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LEUKEMIA – TYPES, CLINICAL APPEARANCES, DIAGNOSIS AND TREATMENT

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Abstract

Leukemia is a tumor originating from hematopoietic cells that is primarily located in the bone marrow and causes leukemia as a sign of the disease. In the vernacular, it is called leukosis, and in medicine it is called leukosis. Leukemia is an oncological condition – blood cancer. The exact causes of the disease are still unknown to medicine, and there are no preventive measures. Children, women, and adults can get this disease. The disease is registered more often in industrialized cities than in rural areas; men are more affected than women. The disease occurs all over the world – both in developed and underdeveloped countries. Leukemia is one of the urgent problems of modern medicine, but it has not yet been thoroughly solved. According to international statistics, the number of deaths from leukemia has been increasing in recent years. About 1% of all causes of death are people who die from leukemia, and about 6% from malignant tumors, and 50% in children and adolescents. Leukemia is a complex disease and is included in the list of diseases that can be treated in the 21st century. If we look at Uzbekistan, 20 years ago, the methods of effective treatment of leukemia were not yet studied to that extent. Until now, treatment methods have been developed to overcome this disease. In leukemia, abnormal blood cells are produced in the bone marrow. Usually, the disease is characterized by the production of abnormal types of leukocytes, which are responsible for fighting infection. In a white blood cell disease, abnormal cells do not perform the same functions as normal leukocytes. Cancer cells grow and actively divide, interfering with the movement of other blood cells. As a result, there is a decrease in the body’s ability to fight infections, loss of control of bleeding, and difficulty in transporting oxygen. Leukemias include a wide group of diseases that differ in their etiology. In leukemias, blood cells of poor quality can arise from immature hematopoietic cells of the bone marrow, as well as from maturing and mature blood cells. Currently, all neoplastic diseases of blood-forming tissues are called hemoblastoses. According to the nature and location of pathological processes, they are divided into two groups. According to the World Health Organization, in recent years, the number of deaths from leukemia has been increasing across countries.

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Introduction

Leukemia is a general name for tumors that arise from blood-forming cells and damage the bone marrow. There are speculations about the viral nature of leukemia. The essence of leukemia is damage to the bone marrow, spleen, and lymph nodes. In leukemia, large numbers of immature leukocytes appear in the peripheral blood, which are usually found only in the bone marrow and lymph nodes. In some cases, the total number of leukocytes in the peripheral blood does not increase, they only change in quality. Such leukemias are called aleukemic leukemias. The exact cause of leukemia is unknown, but it involves a combination of genetic and environmental factors. Leukemia cells develop mutations in their DNA that cause them to grow abnormally and lose the function of normal white blood cells. It is not known what caused this mutation. One type of cellular DNA mutation that is common in leukemia is called a chromosomal translocation. In this process, part of one chromosome is broken and added to other chromosomes. One translocation seen in nearly all cases of chronic myelogenous leukemia, and sometimes in other types of white blood cell disease, is a DNA exchange between chromosomes 9 and 22. This process leads to what is called a Philadelphia chromosome. This creates an oncogene (a cancer-promoting gene) called BCR-ABL. This change in DNA is not passed from generation to generation, but it has an impact on a person's life.

Most cases of leukemia are not hereditary, but some genetic mutations and conditions can be passed down through generations. A condition called Li-Fraumeni syndrome is characterized by an inherited mutation in a tumor suppressor gene called TP53, which increases the risk of developing leukemia and other cancers in people with the condition. Other genetic disorders that pose a risk include Down syndrome, neurofibromatosis type 1, ataxia telangiectasia, and Noonan syndrome.

According to changes in leukocytes in peripheral blood:

1. Leukemic leukemia – leukocytes increase to 100,000-200,000 in 1 mm3 of blood.
2. Subleukemic leukemia – leukocytes increase to 20,000 in 1 mm3 of blood.
3. Aleukemic leukemia – serious changes in the quality of white blood occur while the number of leukocytes is normal and reduced.

