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Guidelines for conducting a practical lesson with 6th year students of the Faculty of Medicine on the topic:

CHRONIC LEUKEMIAS

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Methodological instructions for conducting a practical lesson
with 6th year students of the Faculty of Medicine on the topic:
DIFFERENTIAL DIAGNOSIS AND TREATMENT OF LEUKEMIA

The purpose of the lesson. Students should be able to:

1) make a general assumption about a systemic blood disease;
2) confirm the diagnosis of leukemia based on a blood test and myelogram;
3) determine the nature of the course, the form and stage of leukemia, complications;
4) to carry out a differential diagnosis with syndromic diseases;
5) determine the tactics of treating patients.

Lesson content

Definition. Tumors of the hematopoietic tissue - hemoblastoses - are divided into leukemias and hematosarcomas. Leukemias are tumors originating from hematopoietic cells (class III) and primarily affecting the bone marrow. Hematosarcomas (lymphomas) primarily originate in lymphatic tissue outside the bone marrow.

Leukemias are divided into acute (myelo-, lympho- and monoblastic, undifferentiated) and chronic (myeloid, myelofibrosis, or subleukemic myeloid leukemia, lymphatic, Waldenström's disease, erythremia, multiple myeloma), lymphomas - lymphogranulomatosis (Hodgkin's disease) and non-Hodgkin's lymphomas.

Stages of diagnosis

1. The general assumption of a systemic blood disease is based on the identification of the following syndromes:

- signs of anemia: pallor of the skin and mucus

dry membranes, hypoxic syndrome (weakness, shortness of breath, palpitations, decreased performance, there may be dystrophic changes in organs), peripheral blood analysis (decrease in red blood cells and hemoglobin);

- signs of hyperplasia of the hematopoietic tissue and extra-medullary hematopoiesis (an increase in various groups of lymph nodes, liver, spleen, skin infiltrates);
- hemorrhagic syndrome: hemorrhages and bleeding, symptoms of tourniquet, pinching;
- signs of a decrease in the immunological resistance of the body: infectious-septic and ulcerative-necrotic lesions (pneumonia, tonsillitis, etc.)

2. Confirmation of the diagnosis of leukemia:

- *analysis of peripheral blood: high content of immature cells of a certain type;*- myelogram: hyperplasia of white hematopoiesis due to immature (blast) forms of myelokaryocytes, inhibition of erythropoiesis and thrombopoiesis, an increase in the ratio of leukoforms to erythroforms. Trepanobiopsy data can also be used.

3. Determination of the nature of the course of leukemia.

Index	**Leukemia**	
	Acute	**Chronic**
main cell substrate	blast cells (more than 10-20%)	maturing and mature cells
Leukemic "failure"	Available	All intermediate forms
Leukocytosis	Low, may be leukopenia	More often high
platelets	Reduced	Can be upgraded

Enlarged lymph nodes, liver, spleen	No or little	permanent, pronounced
Ulcerative necrotic processes	Available	Not
Malignancy	high	Not

The malignancy of the process is expressed in the signs of tumor progression: rapid tumor growth within the bone marrow or outside it, inhibition of normal hematopoietic sprouts, refractoriness to previously effective therapy.

Malignant forms include acute leukemia, chronic myeloid leukemia. Chronic lymphocytic leukemia, erythremia, osteomyelofibrosis are considered relatively benign.

4. Determination of the hematological variant: leukemic, subleukemic, aleukemic (depending on the number of leukocytes, the presence or absence of blast cells in the blood), leukopenic.

5. Determination of the nosological form of leukemia: by morphology, cytochemical and cytogenetic (Ph-chromosome) study of cells, as well as by clinical features.

It should be borne in mind that various forms of acute leukemia have a similar clinical picture. The morphology of blast cells often cannot be established without cytochemical studies (undifferentiated leukemia).

