**Hemoblastoses**

Hemoblastosis is a disease of the blood system, a malignant tumor that develops from hematopoietic cells. It is the most common cause of death among diseases of the blood system. The specific cause of hemoblastoses formation has not been determined. However, like other tumor diseases, hemoblastoses are believed to be caused by viruses (DNA and RNA-containing oncoviruses, Epstein-Barr virus), radioactive substances and chemical carcinogens. In addition, genetic factors, heredity (Down syndrome, Philadelphia chromosome), congenital and acquired immunodeficiency syndrome also play a major role in the development of hemoblastoses.

 Several laboratory diagnostic methods are used to determine hemoblastoses:

-morphological method - morphological examination of peripheral blood and bone marrow is considered one of the main methods used in the diagnosis of leukemia. This method allows determining all types of chronic leukosis and 60-70% of types of acute leukosis. With this method, the cell size, shape of nucleus, nucleus-cytoplasm ratio, granularity of cytoplasm is studied.

-cytochemical reaction - reactions with myeloperoxidase, lipid, glycogen, non-specific esterase, acid-phosphatase are carried out in this method. The ability of leukemic cells to differentiate is studied.

-immunophenotypic method – types of acute leukosis (clusters of differentiation CD) are determined

- cytogenetic method - changes in chromosomes are studied

- molecular- biological method - the genome of tumor cells is studied

 **CLASSIFICATION OF HEMOBLASTOSIS**

Depending on the primary localization of tumors, hemoblastoses are divided into two large groups: Leukosis (leukemia) and hematosarcomas (lymphosarcoma or lymphoma).

Leukoses (leukemia) is a malignant tumor that develops from the red bone marrow. Lymphoma (hematosarcoma) is a malignant tumor that develops from regional hematopoietic cells located outside the bone marrow.

In order to classify leukoses, the structure, functional characteristics and differentiation capabilities of leukosis cells should be taken into account. Therefore, they divide Leukoses into 2 groups: acute and chronic.

 Acute (blast) leukoses include acute myeloblastic and acute lymphoblastic leukoses.

**1. Acute myeloblastic leukoses:**

-undifferentiated acute myeloid leukosis-MO

- immature (unformed) acute myeloblastic leukosis -M1

-myeloblast leukosis with some granules formed -M2

-acute promyeloblastic leukosis -M3

-acute myelomonoblastic leukosis -M4

- acute monoblastic leukosis - M5

-acute erythromyeloblastic leukosis -M6

-acute megakaryoblast leukosis -M7

**2. Acute lymphoblastic** **leukoses**:

 -microlymphoblastic leukosis -L1

 -leukosis with lymphoblasts of different sizes -L2

 -macro - or prolymphoblast leukosis -L3

**Lymphocytic, monocytic and myelocytic leukoses belong to chronic (citar) leukoses.**

1**. Chronic lymphocytic originated leukoses**:

- chronic lymphocytic leukoses

- cutaneous lymphoma or Sezary's disease

-paraproteinemic leukoses

These include myeloma disease (plasmacytoma), primary macroglobulinemia (Waldenstrom disease), heavy chain disease (Franklin disease).

**2. Chronic monocytic originated leukoses**:

- chronic monocytic leukosis

- histiocytosis

a) Eosinophilic granuloma

b) Letterer-Siwe disease

c) Hand-Schuller-Christian's disease

**3. Chronic myelocytic** **originated leukoses**:

- chronic myeloid leukosis

- polycythemia vera (Osler- Vaquez syndrome)

- chronic megakaryocytic leukosis (idiopathic thrombocythemia)

or hemorrhagic thrombocythemia disease)

**LYMPHOMAS**

According to histogenesis:

-B-cell lymphomas

- Lymphomas of T-cell origin

**According to clinical morphological features:**

1. Lymphosarcoma

- nodular

-diffuse

Non-Hodgkin's lymphoma

2. Reticulosarcoma

3. Fungal sarcoma

4. Lymphogranulomatosis (Hodgkin's disease)

-local

-spread

**According to the total amount of leukocytes in a unit volume of blood, the following types of leukocytes are distinguished**:

**1. Leukemic leukosis** - the total amount of leukocytes exceeds 30-50 x109 /l. The blast forms of leukosis cells increase.

