

## DIAGNOSTIC AND TREATMENT METHODS OF ACUTE LEUKEMIA

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Acute leukemia is characterized by a proliferation of immature white blood cells in the bone marrow and peripheral blood. There are several types of acute leukemia classified based on the type of cell affected, such as myeloblasts, lymphoblasts, and erythroblasts. Blast cells that cannot be differentiated morphologically are classified as undifferentiated acute leukemia.

If at least one symptom is present, the patient is considered to have a high risk, otherwise, the patient is classified as standard risk. If remission is not achieved after the first phase of induction, the patient is assigned to the high-risk group without regard to other signs.

Morphological classification of acute myeloid leukemia:

- M0. Acute undifferentiated myeloid leukemia.
- M1. Acute myeloid leukemia with minimal differentiation.
- M2. Acute myeloid leukemia with maturation.
- M3. Acute promyelocytic leukemia.
- M3 (variant). Acute promyelocytic leukemia with granulocytic differentiation.
- M4. Acute myelomonocytic leukemia.
- M4. Acute myelomonocytic leukemia with eosinophilia.
- M5. Acute monocytic leukemia.
- M5a. Acute monoblastic leukemia.
- M5b. Acute monocytic leukemia with promonocytes.
- M6. Acute erythroid leukemia.
- M7. Acute megakaryoblastic leukemia.

The main diagnostic tests performed on an outpatient basis include:  
complete blood count (including leukocyte differential count, platelet count);  
myelogram by sternal puncture.

Additional diagnostic tests performed on an outpatient basis include:

- cytokine assay of blast cells;
- cytokine assay of blast cells;
- cytofluorimetry method "for acute leukemia";
- standard cytogenetic studies;
- FISH method and molecular genetic studies;
- general urine analysis;
- coagulogram;
- blood group and Rh factor determination;

biochemical blood tests (total protein, albumin, total bilirubin, conjugated bilirubin, creatinine, urea, ALT, AST, glucose, LDH, C-reactive protein, alkaline phosphatase);

IFA for viral hepatitis markers;

IFA for HIV markers;

IFA for herpes virus markers;

ECG;

Ultrasonic examination of abdominal organs (liver, spleen, pancreas, adrenal glands, lymph nodes, kidneys), small pelvis in women;

skull X-ray.

According to the JSST data, blast cells make up 20% or more in the peripheral blood and bone marrow in acute leukemia.

Cytomorphological features specific to blast cells:

1. Fine chromatin structure of the nucleus;

2. Presence of nucleoli;

3. Basophilic cytoplasm;

4. Nucleus-cytoplasmic ratio of 4:1-8:1.

Peripheral blood changes in acute leukemia

1. Normocytic anemia;

2. Leukocyte count ranging from strong leukopenia to strong leukocytosis (from 1 to  $300 \times 10^9/l$ ):

a) A lymphoid form - leukocyte count of  $1-3 \times 10^9/l$ , absence of blast cells or 1-2% relative lymphocytosis;

b) A sub-lymphoid form - leukocyte count of  $4-14 \times 10^9/l$ , blast cells of 5-10%;

c) A myeloid form - leukocyte count above  $15 \times 10^9/l$ , blast cells above 10%.

3. Thrombocytopenia;

4. "Leukemic hiatus" in the leukocyte formula - presence of blast and mature cells, absence of intermediate cell-lines.

5. Increase of ESR (erythrocyte sedimentation rate).

Changes in bone marrow during acute leukemia:

1. Blast transformation of the bone marrow (blast cells above 30%);

2. Suppression of bone marrow hematopoietic activity of myeloid, lymphoid, and erythroid lines;

3. Acute decrease of megakaryocytes.

Cytotoxic reactions. Blood cytotoxic reactions are based on a colorful reaction of blast cells' enzymatic activity and substrates. Myeloperoxidase, acid and alkaline phosphatase, nonspecific esterase, glycogen and lipid detections have great diagnostic significance. Cytotoxic reactions allow for identification of blast cells, determination of their maturation stage, and the choice of treatment tactics.

