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Oxidative stress and leukemia

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

وَإِذَا مَرَضْتُمْ فَطَرِّبُوا يَدَيْكُمْ

صدق الله العلي العظيم

سورة الشعراء: الآية ٥٠



الاهداء

الى

الذي خط طريق حياتي واحاطني بدفاء قلبة وحنانا لمن كان معلم عند جهلي وقدوتي في
حياتي وخليلي عند شجونني

والدي ... براو وفاء

الى

من خصها الله بالجنة رمزالعطاء الى من ذكراها لايفارقني ماحييت

والدتي ... براو وفاء

الى

من استظل بظلمهم واستنير بنورهم الى مصدر قوتي وفيض روعي اخوتي واخواتي ... عرفانا
بالجميل

الى

كل القلوب المخلصة التي قدمت لي العون وتمنت لي الموفقة والنجاح

اساتذتي الافاضل

اهدي لكم هذا الجهد المتواضع

الباحثون





شكر وتقدير

الحمد لله والحمد حقه كما يستحقه حمدا كثيرا

لا يسعني الا ان اتقدم بجزيل الشكر والتقدير الى **الدكتور زينب نجم عبد الله**
المحترمة لما قدمته لنا من مساعده علمية ولجهودها المبذولة معنا للأرتقاء
بالبحث بهذا الشكل راجين العلي التقدير ان يوفقها لكل خير وسداد ...

كما واتقدم بوافر الشكر والتقدير والاحترام الى الاستاذ الفاضل **اد نبيل عبد عبد الرضا عميد**
كلية العلوم

شكري وتقديري الى **ام د مقداد ارحيم كاظم** رئيس قسم الكيمياء والتدريسين والى الكادر كما
اقدم شكري وتقدير الى والداي لانهما الاساس في الوصول الى هذا المستوى.

الباحثون



Summary

Cancer is a metabolic disorder that affects white blood cells. The most common types of cancer among children, and the majority of cases that are registered among them are of the acute type. Some types of leukemia develop slowly and chronically, and there are other types that come quickly and sharply. The bone marrow in the body produces white blood cells, but in the case of leukemia, the marrow produces abnormal white cells, which lead to overcrowding in normal blood cells. In the case of leukemia, a DNA mutation occurs in the bone marrow cells, resulting in abnormal white blood cells producing large numbers of cells. This causes blood clotting in the blood. Although large, these white blood cells do not function because they are abnormal, resulting in increased susceptibility of the body to infection.

As the disease progresses, leukemia affects the functions and production of red blood cells, that is responsible for the transport of oxygen, platelets responsible for clotting, and wound bleeding. Chemotherapy weakens the process of cell division because of its inability to tolerate the drug. It is possible that deformation occurs in the cells as well as in the transmission of signals and thus cause an increase in production of reactive oxygen species (ROS).

1.1 Introduction

Blood cancer is one of the most common types of human cancers, and the most common, and some sources indicate that the first case was discovered by this disease was a European doctor in the nineteenth century, called the disease name: leukemia leukos, meaning white, and haima, meaning blood. Blood cancer begins with bone marrow the place where the different blood cells are manufactured; O white blood, red blood platelets. In the case of leukemia, the bone marrow begins to produce large numbers of abnormal white blood cells called cancer cells. These cells do not function normally, grow rapidly, and do not stop growing when necessary. Over time, cancer cells begin to compete with normal white blood cells, and this can lead to serious complications such as anemia, bleeding and frequent infections. Cancer cells can also spread to contract lymph nodes or neighboring organs, causing pain and swelling[1].

1.2 Types of leukemia

Blood cancer is divided into several types. It may be classified according to the severity of the disease, the extent of its progression to acute and chronic leukemia, and the type of infected cells classified as leukemia [2].

1-Acute myeloid leukemia (AML) is the most common form of leukemia. The disease occurs in children and in adults, and is also called "acute non-lymphatic leukemia".

2-Acute lymphocytic leukemia (ALL) This is the most common type in young children and is responsible for 75% of childhood leukemia.