According to the degree of differentiation of tumor cells:

1. Sitar leukemias
2. Blastly
3. Undifferentiated

According to the immune phenotype of the tumor cell

Currently, it is possible to more accurately classify tumor cells based on their immune phenotype using CD20, CD5, CD19, light chains of immunoglobulins and other antigenic markers.

From the point of view of this classification, it can be said that the chronic form of leukaemia, as a result of a long and continuous effect of etiological factors (viruses, ionizing radiation, chemicals, etc.), turns into a relatively acute form. That is, in addition to disorders in progenitor cells of

myelo- or lymphopoiesis, disorders specific to acute leukemia develop, “complications” occur in the course of chronic leukemia.

According to the passage

1. Acute – from immature cells (blasts).
2. Chronic – maturing and mature cells.

It should be noted that acute leukemia never turns into a chronic form, and in chronic cases, attacks are not observed. Therefore, the terms “acute” and “chronic” are used only for convenience, the meaning of these terms in hematology is different from the meaning in other medical disciplines. For chronic leukemias, “attacks” are characterized by blast crises, the blood picture of which resembles an acute form.

Acute leukemia is characterized by an uncontrollable proliferation of the youngest (blast) blood cells with a violation of further differentiation, as well as the appearance of pathological foci of hematopoiesis in a number of organs. Its lymphoblastic and myeloblastic forms (acute lymphocytic leukemia and acute myeloid leukemia) are often found in practice. This is the most common form (about 30%) of all leukemias.

The following stages are noted In the course of acute leukemia:

1) Primary; 2) developed; 3) remission (complete or complete was not); 4) relapse; 5) terminal.

Clinical picture. The first clinical signs of acute leukemia are different. In most cases, patients complain of weakness, loss of appetite, pain in the joints and small injuries, bruises on the skin. In other patients, the disease begins acutely, rhinitis, pharyngitis, inflammation of the tonsils, and an increase in body temperature are observed. Sometimes, acute leukemia is detected unexpectedly during a blood test. In the advanced stage of acute leukemia, the clinical picture of the disease is as follows: anemia, hemorrhaging, infection and wound necrosis are manifested as complication syndromes. Anemia syndrome is manifested by weakness, dizziness, pain in the heart area and shortness of breath. When patients are examined, pale skin and mucous membranes are revealed. Manifestations of anemia are different and depend on the degree of reduction of erythropoiesis, hemolysis or bleeding. Hemorrhagic syndrome occurs in almost all patients. Bleeding from the gums, nose, uterus, skin and mucous membranes is observed in them. Large bleeding occurs when a needle is injected to inject medicine under the skin or into a vein. In the terminal stage of the disease, hemorrhages in the mucous membranes of the stomach and duodenum turn into ulcerated necrotic changes. In the promyelocytic type of acute leukemia, a particularly expressed hemorrhagic syndrome is observed. More than half of the patients with acute leukemia develop infectious, wound necrotic complications as a result of developed granulocytopenia, decreased phagocytosis of granulocytes, and violation of antibody production. Slow progressing pneumonia, infectious diseases of the urinary tract, abscesses, stomatitis, gingivitis, and necrotic angina develop in the places where the nose is stung. Such complications are more often observed in patients with severe granulocytopenia and leukemic infiltration of the gums (myelomonoblastic and monoblastic types).

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Laboratory-instrumental tests.

The number of leukocytes in the blood is 100x109/l, even 200x109/l and higher. Although all blast cells are morphologically similar, they can be differentiated by cytochemical reactions. Immature cell forms make up 95 and sometimes 99%. There are no eosinophils and basophils in the patient's blood, the number of other cells decreases not only in percentage but also in number. Thrombocytopenia and anemia are observed due to the crowding out of megakaryocytes and erythroblasts from the bone marrow by blast cells multiplying at a high speed, as well as their direction mainly in the direction of leukopoiesis. As a result of hemorrhages and bleedings characteristic of this disease, as well as due to increased hemolysis of erythrocytes, anemia increases. Blood coagulability and its flow time have changed in many cases, it has increased dramatically. 80-90% of bone marrow smear consists of blast cells and they crowd out other cells.