**2. Subleukemic leukosis** - the total amount of leukocytes does not exceed 30x10 9/l. Blast cells are the majority.

**3. Aleukemic leukosis** - the number of leukocytes is normal. Blast leukocytes are not in the peripheral blood, but atypical leukocytes, their young and blast forms are found in the bone marrow and lymph nodes.

**4. Leukopenic** **leukosis** - the number of leukocytes is less than normal. Blast leukocytes are found in small quantities.

 **DISTINGUISHING CHARACTERISTICS OF LEUKOSES**

**Leukoses** - develop from hematopoietic cells as a result of primary damage to the bone marrow, differ from other malignant tumors from leukocytosis, leukemoid reactions, and the proliferation of hematopoietic tissues located outside the bone marrow. During leukosis, the cells divide and multiply, differentiate, and grow without limits, without obeying the regulatory system and a violation of the ability to undergo apoptosis is observed. Leukosis has a wave-like course, that is, periods of exacerbation and remission replace each other. Although the leukemic infiltrate metastasizes to the tissue, it does not damage it, but only compresses the parenchyma.

**Leukocytosis** is not an independent pathology, but a symptom that accompanies the course of various diseases. The mechanism of development of leukocytosis is related to an increase in the leukopoietic function of the bone marrow.

**Leukemoid reactions** are characterized by leukosis-like changes occurring in the peripheral blood (the amount of leukocytes is more than 30x109 /l, an increase in their immature forms). Unlike leukemia, these changes are reactive in nature, that is, they are observed in infectious diseases, purulent-inflammatory processes. During reactive leukocytosis, an increase in leukopoietins and a decrease in leukopoiesis-inhibiting factors are observed. During reactive leukocytosis, unlike leukemia, anemia and thrombocytopenia are not observed.

Unlike **other malignant tumors**, it is not possible to determine the location of the tumor during leukemia. Because the tumor cells can spread throughout the body through the blood. Leukosis cells first proliferate in the bone marrow, and then they disseminate to the peripheral blood, spleen, lymph nodes and other tissues. Lymphomas are first formed in the lymph nodes, and then they move to the blood and bone marrow. Leukoses develop only from cells belonging to the hematopoietic line, that is, from the cells described in the scheme of hemopoiesis.

**DIFFERENCE OF LEUKEMIA FROM LEUKEMOID REACTIONS**

|  |  |
| --- | --- |
| **Leukemoid reactions** | **Leukoses** |
| - formation of non-carcinogenic factorsbrings | - is caused by the effect of carcinogenic factors. |
| - activation of normal hemopoiesis is noted, transformation does not occur. | -normal hemopoietic cells are transformed into tumor cells. |
| - focal hyperplasia of normal hemopoietic cells is observed. | - widespread hyperplasia of hemopoietic tumor cells is observed. |
| -anemia and thrombocytopenia are not observed. Because the erythroid cells in the bone marrow are not compressed or damaged. | -anemia and thrombocytopenia are observed. Leukemic infiltrate prevents the development of erythrocytes and platelets, compresses them. |
| -degenerative changes occur in leukocytes (toxic granularity, Knyazkov-Dele body, pyknosis of the nucleus, cytoplasm vacuolization). | - an increase in blast cells is observed. |
| - the increase of leukocytes is reactive. It is observed in bacterial infectious diseases. | -blast cells do not obey the regulatory system, divide and multiply without limits, the ability to differentiate is weakened. |
| - does not form leukemic infiltrate in other organs. | - the leukemic infiltrate spreads to the liver, spleen, lymph nodes, lungs and other organs. |

**The most common types of acute leukosis**

**1. Acute myeloblastic leukosis - (M1)** - it is also called acute myeloid leukemia. It refers to bone marrow tumors that develop very quickly. Hemopoiesis originates from the myeloblast cells of the blast stage. During the development of the disease, abnormal blast cells are found in the blood. During the morphological analysis, they are determined as myeloblasts, promyelocytes, monocytes. Normally, blast cells increase in order to fight infection. On the other hand, the bone marrow produces abnormal erythrocytes and platelets. In such patients, due to protoporphyrin (combines with Fe and globulin to form hemoglobin), the bone marrow acquires a green-purulent color, so it is called "pioid bone marrow", that is, purulent bone marrow. During KML, CD13, CD33, CD14, CD65 markers are determined by immunophenotypic method.