The main nosological forms of chronic leukemia have some features:

- myeloid leukemia: a significant increase in the spleen and liver; in the blood, in addition to cells of the neutrophilic series, basophils and eosinophils are noted;
- osteomyeloid leukemia and myelofibrosis: a more benign long-term course. Severe spleno- and hepatomegaly, bone pain, bone changes: thickening, narrowing of the bone canal, compaction of the spongy layer. Often sub- or aleukemic variant, sometimes erythroblastosis, thrombocytosis. There is no Ph-chromosome and alkaline phosphatase in neutrophils;
- lymphocytic leukemia: older age, long-term benign course. Generalized enlargement of lymph nodes of dense elastic consistency, less often - enlargement of the spleen and liver, more often - skin lesions. In the blood: more often leukemic forms, Botkin-Gumprecht cells. Autoimmune crises are possible.

6. Determination of the stage of leukemia (according to the degree of proliferation of leukemic tissue, generalization of the process, complications).

Acute leukemia:

- initial stage - retrospectively;
- deployed - in the presence of the main clinical and hematological manifestations;
- remission - with the normalization of the clinical picture and peripheral blood, mild anemia, leukopenia (up to 1.5-109 / l), thrombocytopenia (up to 100.0-109 / l) are allowed; complete - with the presence of no more than 5% of blast cells in the myelogram, incomplete - up to 6-20%;
- relapse - return of clinical and hematological symptoms;
- terminal - severe anemia, thrombocytopenia, resistance to chemotherapy, dystrophic syndrome, exhaustion, ulcerative necrotic complications.

Chronic leukemia:

- the initial stage - the general condition is satisfactory, moderate changes in the hemogram and organs without signs of generalization and complications;
- extended - phase of exacerbation: violation of the general condition, fever, enlarged lymph nodes and organs, there may be spleen infarcts, mild anemia, hemorrhagic syndrome, blast crises and autoimmune syndrome (fever, hemolytic jaundice, swollen lymph nodes); remission phase: improvement, normalization of temperature, reduction of lymph nodes and organs, improvement of hemogram;
- terminal: blastemia, anemia, thrombocytopenia, complications, cachexia.

7. Carrying out a differential diagnosis.

Disease	Leukemia variant	Features

Leukemoid reaction	Subleukemic form of myeloid leukemia	The presence of the underlying disease (sepsis, tuberculosis, cancer, intoxication, etc.), normal platelet and basophil counts, no Ph-chromosome, normal or increased alkaline phosphatase activity
Aplastic anemia, agranulocytosis	Acute leukemia, aleukemic form, with pancytopenia	Lack of enlargement of lymph nodes and organs, devastation of the bone marrow, lymphoid cells
Lymphogranulomatosis	Chronic lymphocytic leukemia, especially aleukemic forms, with enlarged visceral lymph nodes	Lymphopenia, no Botkin-Gumprecht cells, nodes of different density, fever, pruritus, eosinophilia. Berezovsky-Sternberg cells in a lymph node biopsy.

Making a diagnosis: nosological form, type of course, hematological variant, stage, complications.

General principles for the treatment of leukemia

1. Suppression of leukemic proliferation by using cytostatic drugs, the choice of which depends on the hematological and clinical form of leukemia.

Preparations	**Indications**
Antimetabolites:	
Purine (6-mercaptopurine)	Acute lymphoblastic leukemia, blast crisis in chronic myeloid leukemia
Pyrimidine (cytosine-arabinoside)	Acute myeloblastic and undifferentiated leukemia
Folic acid preparations:	
Methotrexate (ametopterin)	Acute lymphoblastic and undifferentiated leukemia
Antimitotic:	
Vincristine, vinblastine	Acute lymphoblastic leukemia
Alkylating chloroethylamines:	
Cyclophosphamide, dopan	Acute lymphoblastic and chronic lymphocytic leukemia
Leukeran, degranol	Chronic lymphocytic leukemia
Antibiotics:	
Rubomycin	Acute lymphoblastic and myeloid leukemia
Derivatives of sulfonic acid:	
Myelosan, myelobromol	Chronic myeloid leukemia

Enzymes:	
L-asparginase	Acute lymphoblastic and myeloid leukemia
Steroid hormones:	
Prednisolone	Acute leukemia, crises, as part of polychemotherapy
Radiation therapy	Splenomegaly, tumor forms
Operation:	
Splenectomy	Splenomegaly, hypersplenism

2. Treatment of infectious complications: antibiotics, gamma-
globulin, asepsis, skin and mucous membrane care.

3. Fight against anemia: transfusion of blood, red blood cells,
vitamins, iron preparations.

4. Fighting bleeding: transfusion of fresh blood,
plasma, platelets.

5. Stimulation of immunological protection in the stage of induced hypoplasia of hematopoiesis: administration of immunoglobulins, immunocompetent cells (lymphocytes, transplantation of lymphoid organs, bone marrow).

