Understanding Leukemia

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Abstract

"Leukemia" is a commonly recognized yet ambiguous umbrella term that encompasses an array of blood cancers stemming from a large variety of genetic mutations. Because more than six people per hour are diagnosed with leukemia, making it the 10th most common cancer worldwide, leukemia remains a serious health concern internationally. As biomedical research expands, experts work to understand more about the exceedingly complex processes that originate leukemia and develop increasingly effective treatments. However, much remains unknown about the disorder and further development is necessary to erase blindspots in human knowledge in order to produce even stronger treatment options. This paper provides insight into the four most prevalent types of leukemia, including Acute Myeloid Leukemia, Acute Lymphocytic Leukemia, Chronic Myeloid Leukemia, and Chronic Lymphocytic Leukemia; it analyzes diagnosis and risk factors, examines the specific genetic mutations that engender each disorder, and discusses the merits and drawbacks of current treatment avenues available for patients. It aims to provide a digestible profile of leukemia's pathophysiology and instigating processes as well as includes up to date analysis of available and developing treatments for patients.

Intro

Leukemia primarily affects the blood and bone marrow, where blood cells are made, but can develop to affect other regions of the body and patients' overall quality of life as well. All four types of leukemia occur when the body starts producing an abnormal amount of white blood cells. These cells don't work properly and can crowd out the healthy cells, leading to serious health problems, including anemia and other blood disorders. The several types of leukemia are usually categorized based on how quickly they progress and the type of blood cell they affect. For example, leukemia is classified as either acute or chronic, depending on the progression of the cancer. If the disorder is fast developing, it is classified as "acute," whereas if the disorder is slow developing, it is classified as "chronic." Similarly, leukemia cancer is classified also by the type of cell it affects in the bone marrow. If the strain of leukemia affects the myeloblast cells (a type of white blood cell), it is classified as "Myeloid," whereas if it affects the lymphocyte cells (a type of white blood cell), it is classified as "Lymphocytic." The result of this situation, as previously mentioned) is four unique and distinct types of leukemia: acute myeloid (AML), acute lymphocytic (ALL), chronic myeloid (CML), and chronic lymphocytic (CLL). In the United States, the 5-year survival rate for leukemia is 65%, though survival rate statistics contrast each other from subtype to subtype; CLL has a survival rate of 88%, ALL has a survival rate of 71.3%, CML has a survival rate of 70.6%, and AML has a survival rate of 31.7%. These survival rates are

higher than many other types of cancer, largely due to the advances in treatments for leukemia, however there still exists room for improvement.

Causes/Risk Factors

All types of leukemia are caused by genetic mutations, errors in DNA synthesis that result in altered instructions and cells' botched, missing, or excess construction of various proteins. Leukemia-causing mutations vary greatly in location and effect [Table 1]. Though there is no reasonable way to prevent genetic mutations–in fact, the human body is estimated to undergo trillions of genetic mutations per day–certain factors increase one's likelihood of contracting mutations. Behaviors like smoking and exposure to radiation and/or chemotherapy both increase one's proneness to genetic mutations. Furthermore, this proneness is often affected by genetic predisposition. For example, patients with a history of myelodysplastic syndromes or with rare genetic syndromes such as Down Syndrome are of higher risk of developing leukemia. Additionally, adults over the age of 65 are of the highest risk for developing leukemia because more mutations typically occur with age. AML, CML, ALL, and CLL strains are all slightly more common in males than females, though the reason for this is ambiguous.

Table 1: Common/Prevalent Genetic Mutations in Leukemia

Genetic mutation	Type of resulting Leukemia	Specific effects
BCR-ABL 1	CML, AML	The BCR-ABL 1 mutation results in abnormal tyrosine kinase–a type of cell receptor–that drives cancer cell proliferation. Mutated receptors order affected cells to divide at abnormal rates.
FLT3	AML	The FLT3 mutation also results in abnormal tyrosine kinase–a type of cell receptor–that drives cancer cell proliferation. Mutated receptors order affected cells to divide at abnormal rates.
RUNX1	AML	The RUNX1 mutation disrupts normal blood cell development, causing an abnormal number of myeloblast cells to proliferate within the bloodstream and bone marrow.

