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Acute Myeloid Leukemia

There were approximately 43,050 new cases of leukemia in 2010 alone (Leukemia Research Foundation). It occurs in both adults and children- and is the most prevalent type of cancer in children ages one to seven (Leukemia and Lymphoma Society). Having said this, it is important to distinguish between the four major types of leukemia: Acute Myeloid Leukemia, Acute Lymphoblastic Leukemia, Chronic Myeloid Leukemia, and Chronic Lymphocytic Leukemia. What differs is the type of blood cell being affected- as well as the cell's classification of being either an immature, or mature white blood cell. Perhaps one of the more serious types of leukemia is AML, or Acute Myeloid Leukemia. Because it is acute, it develops quickly and rapidly. This paper will mainly focus on AML, although all acute leukemia's are similar in the sense that they affect the white blood cells and progress quickly.

HISTORY

The first written record of leukemia in medical literature was not until 1827, when French doctor Alfred-Armand-Louis-Marie Velpeau explained the symptoms that his 63 year old patient was experiencing. He came to Velpeau with a fever, weakness, urinary stones, as well as excessive enlargement of his liver and spleen (News Medical). The word "leukemia" was named by a well known German pathologist by the name of Rudolph Virchow, in 1856 (News Medical). The word literally translates to "white

blood," which goes in accordance with the high levels of white blood cells physicians typically see in leukemia patients (Leukemia and Lymphoma Society). Virchow is cited as one of the first to actually identify leukemia cells. Yet another renowned physician in the history of leukemia is John Hughes Bennett. He officially diagnosed leukemia in 1845, and named it "leucocythaemia".

The technique of using bone marrow biopsies (method that it still used today) in order to diagnose leukemia was first accredited in 1879, by Otto Naegeli, a Swiss hematologist. He then went on to divide the lymphoblast and myeloid cell into two separate types of leukemia- ALL and AML (News Medical). The development of radiation and chemotherapy in the 1900s helped shape the future of treatment for leukemia, and paved the way for further advances (McGlauflin, Shannon et al.).

Perhaps one of the greatest progressions occurred when James Watson and Francis Crick made the discovery of DNA. This helped in developing a more in-depth look at the genetics of cancer and how certain carcinogens could damage DNA, and potentially cause cancer.

CAUSES/RISK FACTORS

It is important to note that while there are some risk factors that may lead to the development of leukemia, many patients, if not most, do not have any of the risk factors (Leukemia and Lymphoma Society). Having said that, risk factors for leukemia include but are not limited to: high exposure to benzene, genetic disorders like Down syndrome, past chemotherapy/radiation treatments, and a medical history of other blood disorders or cancers. Another aspect that must be taken into consideration is age. Even though age itself is not a risk factor for developing AML, those who are over the age of 60 are at a

higher risk than those who are younger.

DEVELOPMENT

The development of Acute Myeloid Leukemia begins when a stem cell that produces myeloblasts goes through a mutation, resulting in the overproduction of this now abnormal white blood cell. Eventually, the blood marrow becomes full of leukemic cells that overcrowd normal cells. Leukemia cells will eventually leak into the blood stream, where they can potentially spread to the central nervous system (Leukemia and Lymphoma Society).

SYMPTOMS

Once the bone marrow has become crowded with lukemic cells and can no longer produce its own, many problems arise. The bone marrow is where white blood cells, red blood cells, and platelets are produced. As a result of this, the absolute neutrophil count of an individual may drop, putting them at a higher risk of infection. This can lead to symptoms of fever, or frequent infections. When platelet production is decreased, the body can no longer clot blood and stop bleeding after a cut or injury. If an individual's platelet count drops *too* low, they may be at a higher risk for serious internal bleeding as well. Symptoms of low platelet count includes bruising, excessive bleeding, and petechiae- small broken capillary blood vessels that can be characterized by tiny dot-like spots on the body that may be purple or red. When the number of red blood cells drop to a certain level, anemia occurs. Someone with anemia may experience symptoms of fatigue, dizziness, pale skin, rapid heat beat, and headaches. All these symptoms are a result of the body not having enough hemoglobin- a protein that is associated with the transport of oxygen throughout the entire human body (Leukemia and Lymphoma

Society). Those with AML that has spread to the CNS (central nervous system) may experience severe headaches (also can be caused by anemia), seizures, and trouble balancing.