**2. The population of myeloblast leukosis (M2**)-blast cells with some granules formed is morphologically somewhat reminiscent of myeloblasts in the blood and bone marrow. The difference is that the chromatin has a rougher structure and clearly visible nuclei, narrow cytoplasm. In a well-prepared smear, tumor cells can be distinguished from lymphoid cells. it is possible to differentiate. The chromatin of tumor cells has a reticular structure. Sometimes there are crystalline azurophilic and promyelocytic grains in the cytoplasm. Peroxidase reaction is positive in 3% of blasts by means of cytochemical studies.

**3. Acute promyeloblastic leukosis (M3)** - the cells show large nuclei, unclear chromatin structure, a large number of promyelocytic granules and Auer rods. Peroxidase reaction is positive.

**4. Acute erythromyeloblastic leukosis (M6)** - it is also called Di-Guglielmo's disease or acute erythremia. At this time, atypical myeloblasts, monoblasts and other undifferentiated blast cells are found in the bone marrow along with atypical erythroblasts.

**5. Acute megakaryoblastic leukosis (M7)** – originates from megakaryoblasts.

**6. Acute lymphoblastic leukosis (ALL)** originates from lymphoblast cells of the blast stage of hemopoiesis. The disease is called acute leukemia. At this time, a sharp decrease of granulocytes, thrombocytes and erythrocytes is observed. High leukocytosis is noted due to the increase of mononuclear cells. In the blood smear, nuclear chromatin with a not so dense, rigid structure is found. A large number of leukocytes makes it easier to confirm the diagnosis of leukemia. In addition to blast cells, which are characteristic of leukosis, neutrophils with segmented nuclei are also observed. The absence of mature cells between blast cells and mature cells confirms the existence of a **"leukemic abyss".**

**The main features of acute leukosis:**

- It mostly develops in children and young people;

- in blast cells, the nucleus is very large, the chromatin has a fine mesh structure;

- "leukemic abyss" is observed, which is of great importance in establishing the diagnosis;

 - clinical view - weakness, fever, tendency to bleeding, enlargement of lymph nodes, spread of leukemic infiltrate to some organs (liver, spleen, kidney, heart and other organs) is observed;

- blood analysis - hemoglobin, erythrocytes and platelets decrease, leukocytes often increase up to 80%. Blast cells predominate in the leukocyte formula. However, aleukemic leukemia is an exception. In this type of leukemia, against the background of leukopenia, anemia, thrombocytopenia, there are almost no blast cells in the peripheral blood. They are found in large quantities in the bone marrow;

- there is an increase in uric acid;

 - hyperplasia, anaplasia and metaplasia are found in the bone marrow and lymphoid organs. leukemic blast cells increase, 30-90%, and erythroid, megakaryocytic and granulocytic cells decrease.

**CHRONIC LEUKOSES**

 Chronic lymphocytic leukosis

 CLL disease develops from lymphoblasts, B-cell origin and T-cell origin. CLL of B-cell origin is mainly observed (95% of cases). Lymphocytes (80-90%) make up the main mass of leukosis cells of the blood.

 CLL takes its origin from the maturing cells of class V of lymphopoiesis. This type of tumor develops gradually. Because the abnormal cells increase gradually. Detection of lymphocyte remnants with fragmented nuclei in the blood smear - Botkin-Gumprecht shadows is a characteristic feature of chronic lymphocytic leukosis. Other blood cells (erythrocytes, platelets, granulocytes, monocytes) are present in small quantities. In this disease, the ability of B-lymphocytes to synthesize antibodies is weakened. Although erythropoiesis is weakened, patients can live for a long time. During a bone marrow puncture, lymphocytes are more than 30% in the myelogram. Prolymphocytes and Botkin-Gumprecht shadows are observed in the punctate. During CLL, the expression of CD19, CD20, CD23, CD5 antigens is observed in lymphocytes of B-cell origin. Cytogenetic disorder (pathology of chromosome 13 and trisomy of chromosome 12) is noted in some patients.