TP53 (p53)	AML, CLL	The TP53 mutation results in cells being unable to recognize themselves as cancerous and as a result, do not undergo apoptosis–otherwise known as cell suicide–following DNA damage.
IDH1	AML	The IDH1 mutation results in blood cells becoming stuck in a premature stage; they are unable to complete their full development. As a result, these cells crowd and infiltrate the bloodstream and bone marrow.
JAK2 (Janus kinase 2)	CML	The JAK2 mutation drives cell proliferation, resulting in an abnormal amount of myeloblasts in the bloodstream and bone marrow.
ETV6	ALL, AML	The ETV6 mutation disrupts normal gene regulation and results in rapid cell proliferation. As a result, an abnormal amount of mutated blood cells crowd and infiltrate the bloodstream and bone marrow.

Symptoms and Diagnosis

Symptoms of leukemia may depend on the specific type of the disease, but fever, fatigue, easy bleeding and bruising, pale skin, and swollen lymph nodes often present themselves in patients with leukemia and are often used in diagnosis. In chronic types of leukemia, individuals often display no symptoms in early stages. When leukemia is suspected in patients, doctors may use physical exams, blood exams, and bone marrow exams to gather further evidence. In physical exams, doctors look for suggestions of leukemia including pale skin, swollen lymph nodes, and liver or spleen enlargement. In blood tests, doctors look for an abnormal number of red or white blood cells. In bone marrow exams, medical professionals look for the leukemic cells themselves, often working to gain understanding and determine the best treatment plan by performing specific tests on the cancerous cells.

Treatment Options/Survival Rates

After a leukemia diagnosis, doctors work to determine a treatment option based on the health of the patient, the type of leukemia, and the stage to which the cancer has developed. Chemotherapy is the major form of treatment for leukemia patients; it works by attacking cells rapidly undergoing mitosis, or cell division. However, chemotherapy patients often report excessive fatigue, nausea, and hair loss. If the leukemia has spread outside the bone marrow and blood, doctors may sometimes prescribe radiation therapy, a process of exposing the patient to an external beam of radiation to the specific part of the body that the cancer has infected. This form of treatment targets and kills cancer cells, but it has been reported to cause fatigue, nausesa, skin burning and peeling, headaches, and lowered blood cell counts. After excessive radiation destroys a leukemia patient's cancerous bone marrow, doctors may also choose to perform a bone marrow transplant, or a process in which a donor's healthy stem cells are infused into leukemia patients with the goal of rebuilding their cancerous bone marrow using cancer-free stem cells. While bone marrow transplants assist patients greatly in their fight against leukemia, they can also be known to cause organ damage, infections, infertility, new cancers, and death.

Recent Research and Developments

By providing better, safer, and more tolerable drugs patients can hopefully be more easily cured of these diseases and at a lower financial and physical cost. As experts continue to learn more about leukemia, experts continue to engineer new forms of treatment and improve existing ones. Clinical trials test the effectiveness of various treatments and can be used to understand the future of leukemia treatment. Currently, hundreds of clinical trials are taking place across the world for these reasons. To fight ALL, clinical trials determining the effectiveness of combining less-toxic therapies, done with hopes of decreasing harmful side effects; immunotherapy, used to strengthen the body's immune system; and CAR T-cell therapy, the genetic modification of a patient's immune cells, are all taking place. To fight AML, researchers are using clinical trials to test the effectiveness of targeted therapies, drug-induced genetic modification and immunotherapy. To fight CML, current clinical trials involving protein blocking, the thwarting of any abnormal leukemia-inducing protein synthesis; combination therapy, the combination of various treatment avenues; and medication discontinuation are taking place.To fight CLL, researchers are monitoring clinical trials examining the effects of targeted therapy, the utilization of treatment that attacks specific molecules cancerous cells are dependent upon and immunotherapy. Fortunately, because of these ongoing developments, the 5-year survival has increased over the last 40 years from 33% in 1975 to 69% as of 2016. Overall, as the face of medicine advances, so do the potential treatment avenues for leukemia.

Conclusion

Leukemia envelopes an array of blood cancers all stemming from incredibly complex genetic mutations. A myriad of risk factors can affect one's likelihood for developing the disorder, though

their presence is not imperative for leukemia's development. Thus, treatment of leukemia is exceedingly difficult because of its various forms and complex nature. Because experts are still developing their understanding of this mutational ailment, the field of treatment is continuously expanding. Ultimately, with new developments in transplant, immune, and genetic therapies, treatment is becoming increasingly effective. Additionally, a better understanding of the risk factors and genetic background of leukemia which may make certain people more susceptible could allow for the disease to be stopped before it ever develops. Overall, leukemia continues to affect individuals across the world, and, while great progress in understanding and treatment has been made, there is still more to be learned about this complex disorder. It is through greater understanding that we can assist patients through more effective and accessible treatment avenues.

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