DIAGNOSIS

From here a proper diagnosis must be made. Physicians will normally order a CBC blood test in order to look at a patient's platelet, red blood cell, and white blood cell count. Patients with leukemia will generally have a high white count, accompanied by a low platelet and red blood cell count. A peripheral blood smear will also be done in order to determine the amount of immature or abnormal white blood cells present in the body. The next step in diagnosing AML is a bone marrow biopsy and aspiration (Leukemia & Lymphoma Society). First, a small sample of liquid is taken from the marrow. From here, the physician will also take a sample of bone from the marrow. These two samples will be tested in order to determine the number of leukemic cells present in the bone marrow (Leukemia & Lymphoma Society). When at least 20 percent of the marrow is made up of blast (leukemic) cells, a positive diagnosis for AML can be made. The cell type will then be determined, along with any abnormal changes. Cytogenetic analysis and immunophenotyping are lab tests in which changes to chromosomes and genes are distinguished, as well as the involvement of antigens on blast cells in the marrow (Leukemia & Lymphoma Society). It is estimated that approximately 60 percent of those with AML have an abnormal number, or structure of their chromosomes (Leukemia & Lymphoma Society). Trisomy 8, trisomy 21, monosomy 7, and monosomy 21, are all the major chromosome changes that can occur in AML patients. Some may even lose an x or y chromosome (Leukemia & Lymphoma Society). With this information, a subtype will

be determined and the best possible treatment plan will begin.

TREATMENT

For patients who have been newly diagnosed with AML or other acute leukemia's, treatment usually starts right away (The Leukemia & Lymphoma Society). The most common treatment plan for AML patients includes chemotherapy, radiation (if disease has spread to CNS), stem cell transplantation, and other anti-cancer drugs that may be used for other subtypes of AML, such as subtype M3; also known as acute promyelocytic leukemia (The Leukemia & Lymphoma Society).

The first phase of treatment begins with induction, where the goal is to kill as many cancer cells as possible, and to get the patient into remission. High levels of chemotherapy are used during induction. Not only does chemotherapy destroy cancer cells, but it also destroys the bodies own healthy cells as well. As a result, chemotherapy can significantly decrease the body's blood counts. In the days/weeks following chemotherapy, patients may experience the unpleasant side effects of treatment. Some of these side effects may include nausea, difficulty eating, muscle/joint pain, hair loss, higher risk of infection, anemia, and low platelet count. This however, is only temporary. Usually one to two weeks following treatment, the body will begin to make its own cells again (The Leukemia & Lymphoma Society). Induction generally brings remission in about 70% to 80% of adults under the age of 60, and over 90% in children (National Marrow Donor Program). Once the induction phase is complete, patients go on to post remission therapy- also known as consolidation therapy. It is during this phase that the remaining leukemia cells in the body are targeted. Without it, almost all patients would be likely to relapse. It is also during this phase that stem cell transplantation occurs. Stem

cell transplantation is more common in adults and in relapsed or refractory patients (Poinier, Anne, et al.) The process begins by using high levels of chemotherapy and/or radiation in an attempt to destroy the body's own bone marrow. It is at this time a donor's stem cells will be released into the patient's body, and into their bone marrow. If the transplantation is successful, the bone marrow will now be able to produce normal, healthy, white blood cells-as well as red blood cells and platelets. It is also important to note that this procedure can only be done when the donor's stem cells are a close match with the patient's.

Throughout treatment, patients who did not have leukemic cells present in their spinal fluid still receive chemotherapy in the central nervous system in order to prevent it from spreading there. Many patients still receive maintenance therapy, or low dose therapy after these stages have been completed.

RESEARCH

A vast amount of research has been done in order to improve treatment and decrease morality rates. In a recent study done by Pediatric Hematology and Oncology at a University Children's Hospital in Germany, researchers found that patients with a large number of leukemia stem cells at the time of diagnosis were more likely to relapse and respond poorly to treatment. They compared these patients with those who had a low overall amount of leukemic stem cells at diagnosis, and found that the patients with low LSC had a higher rate of survival. It was also noted that "most immature leukemia cells are more resistant to therapy and subsequently initiate relapse" (Department of Hematology/Oncology, University Children's Hospital).

Over the years, the treatment for Acute Myeloid Leukemia has significantly

improved. Just in 2010 alone, the Leukemia and Lymphoma Society has donated over 72 million dollars in blood cancer research. Survival rates have increased, and new medications and therapies have paved the way for even better results. Technology and science have further increased our understanding and knowledge in the way cancer works. With stem cell research and other therapies being studied, it is only a matter of time before these new and promising therapies can help us find a cure.

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