3-Chronic lymphocytic leukemia (CLL) Although this type is very common and appears mainly in adults, the patient can feel good for several years without the need for any treatment. It is almost invisible to children.

4-Chronic myeloid leukemia (CML) - This type of leukemia appears mainly in adults. His appearance is due to a defect in the chromosome called the Philadelphia chromosome, which is responsible for producing a genetic mutation in the BCR ABL gene.

This gene produces an abnormal protein called tyrosine kinase and scientists and doctors believe it is the cancer cells that can develop and multiply.

A person with this type of leukemia may experience a few symptoms, over a period of months or even years, before the onset of the stage in which disease cells grow and multiply very quickly [3].

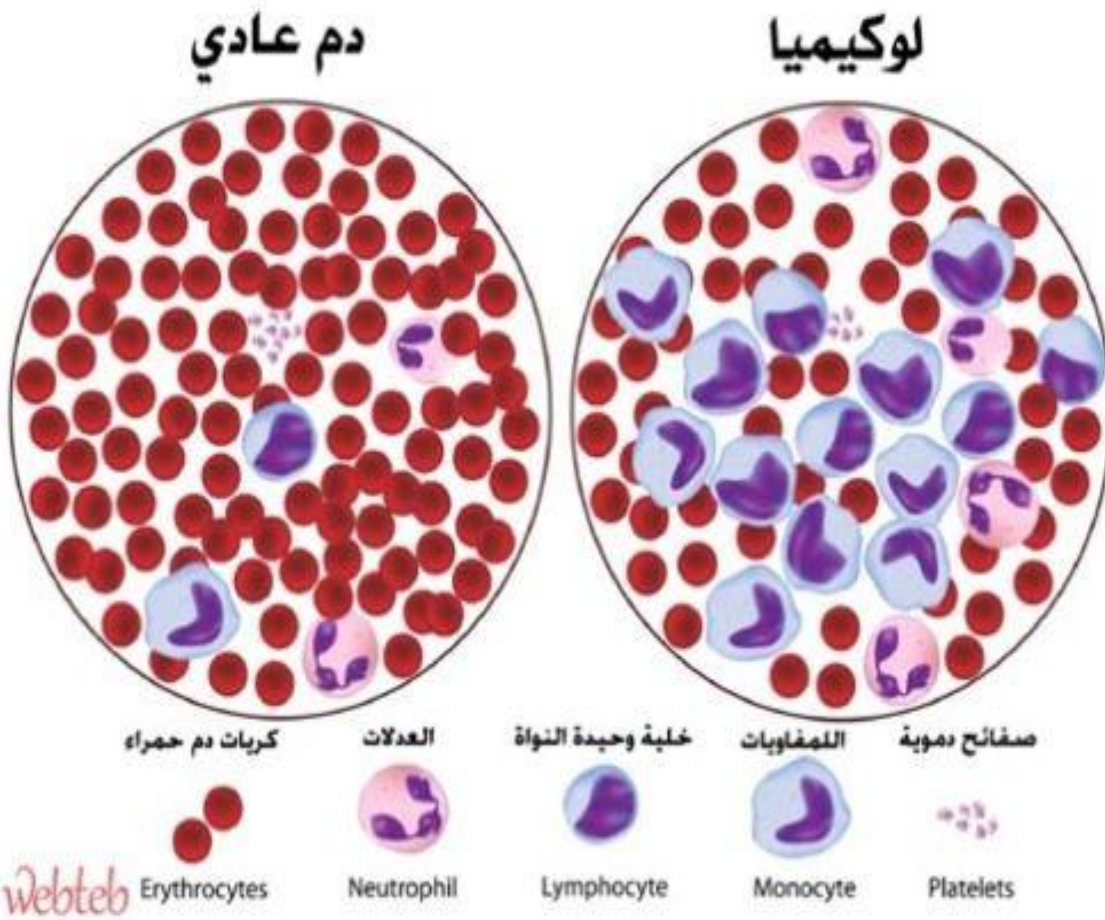


Figure 1: Leukemic and non-leukemic blood cells

1.3 The Symptoms of leukemia

The most common symptom is frequent tiredness and stress; the result of less stressful effort.