 The disease passes without symptoms for a long time. Only when examining the cells in the peripheral blood, the detection of absolute lymphocytosis can attract the attention of the doctor.

**Diagnosis of CLL**

- there is lymphocytosis in the peripheral blood;

- lymphocytosis in the bone marrow exceeds 30%;

- Antigens (CD19, CD23, CD5) are detected in lymphocytes of B-cell origin. The expression of CD5 confirms the presence of XLL of B-cell origin immunologically;

- in the terminal stage - anemia, granulocytopenia, thrombocytopenia develops.

CLL of T-cell origin is rare (3-5%). Its main features are: frequent damage to the skin with leukosis infiltrate, presence of polymorphous nuclei (bean-shaped), determination of coiled (brain-like) chromatin and detection of CD2, CD3, CD4 in lymphocytes of T-cell origin.

**Cutaneous lymphoma or Sezary's disease**

It is a malignant tumor of the skin. It originates from T-lymphocytes. In Sezary's disease, which damages the skin, 3 clinical signs are observed: erythroderma, lymphadenopathy, and the finding of cells with specific convoluted nuclei in the blood. The diagnosis of the disease is based on clinical signs, blood analysis and skin biopsy. In contrast to fungal mycosis, skin dyschromia is more clearly visible.

The presence of lymphadenopathy, erythroderma in the patient and the finding of Sezary’s cells in the blood analysis are of great importance in establishing the diagnosis. These cells are a special type of white blood cells, they are lymphocytes that are not so large and have an irregularly shaped nucleus. Characteristic sign: loss of DNA on chromosomes 10 and 17 or addition of DNA on chromosomes 8 and 17 is observed.

Differential diagnosis should be made with benign dermatological diseases. It is mainly differentiated by atopic dermatitis, psoriasis, true eczema, systemic ringworm diseases. Symptoms of erythroderma in these diseases are secondary in nature.

**PARAPROTEINEMIC HEMOBLASTOSIS**

Paraproteinemic hemoblastoses - tumors of B-cell origin - myeloma disease, Waldenstrom macroglobulinemia and heavy chain disease belong. In this type of leukoses, the ability of B-lymphocytes to differentiate into immunoglobulin-secreting cells is preserved. However, secreted immunoglobulins differ in their structure. These proteins synthesized by leukosis cells consist of either heavy or light chains of immunoglobulins, or immunoglobulins that have changed their structure.

**Myeloma disease**

It refers to tumors of B-cell origin. It is also called generalized plasmacytoma, Rusty-Kahler disease. Immunoglobulins secreted during the disease differ in their structure. The disease is caused by proliferation of lymphoplasmacytic cells of tumor origin.

The disease is characterized by the accumulation of abnormal plasmatic cells in the bone marrow and the high amount of proteins in the blood. In 20% of myeloma cases, tumor cells can synthesize only the light chain of immunoglobulins. IL-6 plays a major role in the pathogenesis of myeloma. IL-6 stimulates the division of plasma cells and inhibits their apoptosis. It is believed that IL-6 causes the lysis of bone tissue and the activation of osteoclasts (macrophages that destroy osteocytes). Due to the formation of hypercalcemia, damage occurs in the bones, kidneys, nervous and cardiovascular system. Because the bone tissue loses a lot of Ca, the patient develops pathological fractures. In the delayed forms of myeloma, the excretion of Ca in the urine accelerates, as a result of the precipitation of calcium salts in the renal tubules, the epithelial cells of the tubules become calcified. These changes cause oliguria, and in severe cases, anuria.

**Changes in the blood during myeloma disease** - at the beginning of the disease, the amount of Hb and erythrocytes is normal, and platelets may increase. As the disease progresses, the concentration of Hb in the blood, the amounts of erythrocytes and platelets decreases, anemia develops and the ESR increases sharply (50-70 mm/h). If these symptoms are present, one can suspect myeloma. But not every blood count means multiple myeloma. Therefore, a bone marrow puncture should be performed to confirm the diagnosis. If the plasma cells in the punctate are more than 30%, the possibility of myeloma disease increases.