Treatment. Treatment of acute leukemia is carried out as early as possible, depending on the form, stage, course of the disease in hospital and outpatient settings. Chemopreparations, which mainly act in different periods of cell mitosis, are given in different combinations.

In lymphoid treatment of acute leukemia

VAMP (10 days) Vincristine 2 mg/m2 intravenously on days 2-3 of the course + Amethopterin (methotrexate) 20 mg/m2 intramuscularly or intravenously on days 1, 5, 9 of the course + 6 Mercaptopurine 60 mg/m2 daily to drink + Prednisolone 40 mg/m2 to drink every day.

When neuroleukosis develops, it is also recommended to inject drugs into the cerebrospinal fluid by spinal cord puncture.

In the treatment of myeloid type of acute leukemia

SOSP (4 days): Cyclophosphan 50 mg/m2 intravenously every 8 hours on the 1^{st} – 4^{th} day of the course + Onkovin (vincristine) 2 mg/m2 intravenously on the 1^{st} day of the course + Cytozar 50 mg/m2 intravenously every 8 hours on the 1^{st} of the course - 4- day + Prednisolone 60 mg/m2 to drink every day.

When acute leukemia relapses or to prevent relapse, it is necessary to perform allogeneic bone marrow transplantation and immunotherapy procedures. In the treatment of infectious complications, a wide range of antibiotics and sulfonamides are used. In order to prevent infection complications, it is necessary to take care of skin and mucous membranes, place patients in aseptic rooms, and sterilize the intestine by giving non-absorbable antibiotics. For the treatment of hemorrhagic syndrome, blood, platelet mass, and plasma are transfused, and in DVS (distributed blood coagulation syndrome in many vessels of the body), epsilonaminocaproic acid is given at 1.5-3 mg/kg per day and heparin. It is necessary to create conditions that calm the nerves and mental state. It is necessary to prevent and treat various complications of the disease (abscesses, bedsores, intoxication).

Chronic myelogenous leukemia is the most common type of leukemia and originates from the stem cells of myelopoiesis. It includes myeloid hyperplasia of the bone marrow and the spleen, liver, lymph nodes and other a The Philadelphia chromosome is detected in myeloid stem cells. Chronic myelogenous leukemia is more common in people aged 20-45 years. Chronic myelogenous leukemia ranks fifth among dangerous diseases of the blood system (hemoblastoses), 8.9% of all types, and the incidence is 1.0-1.7 per 100,000 people. It occurs relatively rarely (3.2%) in

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childhood and adolescence, the disease occurs equally in both men and women.The clinical picture of the disease passes through three stages (initial, advanced and terminal). The initial stage is hidden, and the main signs are observed in the advanced stage.

Clinical picture. The patient complains of general weakness, heaviness and pain under the left ribs, profuse sweating, bleeding gums. When examined, the spleen is significantly enlarged (like the bone marrow, the spleen undergoes myeloid metaplasia and becomes very large and descends to the pelvis) up to 40 cm in diameter and up to 7 kg in weight. It turns out that it occupies a large part of the abdomen, the lymph nodes are enlarged, the skin turns pale, the patient loses weight. The body temperature rises, blood tests reveal immature forms of myeloid leukocytes, promyelocytes, metamyelocytes, myelocytes, the number of leukocytes increases significantly (leukocytosis up to 200-400x109), a large amount of myelocyte and promyelocytlam is detected when the sternum is punctured. Anemia, thrombocytosis are noted. The disease is wavelike, periodically repeating attacks and remissions. The following clinical and hematological types of chronic myelogenous leukemia are distinguished:

Leukemic (significant increase in the number of leukocytes and the appearance of a large number of granular elements in the peripheral blood).

Subleukemic (with a moderate increase in the number of leukocytes and a shift to the appearance of myelocytes and promyelocytes in the blood formula).