1-Persistent fever, high body temperature.

2-Recurrence of multiple diseases, and recurrence due to lack of body immunity.

3-Loss of appetite without causes, and therefore lose weight dramatically and suddenly.

4-Frequent and severe hemorrhage, and long-term bruising, due to lack of blood platelets, which reduces the ability of the body to form clots, and stop bleeding.

5-Difficulty breathing when climbing or running.

6-Internal bleeding occurs, showing red spots on the skin due to bleeding.

7-Anemia; due to lack of hemoglobin in the blood.

8-The incidence of bacterial and viral infections, as a result of increasing the number of white blood cells incompletematurity, which reduces human immunity to disease resistance.

9-Inflammation and swelling in the lymph nodes circulating

10-Frequent pain in the bones; the result of bone marrow cancer.

11-It should be noted that the symptoms of leukemia vary according to the degree of disease, and the extent of progression, the initial symptoms may be very similar to the symptoms of influenza and colds[4].

1.4 Diagnosis of leukemia

Blood cancer is detected by a complete blood image analysis, and if the doctor notices abnormal changes in the outcome of the analysis, such as increased white blood cells significantly, other tests are performed [5].

1-A bone marrow biopsy is withdrawn and is examined and examined to detect any cancerous cells that may exist.

2-Physical detection is performed; to see if there are swelling in the lymph nodes or not.

3-A fluid is taken from the bone marrow to be examined under the microscope, and dyed in a special dye to see the cancer cells, and their type[6].

1.5 Causes and risk factors for leukemia

Scientists and doctors have not found definitive causes of leukemia, which is a sudden change of blood cells, leading to a crazy breeding that cannot be stopped, but doctors found that there are several reasons and factors that may increase the risk of leukemia [7].

1-Genetics, and plays a major role in the incidence of leukemia, where genes are transmitted from parents to children, and Down's syndrome or Mongolian nonsense, increase the incidence of leukemia.

2-Exposure to chemicals, as well as radiation used in the treatment of other types of cancers, such as breast cancer, lung cancer and others.

3-Exposure to a nuclear explosion and atomic radiation, as in Japan, expose people to high blood cancer, as blood cells are affected by nuclear and atomic radiation.

4-Smoking, which affects tobacco and constituents of cigarettes in blood cells, reduces its ability to grow and function, causing malfunction and appearance of cancerous properties.

5-The removal of a cancerous tumor using the laser, which spreads the cancer in the vicinity of it; and the injury of blood cancer, and this is the result of wrong diagnosis of the tumor, and the lack of suspicion of being a malignant tumor [8].

1.6 Definition of oxidativestress (OS)

It can be known as an increase in oxidizing substances in and around the cell, which result in damage to cellular structures such as destroying DNA, RNA and proteins.

In high-end neighborhoods, there are many diseases such as Rheumatoid Arthritis, Inflammatory Bowel Disorders, arteriosclerosis, neuropathic diseases, some cancers, pyelonephritis, infections, diabetes and help to accelerate the growth of cells, as it is one of the important causes of mutagenesis and tumors. In bacteria it affects or inhibits chemical

attraction of food and other conditions that are not in favor of the cell.

Oxidative stress is obtained when its degree is greater than the defenses of cellular systems, and can be increased when exposed to environmental conditions or food or a satisfactory condition, in addition to the internal causes of the cells [9].

1.7 Oxidative stress and the Reactive Oxygen Species (ROS)

Oxidative Stress: is a biochemical condition that occurs when intracellular antioxidants are unable to neutralize pro-oxidants, such as ROS. Mitochondria are the primary sites for oxidative phosphorylation, which produces massive highly reactive and unstable oxygen, thus oxidizing a large number of molecules to form ROS. ROS are generated intracellularly within various compartments and through multiple mechanisms[10].