If there is doubt about the accuracy of the diagnosis, the bone marrow puncture is either repeated or a trypanobiopsy is applied.

Morphologically, when examining plasmatic tumor cells, multinucleated cells are detected in the blood smear. Polymorphism and atypicality of tumor cells are observed in patients. The shape of the nucleus is deformed, the nuclei are enlarged, there are granules in the cytoplasm.

One of the main characteristics of myeloma disease is the finding of Bence-Jones protein in the urine of patients, and the light chain of immunoglobulins in the blood. Paraproteins with a small molecular weight can be easily filtered by the renal glomeruli and pass into the urine (Bens-Jones proteinuria). Accumulation of Bence-Jones paraproteins in the kidney results in the development of myeloma nephropathy. Patients develop secondary amyloidosis.

**Myeloma diagnostic criteria:**

- in the bone marrow, plasmatic cells are more than 10 - 30 %;

- paraprotein is found in the blood;

- Bence-Jones protein is determined in urine by electrophoresis;

- hypercalcemia is observed;

- kidney failure develops, the amount of creatinine in the blood increases;

- anemia is observed, hemoglobin is less than 100 g/l;

- sensitivity to infection;

- the amount of Ca in the blood increases;

- the amounts of proteins in the blood increases;

-mainly flat bones (ribs, skull bones) and vertebrae are damaged, osteolysis centers are formed.

During non-tumor paraproteinemias, there are no proliferation of plasmatic cells and foci of osteolysis in the bone marrow. Bence-Jones protein is not found in the urine.

**Primary macroglobulinemia**

It is also called Woldenstrom disease. It refers to malignant tumors of B-cell origin. Tumor cells synthesize large amounts of pathological IgM into the blood. The thickness and viscosity of the blood increases, hepatosplenomegaly, widespread lymphadenopathy, SLAC phenomenon, anemia, increase of ESR, vascular damage, bleeding observed. Patients are prone to infection. Sometimes Bence-Jones protein is detected in the patient's urine. However, unlike myeloma, its amount is small. The diagnosis is confirmed on the basis of bone marrow examination and the increase of protein M.

Bens- Jones proteins combine with other proteins in the urine (often Tamm-Horsfall protein) to form crystalline cylinders.

**Heavy chains disease**

During this disease, atypical B-lymphocytes synthesize the heavy chain of one of the immunoglobulin classes. The disease belongs to neoplastic plasmatic cell pathology and is characterized by excessive synthesis of the heavy chain of monoclonal immunoglobulins.

Monoclonal immunoglobulins (M-proteins) are often synthesized during plasma cell diseases. In the case of heavy chain disease, incomplete monoclonal immunoglobulins (true paraproteins) are formed with a changed structure. They consist only of the heavy chain component (alpha, gamma or delta).

Anemia, leukopenia, thrombocytopenia, eosinophilia, atypical lymphocytes and plasma cells are noted in the general blood analysis. The diagnosis is confirmed based on the detection of monoclonal alpha chain in blood and urine. If it is not found in the blood and urine, then a biopsy of the intestines is performed. Sometimes the abnormal protein is also found in the intestinal juice. Bence-Jones protein is not found in urine.

**Chronic myelocytic leukosis**

CML is a tumor of myeloid tissue. The morphological substrate of the tumor consists of maturing and mature granulocytes. Unlike acute myeloblastic leukosis, "leukemic abyss" is not observed. The chromosomal marker of the tumor clone is the Philadelphia (Ph) chromosome. This specific chromosomal marker is found in granulocytes, erythrocytes and megakaryocytes in 85-95% of cases. The Ph-marker appears as a result of the deletion of the 22nd pair of chromosomes or the translocation of the distal part of the long arm of the 22nd chromosome to the 9th chromosome t (9:22). As the disease progresses, new tumor clones and additional chromosomal abnormalities arise. The disease develops in 3 phases:

1. chronic phase

2. acceleration (progressive) phase

3. terminal phase (blast crisis)

**The criteria for the chronic phase of CML include:**

- clinical view - the patient's mood is relatively good, the spleen and sometimes the liver are slightly enlarged, there is leukocytosis (due to the increase in granulocytes);

- left bias of neutrophils (up to promyelocytes);

- lack of gross degenerative changes in neutrophils (toxic granularity);

- increase in eosinophils or basophils;

- hyperplasia of granulocytic derivatives in the bone marrow;

- Presence of Ph-chromosome;

The diagnostic criteria of the acceleration phase during CML refer to:

\*the number of blast cells in the blood or bone marrow is up to 10-19 %;

\* the number of basophils in the blood or bone marrow exceeds 20 %;

\*untreated thrombocytopenia or thrombocytosis develops;

\*untreated, progressive splenomegaly is observed;

\*additional chromosomal abnormalities occur.

Diagnostic criteria of the terminal stage during CML refer to:

\*the amount of blast cells in the blood and bone marrow exceeds 20%;

\*accumulation of large blast cells is observed in trepanobioptate;

\*additional abnormal chromosomes are found;

**Polycythemia vera (erythremia)**

It is also called Vakez-Osler disease. Although it is of tumor origin, it has a benign course. The disease is asymptomatic for a long time. The role of transformation of stem cells in its etiology is noted. Mutation of tyrosine kinase occurs, replacing valine with phenylananyl. The disease originates from myelopoiesis cells. The main substrate of tumor cells is erythrocytes.

The main hematological indicators of the disease:

-increased erythrocyte mass. Erythrocytes are 6-8×1012/l and more, Hb is 180-220 g/l, color index is 0.7-0.6. Due to the increase in erythrocytes, the volume of circulating blood increases;

- increased hemoglobin concentration;

- an increase in the hematocrit index and more than 65% is observed;

- due to the regeneration of erythrocytes, the amounts of reticulocytes in the blood increases by more than 15-20%;

- due to neutrophils, the amounts of leukocytes increase by 1.5-2 times. The nuclear orientation of leukocytes tends to the left;

- the amounts of platelets increase (400-600×109/l and more);

- an increase in the thickness of the blood is noted;

- ESR decrease (1-2 mm/h), increase of uric acid is observed.

**Complications of polycythemia**

Complications can occur due to thrombosis and embolism of brain vessels, spleen, liver, lower limbs. Ischemic stroke, heart attack of myocardium and spleen, cirrhosis of the liver, thrombosis of the femoral vein can develop. In addition to thrombosis, ulcers and bleeding of the duodenum and stomach are also noted. Stones are often formed in the gall bladder and kidney and nephrosclerosis is observed.

The disease is diagnosed based on the following symptoms:

- hematological and biochemical indicators change (increase of erythrocytes, Hb, leukocytes, reticulocytes, platelets);

- the patient's skin and visible mucous membranes become hyperemic;

-spleen and liver grow;

- the patient is prone to thrombosis;

- the patient's weight decreases;

- sweat secretion increases;

-genetically abnormal cells (with the exception of Philadelphia chromosomes) are found in the bone marrow;

-alkaline phosphatase increases (even in the absence of infection);

- the amount of erythropoietin is low;

- histological examination of the punctate during trypanobiopsy shows an increase in megakaryocytes.

**Difference between true polycythemia and secondary absolute and relative erythrocytosis**

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| **Polycythemia vera**-tumor proliferation of myeloid cells is observed in the bone marrow;- the level of erythropoietin in blood and urine is normal or decreased;- peripheral blood has thrombocytosis, neutrophilia, monocytosis;- the color index decreases as the ratio between the rate of proliferation of erythroid cells and the synthesis of hemoglobin is broken;- abnormal cells are found in the bone marrow;-spleen and liver grow;- the patient's skin and visible mucous membranes are red. | **Secondary absolute erythrocytosis**- observed during hypoxia, kidney ischemia, cardiovascular system pathologies;- the synthesis of erythropoietin increases;- non-tumor proliferation of erythroid cells is observed in the bone marrow;- thrombocytosis and leukocytosis are not observed;-relative erythrocytosis is temporary, observed during pathological processes that cause blood clotting (continuous vomiting, severe diarrhea, etc.);- a hereditary form of erythrocytosis also develops as a result of a lack of 2,3 diphosphoglycerate in erythrocytes and a genetic defect of globin in the hemoglobin molecule. The ability of oxygen to combine with Hb increases, as a result, hypoxia develops. |