Aleukemic - forms of osteomyelofibrosis (the number of leukocytes is normal or even reduced and there are no immature cells in the peripheral blood). In osteomyelofibrosis, puncture of the sternum and examination of the puncture are of great importance: a large number myeloblasts and promyelocytes are found (normal bone marrow does not contain many myeloblasts).

Atypical types of chronic myeloid leukemia are also observed: eosinophilic myeloid leukemia, characterized by the presence of acidophilic granulocytes (eosinophilia) in the peripheral blood (about 75%) and basophilic myeloid leukemia (a large number of basophils in the peripheral blood). The most serious complication is hemorrhagic diathesis, which passes with a lot of bleeding. In addition to clinical symptoms, detection of the Philadelphia chromosome in the sputum plays a decisive role in the diagnosis of chronic myelogenous leukemia.

Laboratory-instrumental tests. When the blood smear is examined, mainly cells belonging to the granulocyte series are detected, which make up 95-97% of white blood cells. Among these elements, immature myelocytes, promyelocytes and even myeloblasts are identified in large numbers. During the exacerbation of the disease, the number of abnormal forms increases sharply, only the youngest cells – myeloblasts and a small amount of mature granulocytes – types with rod and segment nuclei are detected in the blood. Usually, intermediate forms of cells are not found in the blood (leukemic cavity). Basophils and eosinophils are sometimes present in the smear, and the ratio of percentages may even be high. A basophil count of 4-5% is one of the signs of myelogenous leukemia. In severe cases, a sharp decrease in the number of lymphocytes and monocytes observed with obvious leukocytosis by 3-0.5% is detected, but their absolute amount in the blood does not change significantly. Changes in red blood cells are observed only in the II and III stages of the disease, when anemia develops. As the amount of erythrocytes in the blood decreases in proportion to the hemoglobin index, the color index is within the normal range, i.e.

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around 0.8-1.1. In the last stages of the disease, thrombocytopenia and high ECHT (30-70 mm/s) are detected. The amount of erythrocyte stem cells in the punctured bone marrow smear decreased sharply, especially near the last stage of the disease, the myeloid line increased mainly due to young forms – promyelocytes, myelocytes and myeloblasts. In the first half of the disease, an increase in the number of mikaryocytes, basophils and eosinophils, promyelocytes and myelocytes is characteristic. They die as a result of worsening general emaciation, severe anemia, hemorrhagic complications or infection.

Treatment. In the advanced stage of the disease, it is mainly treated with chemopreparations in order to reduce the amount of tumor cells. Cytostatics myelosan (mileran, bisulfan) is given at 2, 4, 6 mg per day. When the number of leukocytes reaches 15-20x109, myelosan is given in small amounts 2 mg 1-3 times a week. Myelobromol is given at 250 mg per day, 6 mercaptopurine at 100-150 mg per day.

Polychemotherapy is prescribed when the indicated drugs do not give good results and in the terminal stage of the disease. Splenectomy, light therapy, leukocytophoresis can be used. Complications of infectious, hemorrhagic anemia should be treated (antibiotics, hormones, drugs that stop blood flow, blood transfusion). The patient should be physically and mentally calm, create sufficient antiseptic conditions and feed him with nutrients rich in vitamins. Patients are under constant dispensary supervision. In severe anemia, blood or erythrocyte masses are transfused.

VAMP (10 days) Vincristine 2 mg/m2 intravenously on days 2-3 of the course + Ametopterin (methotrexate) 20 mg/m2 intramuscularly or intravenously on days 1, 5, 9 of the course + 6 Mercaptopurine 60 mg/m2 daily to drink + Prednisolone 40 mg/m2 to drink every day.

Chronic lymphocytic leukemia is currently a benign tumor of immunocompetent tissues. Its hematological basis is B-lymphocytes (morphologically mature, but functionally immature). Chronic lymphocytic leukemia is characterized by hyperplasia of the lymphatic system, lymphoid metaplasia of the spleen, bone marrow, and other organs. Chronic lymphocytic leukemia is a common disease in middle-aged and elderly people (35-70), and it is rarely observed in young people.