1.8 Association between OS and chemotherapy during leukemia treatment

The current therapy for leukemia primarily consists of high-dose cytotoxic chemotherapy with or without allogeneic stem cell transplantation. However, chemotherapeutic treatments are often

accompanied by elevated ROS levels, and cause drug-intolerance or resistance correspondingly. The underlying mechanisms may be closely associated with the aforementioned ROS-mediated signaling pathway. Chemotherapy impairs the mitotic and metabolic process of cancer cells, involving various signal transmission abnormalities or sub-cellular organ damage, thus causing excess ROS production. Angsutararuxand others studied doxorubicin (DOX)-induced cardiotoxicity, and proposed that DOX is particularly harmful to the heart due to its exceptional effects on mitochondria, which are the home of ROS. Petrolaand others performed a clinical trial to evaluate OS through detecting the levels of MDA and nitrite in patients with CML [11].

1.9 Polyphenol-induced Oxidative Stress in Leukemic Cells

status of the cancer cells, they seem to be more susceptible than normal cells to treatment with agents that cause oxidative stress, as epitomized by the study using PEITC(41). Our findings that C-3-R, also a natural product commonly found in fruits and vegetables, selectively induces the accumulation of peroxides in

the leukemic cell line HL-60 but not in normal PBMC, point in the same direction and suggest that this approach is valid in seeking new generation of therapeutic agents with lower side effects, considering that many anticancer drugs currently used in the clinic have strong [12].

1.10 Treatment of leukemia

1-There is a type of leukemia in which the tumor is located in a specific area of the body, and does not spread to the rest of the body, in which case can be surgically removed tumor, to treat cancer [13].

2-In other cases, it is the worst and most difficult method of treatment, in which the cancer is present in the blood, and is widespread, there is no tumor that can be surgically removed.

3-In this case, the treatment is complex, and begins to provide the patient with many vitamins and tonics and anti-virus and bacteria, which attack his body because of the weakness of the immune system.

4-There are also several ways in which to try to eliminate leukemia, and prevent its spread and penetration in the body:

A-Chemotherapy.

B-Radiotherapy.

C-Bone Marrow Transplantation Bone Marrow Transplantation.

D-Stem Cells Transplantation[14].

1.11 Protection Against leukemia

1-Plenty of fruits and vegetables and make sure that green salad is present in all meals. Contains essential vitamins needed by the body [15].

2 - A lot of food rich in dietary fiber.

3. Eat garlic and onions and add them to meals. Act as an antibiotic and protect the body from cancer.

4 - Exercise every day until walking. Maintains blood circulation and prevents the formation of cancer cells.

5 - Reduce as much as possible of grills and smokers. Studies have shown that these foods contain carcinogens.

6 - Try to lose weight in the case of obesity to protect the body from many diseases.

7. Refrain from smoking. Tobacco contains substances that cause many cancers such as lung cancer, liver cancer and stomach cancer, not just leukemia.

8-Eat green tea. Contains antioxidants[16].

1.12 A dietary system to be followed with a leukemia patient

1- Divide the food into small meals divided during the day; so that the stomach can digest well, and the patient does not feel bloated or indigestion.

2-Add lemon juice to the food to give it a grainy taste for the patient, as well as for the benefit of large lemon food is rich in multivitamins.

3-Eat foods containing energy and calories, to give the patient activity and strength such as milk and honey.

4-Try to open the patient's appetite for food, by decorating the food, and put it in beautiful and colorful utensils.

5-If the mouth is dry from chemotherapy, it is preferred that the patient take the vegetable soup, it helps to increase the saliva in the mouth and also can eat foods containing sugars, it also helps in this.

6-Care should be taken when the patient is infected with ulcers and infections in the mouth; as a result of chemotherapy, in which case you should stay away from sweets, acids and spices of all kinds, so as not to worsen the situation, and prefer to mash the food so easy to swallow.

7-It is recommended to avoid frying and fat in food, as well as to reduce the drinking of liquids, such as water and juices while eating, and can be used to eat dry bread is useful in the case of nausea.

8-It is preferable to avoid sugar in foods and beverages and replace it with white honey[17].

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