**Diagnosis of chronic leukosis**

The most common form of chronic leukosis is chronic myeloid leukosis. At this time, cell elements can retain their ability to differentiate and mature for a long time. Tumor cells are collected both in bone marrow and peripheral blood. There are many myelokaryocytes in the punctate of the bone marrow. Megakaryocytes are almost not found in the bone marrow. If the blast cells are more than 30%, the presence of acute leukosis is confirmed, if it is less than 30%, the development of chronic leukosis is confirmed. In chronic myeloid leukosis, the chromosomal marker of the tumor clone is the Philadelphia chromosome (Ph).

**Differences between chronic myeloid leukosis** **and chronic lymphocytic leukosis**

**CML CLL**

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| It develops at the age of 30-40;-pioid (purulent) bone marrow is observed;- cells have 100% Ph- chromosome;-spleen grows too much, blast crisis develops;- there are leukosis infiltrates in the liver. | It develops at the age of 40-60;-bone marrow is red (raspberry);- There is no Ph-chromosome;- the spleen enlarges, hemolytic anemia, thrombocytopenia noted;- there are leukosis infiltrates along the portal tracts of the liver. |

**The main features of acute and chronic leukemia**

**Acute Chronic**

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| -children and young people get sick;- "leukemic abyss" occurs;- hemorrhagic syndrome and ulcerative-necrotic processes in mucous membranes are clearly observed;-spleen, liver, lymph nodes are slightly enlarged;-tumor cells in the bone marrow and peripheral blood consist of undifferentiated or poorly differentiated blast cells;- on the basis of morphological studies, it is not possible to determine whether blast cells belong to myeloid or lymphoid cells. | middle-aged and elderly people get sick;-all cells (mature, maturing) are present. Blast cells are more than normal;- hemorrhagic syndrome and ulcerative-necrotic processes in mucous membranes are observed only when the disease is aggravated (crisis of blast cells);-spleen, liver, lymph nodes become very enlarged;- has the ability to differentiate tumor cells;- on the basis of morphological studies, it is determined which cell line the blast cell belongs to. |

**Difference between Hodgkin's lymphoma and non-Hockin's lymphoma**

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| Hodgkin's lymphoma- in 90% of cases, neck lymph nodes are damaged;- the cell population is polymorphic;- observed at young ages;- the prognosis is good in 80% of cases;-Epstein-Barr creates the virus;- Reed-Sternberg cells are found in the damaged lymph node. | Non-Hockin's lymphoma- various localized lymph nodes join the process. It is not known which lymphoid tissue starts from the lymphopoietic cell;-cell population is monomorphic;- often occurs after the age of 40;- the prognosis is bad. |

**Prognostically unfavorable signs:**

- the presence of many conglomerates (more than 5 cm in diameter) in the peripheral lymph nodes;

- damage to more than 3 lymph nodes at the same time;

- the presence of signs of intoxication and ESR exceeding 50 mm/h;

- the patient's age is over 40.

**Disseminated Intravascular Coagulation Syndrome**

Disseminated intravascular coagulation syndrome (DIC-syndrome) is a widespread coagulation of blood inside a vessel, characterized by the formation of a large number of microthrombi and microaggregates that disrupt microcirculation in organs and tissues.

DIC-syndrome is a complication of other diseases, according to its clinical course, acute, subacute and chronic forms are distinguished. Acute DIC-syndrome develops suddenly within 24 hours, subacute DIC-syndrome lasts 1-3 weeks and chronic DIC-syndrome lasts more than 1 month. Acute DIC-syndrome occurs as a complication of the following pathologies:

• OBSTETRICAL AGGRAVATIONS:

- Premature separation of the placenta;

- Fetal flat water embolism;

- Rhesus incompatibility of mother and fetus;

- Septic abortion;

- Ectopic pregnancy;

• VASCULAR PATHOLOGIES

- Aneurysm

- Coarctation of the aorta

- Congenital heart defects

- Pulmonary artery thromboembolism

- Surgical angioplasty, etc.