6. Removal of leukemia cells from the body (cytopheresis).

Tactics for the treatment of acute leukemia.

1. Induction of complete remission (usually with lymphoblastic leukemia) with the help of intensive courses of polychemotherapy for 4-6 weeks. before the development of hematopoietic hypoplasia (courses of 5-7 days with a break of 10-14 days).

Polychemotherapy (for simultaneous impact on different phases of the mitotic process of leukemia cells) is carried out according to various programs: VAMP - vincristine, amethopterin, 6-mercaptopurine, prednisolone; TsVAMP - cyclophosphamide + VAMP; CLAP - cyclophosphamide, L-asparginase, prednisolone; AVAMP - cytosinorabinoside + VAMP, etc.

Doses of cystostatic drugs are halved with a decrease in leukocytes to 2.0-109/l and platelets to 40.0-109/l. Cytostatic therapy is canceled when the level of leukocytes is less than 1.0-109/l, ulcerative stomatitis, diarrhea, severe vomiting.

When induced hypoplasia of hematopoiesis is achieved, measures are taken to combat anemia, bleeding, and to prevent and treat infectious complications. When restoring the number of leukocytes more than 2.5-109/l and platelets more than 50.0-109/l, cytostatic therapy is resumed.

With neuroleukemia - additional endolumbar introduction of cyclophosphamide.

2. Strengthening (consolidation) of remission by additional 2-3 courses of intensive chemotherapy.

3. Maintenance therapy during remission with

3-6-week courses of monochemotherapy mainly with antimetabolites (with lymphoblastic leukemia for at least three years under the control of peripheral blood tests and myelograms).

Tactics for the treatment of chronic leukemia.

In stage I, partially in stage II, mainly general strengthening measures, observation, sanitation of foci of infection are carried out, primary restraint therapy is possible (with leukocytosis up to 50.0-109 / l, with a tendency to increase and shift in the leukocyte formula to myelocytes; the spleen is not enlarged or slightly enlarged).

Control blood tests at least once a month.

Indications for active course cytostatic therapy:

- leukocytosis more than 120.0-150.0-109/l;
- tendency to anemia and thrombocytopenia;
- progressive enlargement of lymph nodes, organs, compression syndrome;
- dystrophogenic disorders (weight loss, etc.).

The course of treatment is 2-3 weeks until the number of leukocytes decreases to 10.0-15.0-10%.

Control blood tests 1 time in 5-7 days.

Features of the treatment of chronic myelo- and lymphocytic leukemia.

Stage	myeloid leukemia	lymphocytic leukemia
Initial	Primary restraint therapy (myelosan 2-4 mg once every 7-10 days) on an outpatient basis.	Restorative measures, observation
deployed	Course chemotherapy Mielosan Mielobromol Dopan Radiation treatment	Course chemotherapy Leukeran Cyclophosphamide Degranol Splenectomy Radiation treatment
Blast Crisis	Polychemotherapy	Prednisolone
Terminal	Polychemotherapy Symptomatic treatment	Symptomatic treatment

In the stage of remission with a decrease in the number of leukocytes to 15.0-20.0-109 / l with almost complete normalization of the blood count and the size of the spleen, they switch to maintenance therapy with the introduction of a medication 1-2 times a week. With the recurrence of the disease, the course treatment is repeated.

With erythremia, bloodletting is first performed, with ineffectiveness - imiphos, myelobromol, myelosan, anticoagulants, acetylsalicylic acid.

With multiple myeloma - sarcolysin, cyclophosphamide, prednisolone, anabolic steroids.

Summary.