Medical report

Patient Maganova Maria Sergeevna, date of birth April 3 1975, stayed in the Department of chemotherapy of leukosis of State Science Center RAMS from 01.06.2010. Diagnosis: acute myelogenous leukemia (escape from MDS). Concomitant disease: uterine fibroid.

Anamnesis morbi: from May 2010 weakness; in the blood analysis dated 29.05.10: WBC 5.7 thous., bl.1%, myel.3%, metamyel.1%, band 10%, segm 41%, mon. 13%, Нв 57- 52g/L, Plt.94 thous., LDH 596 U/L.

Allergic anamnesis: not burdened. Blood group A2B (IV)CcDee.

Assessment in June 2010 in State Science Center:

- **Bone marrow** (01.06.10г.): bl..26%. pmyel.0.4%, myel.28%, myel. eos. 1.8%, metamyel. 6.2%, myel.eos. 0.4%, band 9.4%, band eos. 0.2%, eos. 2%, bas.0.2%, segm 9%, lymph.6%, mon. 0.8%, RBC/bl. 7.8%, BM is cellular. MKC in moderate amount. Cytochemistry: MPO + in 13%, nonspecific esterase of moderate activity, NaF is not suppressed, PAS-positive material in the diffuse-granular form; conclusion - myeloblastic variant; phenotype CD34+-/HLA-DR+/CD13+/CD117+-/MPO-1; proliferative activity level is 7%, the total content of CD34+ 14%, total content of CD117 + 21%. The phenotype corresponds to myeloblasts;
- Cytochemistry of bone marrow (07.06.10): Blasts 10%, MPO+, partly contains azurophilic granulation and Auer bodies; 65% sideroblasts, of which 4% have ring-forms, the content of polysaccharides in erythrokaryocytes is normal 4%;
- trephine (08.06.10): the fat cells are almost absent. Myelokaryocytes are tight. Erythropoiesis is sharply stenosed. Granulocytopoiesis is not stenosed, represented mainly by intermediate forms, there are quite a lot of mature forms, immature forms are few. Eosinophilic forms are frequent. The number of megacaryocytes is significantly reduced, they are unevenly distributed, exist one by one, dominated by microforms and bare nucleus forms. A very large number of scattered cells of monocytoid type (blasts?) is seen, and also single mitoses. There are single lymphocytes. Conclusion: The pattern is abnormal for the presence of blast transformation of CMML, we can not exclude acute leukemia de novo. Immunohistochemistry: Glycophorin A + erythrokaryocytes in sufficient quantity, the number of MPO+ granulocytic elements are reduced, scattered and exist in groups of CD34 + blast cells (about 10%). Staining for CMV-, HSV-HHV8-, HBsAg-, some cells EBV + and HSV2 +, there are few cells HCV +; PCR in bone marrow DNA-CMV-, DNA-EBV+;
- karyotype 46, XX [20];

- By FISH method 200 interphase nuclei were analyzed with each DNA-probe: a chimeric gene BCR/ABL (probe D-BCR-ABL), monosomy and deletion 5 (probe LSI EGR1 (5q31)) and 7 (probe LSI D7S522 (7q31) / CEP7) chromosomes, trisomy of 8 chromosome (DNA probe to the centromere), division of chromosome 20 (probe LSI D20SI08), monosomy of chromosome 3 (probe LSI BCL 6) **have not been identified**;
- Thoracic CT scan (15.06-10): pretraheoretracaval lymph node 10.5mm; in the peripheral regions S3 of both lungs single low-intensity areas of alveolar infiltration of type "diffusing screen" are determined, limited areas of enriching lung pattern with fine intralobular perivascular foci: in other regions no changes are seen; (09.07.10): almost complete restoration of pneumatization of the lung tissue;