• Sepsis

• Shock (traumatic, hemorrhagic, septic, burn, anaphylactic)

• Transfusion of incompatible blood

• Crash syndrome, massive tissue damage during surgical operations

• Acute intravascular hemolysis

• Massive hemotransfusions

The reasons for the development of the semi-acute DIC-syndrome are:

• Subacute glomerulonephritis

• Hemorrhagic vasculitis

• Immune complex vasculitis, etc.

Chronic DIC-syndrome can occur as a complication of the following pathologies:

• Systemic urticaria

• Tumor diseases (leukemia, cancer)

• Dehydration of the body

• Artificial prostheses of heart valves

• Chronic hemolysis, etc.

Hypercoagulation, consumption coagulopathy and hypocoagulation stages are distinguished in the pathogenesis of DIC-syndrome.

Hypercoagulation stage - when the generation of active thromboplastin accelerates, most of the prothrombin in the blood turns into thrombin. Thrombin accelerates the conversion of fibrinogen to fibrin, at the same time activates other coagulation factors and aggregates platelets;

Wasting coagulopathy - when a large amount of thromboplastin enters the blood vessels, most of the coagulation factors of the blood plasma are consumed, and most of the fibrinogen is converted into fibrin. At this time, circulating microaggregates and microthrombi are formed in the vessels. Also, due to the decrease in the amount of fibrinogen, the blood does not clot.

Hypocoagulation stage - bleeding occurs. Bleeding is caused by the increased consumption of platelets, coagulation factors and plasminogen.

The diagnosis of DIC -syndrome is based on a general examination of the blood and the determination of a coagulogram.

Changes in the following indicators are of great importance in the laboratory diagnosis of the hypercoagulation stage:

• Blood clotting time ↓

• Activated partial thromboplastin time ↓ (less than 45”

• Ht ↑ (40 and ± )

• Fibrinogen ↑

• Plasma recalcification time ↑ (over 45”)

• Thrombin time ↑(more than 10”)

• Degradation products of fibrin ±

• Soluble complexes of fibrin monomers ±

• Tests: ethanol, protamine sulfate ±

Characteristic for wasting coagulopathy:

• Platelets ↓

• Fibrinogen ↓

• Antithrombin III ↓

• Hypoproteinemia, hypoalbuminemia

• Fibrin degradation products ↑

• Activated partial thromboplastin time ↑ (≥ 65" )

• Plasma recalcification period ↑

• Prothrombin and thrombin time ↑

• Blood coagulation time, bleeding time and Ht either decrease or are in the lower and upper limits of normal

Laboratory diagnosis of the hypocoagulation stage is based on the following indicators:

• Blood clotting time, bleeding time ↑

• Fibrinolytic activity ↑

• Fibrinogen ↓

• Hb ↓ Ht ↓

• Erythrocytes ↓

• Antithrombin III ↓

• Coagulation factors I, II, IV, V, VIII, XIII ↓

• Plasminogen ↓

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| **Laboratory indicators** | **Norm** | **I stage** | **II stage**  | **III stage** |
| **Platelet count (x109/l)** | 150-400 | 300 | 150 | ≤100 |
| **Coagulation time (min)** | 5-10 | <4 | 10-20 | 12-20 |
| **Prothrombin time (seconds)** | 12-15 | ≤12 | ≥15 | 18-22 |
| **Activated partial thromboplastin time (seconds)** | 45-55 | <40 | 50 | >60 |
| **Thrombin time (sec)** | 18-20 | <18 | 25-28 | 30-35 |
| **Fibrinogen (g/l)** | 2-4 | 2-3 | <2 | <1,5 |
| **Fibrin degradation products (mcg/ml)** | 0-10 | ≥20 | ≥15 | 20-25 |
| **D-dimer (mcg/ml)** | <0,5 | 5-10 | 10-20 | 10-20 |