphomas increased by 45%, from 2,520 to 3,668 patients annually (Hahn, 2013).

However, with a stem cell transplant there can be serve complications. The transplant puts the patient into a very high risk of developing graft-versus-host disease (GVHD). Allogeneic hematopoietic stem cell transplantation is used to treat a variety of disorders, but its efficacy is limited by the occurrence of graft-versus-host disease (GVHD) (Blazar, 2012). This is a disease that can occur after a stem cell transplant where the donor cells attack the patient's own normal cells. Graft-versus-host disease can range from mild to life threating. If the patient is older, the risk is much higher for a more serious reaction. Because GVHD can be so severe, it is important to be able to recognize symptoms right way. Some symptoms may include nausea, body rash, mouth ulcers, and jaundice. Once diagnosed, the oncologist will make a treatment plan for the patient. Graft-versus-host disease is usually treated with immunosuppressant drugs. These types of drugs decrease the chances of the body rejecting a transplant. These drugs may include corticosteroids (prednisone), monoclonal antibodies (basiliximab), and cyclosporine. New insights from basic immunology, preclinical models and clinical studies have led to novel approaches for prevention and treatment (Blazar, 2012). If a patient has had the leukemia relapse and still wants to pursue treatment, the next option would be to participate in a clinical trail. Firstly, we need to define exactly what is meant by a 'clinical trial': briefly the term may be applied to any form of planned experiment which involves patients and is designed to elucidate the most appropriate treatment of future patients with a given medical condition (Pocock, 2013). These studies are specifically useful for patients diagnosed with leukemia. However, in order to participate in a clinical trial, there is certain criterion that an individual must meet. The protocol of a clinical trial plays a key role in study planning, conduct, interpretation, oversight, and external review by detailing the plans from ethics approval to dissemination of results (Chan, 2013). This criterion is based on a variety of different aspects including age, stage of disease, current medications, and existing medical conditions. Being that there is a protocol that the patient must meet, this means that the patient will endure frequent testing. The health of the patient is monitored before the clinical trial in order to have a baseline when assessing how effective the trial is over time.

Currently, there are specific agents being researched and studied in clinical trials for patients with acute lymphoblastic leukemia (ALL). These agents include proteasome inhibitors, antimetabolites, janus kinase (JAK) inhibitors, and immunotherapies. A drug called Velcade is a type of proteasome inhibitor that is being studied to treat relapsed pediatric-ALL patients and patients with T-cell ALL. A drug called Clolar is a type of antimetabolite that is being studied to treat relapsed ALL. Jakafi, a type of Janus kinase inhibitor (JAK), is being studied to treat pediatric relapsed ALL. An immunotherapy drug called Rituxan is being studied to use in a clinical trial for ALL. Rituxan is made up of monoclonal antibodies, which are antibodies that are made by cells of a single clone. They are used in cancer treatment to target cancer cells (Leukemia & Lymphoma Society, 2016).

VI. CONCLUSION

Leukemia is one of the most prominent blood cancers in medicine today. Starting with diagnosis to treatment and remission is a long journey. Leukemia comprises a person's whole life and is very taxing on their body. The four different types of leukemia include Acute Lymphoblastic Leukemia (ALL), Chronic Lymphocytic Leukemia (CLL), Acute Myeloid Leukemia (AML), and Chronic Myeloid Leukemia (CML). The two main subtypes of ALL are classified as B-cell and T-cell ALL. Other subtypes of ALL include precursor B-cell, early T-cell precursor ALL, Burkitt-type, and Philadelphia chromosome positive ALL. These are a result of type of lymphocyte affected.

Acute lymphoblastic leukemia (ALL) is one type of leukemia that is commonly seen today. It is a cancer of the blood that occurs in the early forms of lymphocytes. These lymphocytes turn into lymphoblasts and take over the bone marrow. Many tests are performed in order to confirm the diagnosis. These tests comprise of complete blood count (CBC), cytogenetic analysis, lumbar puncture, and bone marrow aspiration and biopsy. Once diagnosed by an

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oncologist, it is then aggressively treated. The oncologist will then formulate a treatment plan based on the stage and type of leukemia the patient possess. Treatment options include chemotherapy, stem cell transplant, and participation in a clinical trial. However, with a stem cell transplant there can be serve complications such as developing graft-versus-host disease (GVHD).

There is current research being conducted on new treatment drugs for patients with acute lymphoblastic leukemia (ALL). These agents are being studied in clinical trials that patients with acute lymphoblastic leukemia are enrolled in. These agents include proteasome inhibitors, antimetabolites, janus kinase (JAK) inhibitors, and immunotherapies. Treatment options and prognosis is looking promising in the near future for ALL. Researchers and patients are eager for new technological advances that provide for finding a cure to ALL.

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