General blood test results in acute leukemia: hemoglobin - 72 g/l, erythrocytes -  $1.7 \times 10^{12}/l$ , hematocrit - 22%, MCV - 100 fl, MCH - 31 pg, leukocytes -  $17.0 \times 10^9/l$ .

Leukocyte formula: blast cells - 75%, segmented neutrophils - 8%, lymphocytes - 15%, monocytes - 2%, platelets -  $5.0 \times 10^9/l$ , reticulocytes - 0.1%, ESR - 65 mm/hour.

Hospitalization indications: immediate hospitalization in an isolation ward upon the diagnosis of acute leukemia.

Recommendation for chemotherapy courses for hospitalization in a properly equipped hospital.

Treatment. Nowadays, modern, continuously updated, internationally approved polychemotherapy protocols are used to treat acute leukemia, which include stratification according to the cytogenetic and immunological variant, providing a targeted approach to the therapy. Treatment consists of the following steps:

Indication of remission. At this stage, a significant decrease in leukemia cells is observed.

Consolidation - the eradication of residual leukemia cells.

Neuroleukemia prophylaxis, including lumbar puncture for the administration of chemotherapy.

Remission maintenance therapy - administration of chemotherapy to eliminate residual clones.

Polychemotherapy uses a combination of cytostatic drugs based on different mechanisms of action, selective targeting of blast cells in different histogenetic and cell-cycle phases, and taking into account the interval between courses. Chemotherapy drugs are classified into the following groups according to their mechanism of action against leukemia: antimetabolites (mercaptopurine, thioguanine, methotrexate, cytarabine), alkylating agents (cyclophosphamide, daunorubicin, asparaginase, etoposide, carmustine), and hormones (glucocorticoids). Polychemotherapy allows complete clinical and hematologic remission to be achieved, characterized by the normalization of lymph nodes, liver and spleen size, and the absence of neuroleukemia symptoms.

Hemoglobin levels should not be less than 100 g/l, the number of granulocytes should not be less than  $1.0 \times 10^9/l$ , and the number of platelets should not be less than  $100 \times 10^9/l$ , and there should be no blast cells. The composition of blast cells in the bone marrow should be less than 5%, and lymphocytes should not exceed 30%.

Polychemotherapy courses are only carried out under stationary conditions.

Prognosis. Modern approaches to diagnosis and treatment, as well as the state's attention to this issue, lead to successful outcomes. In recent years, the mortality rate from acute leukemia has decreased, and 60-80% of patients achieve complete remission.

The unfavorable consequences of the disease are largely due to delayed diagnosis, poor response to polychemotherapy, and the combination of signs indicating a high-risk group. The most common causes of death are myelosuppression and infection.

Surveillance. During 1-2 years of remission, a hematologist and a general practitioner should conduct clinical examinations once a year; during 3-5 years, examinations should be conducted every 3 months.

Monitoring laboratory indicators: blood analysis to determine the number of platelets - once a week during supportive therapy; once a month after the completion of therapy; during 3-4 years of remission, every 2-3 months.

Monitoring biochemical indicators (bilirubin and its fractions, ALT, AST, alkaline phosphatase, C-reactive protein, glucose, creatinine, urea) - once a month during supportive therapy, and twice a year after its completion.

Hepatitis B virus, hepatitis C virus, cytomegalovirus, Epstein-Barr virus, HIV - should be checked twice during the first 1-3 years, and then according to the recommendations.

Coagulogram, immunogram, trepanobiopsy, myelogram, lumbar puncture - according to the protocol.

Functional methods (ECG, ultrasound) - every 6 months for 1-2 years, and then once a year.

Instrumental methods (fibrogastroduodenoscopy), X-ray, CT - according to the recommendations. Ultrasound examination of abdominal organs - every 6 months for 1-3 years, and then once a year.

Examinations by specialists: hematologist - every 3 months; neurologist - every 6 months; cardiologist, gynecologist, urologist, endocrinologist - according to the recommendations.

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