Pathogenesis. In chronic lymphocytic leukemia, the production of blood cells changes from the normal development path to the development of many lymphocytes, therefore, lymphatic metaplasia of the bone marrow develops, and lymphocytes take the place of granulocytic cells. Patients develop granulocytopenia, anemia and thrombocytopenia. As a result of hypoxia associated with anemia, dystrophic and degenerative changes occur in the heart, liver, kidneys and other internal organs. Thrombocytopenia leads to hemorrhagic diathesis. Enlarged lymph nodes (often in the form of large cysts) and tissue infiltrates compress adjacent organs, nerves and vessels.

Clinic Three types of chronic lymphocytic leukemia are noted: leukemic, subleukemic and aleukemic. In addition, the following types of atypical course of the disease are observed. There are three stages of chronic lymphocytic leukemia. The first, the initial period is relatively long (2-3 years in some patients), while the patient's condition is satisfactory, the enlargement of the lymph nodes, spleen and liver, changes characteristic of the disease in the blood and bone marrow are detected by chance. . Second, in the period of exacerbation of the disease, lymph nodes, liver and

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spleen increase in size, changes in the blood increase, anemia and thrombocytopenia develop, weakness, frequent sweating, temperature rise are noted, and hemorrhagic changes are observed. An autoimmune process develops. The third stage is the terminal stage, in which resistance to infection develops. In the course of the disease, periods of exacerbation and remission are observed. In this type of leukemia, the patient does not lose much of his ability to work compared to chronic myelogenous leukemia. But severe types of the disease can lead to severe anemia and death of the patient within 1-2 years.

Diagnosis. Clinical signs of the disease, changes in the blood and bone marrow play a decisive role. Comparative diagnosis of chronic lymphocytic leukemia is made with the following diseases: lymphocytosis in infectious diseases (in children), infectious mononucleosis, lymph node tuberculosis, lymphogranulomatosis and lymphosarcoma.

Laboratory-instrumental tests. In the leukemic type of the disease, a large leukocytosis (up to 200-300x109/l) develops, mature lymphocytes make up 80-90% of the total, prolymphocytes make up 3-4%, and lymphoblasts make up 1-2%. Neutrophils make up 4-5%. In the early stages of the disease, there are no changes in red blood, then anemia develops, the number of platelets decreases. Damaged lymphocytes Gumprecht corpuscles are found in the blood smear. In the subleukemic type, the number of leukocytes is equal to 20-30x109/l, in the aleukemic type, the number of leukocytes does not increase (6-8x 109/l). Lymphatic metaplasia of the bone marrow is detected when the sternum is punctured. Especially in the aleukemic type of the disease, this examination is of decisive importance, without changes in the peripheral blood, the number of lymphocytes in the sputum is more than 20-30%, and in some cases it is 60-90%. .

Treatment.In the early stage of the disease, active treatment is carried out, such as chronic myelogenous leukemia. The main focus is on organizing work and rest, taking enough walks in the open air, following a complete diet with a large amount of vitamins and proteins.

1. In order to reduce the growth process of tumors, chemotherapy and cytostatic treatment are carried out.
2. Hormonal drugs are used to treat autoimmune hemolytic anemia, splenectomy is recommended.
3. Antibiotics are given to treat infectious complications of the disease.
4. Retabolil, vitamins, u-globulin to increase the body's defenses.

Chemotherapy is used during the disease outbreak. Chlorbutin (leucaran) 10-15 mg per day for 4-6 weeks, cyclophosphan 200-600 mg per day or intramuscularly for 4-6 weeks, degranol 50-75 mg intravenously 5-10 times per day. Hormonal hemolytic anemia and thrombocytopenia will be assigned when it appears. In the terminal stages of the disease, when it is severe, polychem ion therapy is carried out. Enlarged lymph nodes, spleen are treated with radiation. Leukophoresis can be performed several times.

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