(19.10.10): area of limited fibrosis in the lower lobe of left lung (probably as a consequence of the pleuropneumonia in August 2010) in tissue of the mediastinum retrocaval-paratracheal lymph nodes of 12.3mm are visualized; (02.11.10): a decrease in the anterior mediastinum lymph nodes to 7 mm, induration of their structure, changes in the lower lobe of the left lung underwent regression and. apparently were caused by residual inflammation;
- ECG (01.06): sinus rhythm, heart rate 81;
echocardiogram (16.06): the cavities are not dilated, the wall thickness is normal, the valves are not modified, lumen of the aortic root is not expanded, contractility is satisfactory, systolic and diastolic function are not violated: in the cavity of the left ventricle there is the additional apical diagonal trabecule (hemodynamically insignificant):
- Ultrasound examination (2.6): liver right lobe 145x93mm, left lobe 105x40mm, V.portae 12mm, v.lienalis 7mm, spleen 122x50mm; modified lymph nodes were not found; the size, echogenicity of kidneys are not changed, in the projection of the lower pole of left kidney – a cyst 8mm. Size, echogenicity of thyroid gland is not changed, in the left lobe - anechoic inclusion 5x3mm of involutive nature. Uterus - myoma nodes up to 30mm, M-echo 14mm; left ovary 42x28, has follicular? inclusion 27x21mm, right 34x30mm; no abnormalities.
- Antiplatelet and antileucocytal antibodies were not found (10.06.10);
- RW, HBsAg, a/HCV, a/HIV - neg (02.06.10); HBsAg, a/HCV, RNA-HCV, DNA-HBV - neg. (24.11.10.):
- DNA-CMV-, DNA-EBV-, DNA-HSV 1-2 - neg. (10.08.10, 21.10.10); DNA-HHV 6 neg. (21.10.10); DNA-CMV- neg. (24.11.10)

Treatment: -*16.06 -13.07.2010: course of low-doses of cytozare* (5-10mg subcutaneously x 2 times a day). **Bone marrow** (03.08): bl..37.2%, nmyel1.6%, myel.18%, myel.eos.1,2%, metamyel 4.4%, metamyel.eos.0.8%, band 9.2%, segm 6.8%, eos.2.3%, bas.2%, lymph. 13,6%, mon.2%, erythrokaryocytes 0.8%, MKC in moderate amount, BM is cellular;
- 06.08 - 12.08.2010. «7+3» with idarubicine (scheme of acute myeloid leukemia). Complications: thrush, bilateral pneumonia. **Bone marrow** (14.09.10): Bl . 24%, myel.3.2%, metamyel.1.2%. band 6.8%, segm 8.4%, eos.4.8%, bas. 6.4%, lymph.32%, monocyt.cells 12.8%, eritrocariocytes are not found, plasma 0.4%, MCC isolated., BM moderately cellular, many damaged cells, counting is partially selective. Karyotype 46, XX [20]: by FISH 200 interphase nuclei were analyzed with each DNA probe: a chimeric gene BCR / ABL (probe D-BCR-ABL), monosomy and deletion of the 5 (probe LSI FGR1 (5q31)) and 7 (Probe LSI D7S522 (7q31) / CEP7) chromosomes, trisomy of 8 chromosome (DNA probe to centromere), deletion of chromosome 20 (probe LSI D20S108), monosomy of chromosome 3 (probe LSI BCL 6) were not re-identified.
- Trephine (16.09.10): The focal resorption in trabeculae of bone, a wide bone marrow cavities sharply hypoplastic blood-forming tissue, elements of the three germs of hematopoiesis are determined, the ratio of the granulopoiesis cells and erythropoiesis is close to normal; granulocytopoiesis is represented mainly by cells of mature and ripening forms along which clearly separate intermediate forms, the number of megacaryocytes is decreased, they are presented by microforms: single cells of monocytoid type, cyderophages, small lymphoid cells are identified; coarsers in stromal areas.
- *05.10 - 09.10.2010.: HAM (*cytosar 4.5g intravenously x 2 times a day 1 -3 days, novantron 15mg intravenously 3 -5 days). Complications: Candida esophagitis. Gram-negative sepsis (E.coli). **Bone marrow** (12.11.10): bl..40%, myel.10%, myel.eos.0.5%, metamyel.0.5%, myel.eos.0.5%, band2%, segm9%, eos.1%, lymph.29.5%, mon.7%, eritrocariocytes and MCC are not found; many lysed cells, counting is selective. **Bone marrow** (19.11.10): bl..27%, myel. 14%, myel.eos.2%, metamyel.2%, band3.5%, segm8.5%, lymph.38.5%, mon.3%, eritrocariocytes 1.5%, MCC are not found,

BM is poorly cellular. Trephine (24.11.10): Bone tissue with signs of severe resorption; cavities are broad, and include a significant increase in fat cells, nuclear forms of erythropoietin are identified in the reduced amount, in even more reduced – of granulopoiesis, with very little mature generations, single megacaryocytes, blasts a few, many syderophages. Staining for CMV-, HCV-, HBsAg-, all of megacaryocytes EBV. When PCR in bone marrow DNA-CMV, RNA-HCV, HBsAg are not detected.

- **Bone marrow** (09.12.2010: Bl . 15%, myel. 7%, metamyel. 1%, band (n) 4.5%, segm 24.5%, lymph. 44.5, mon. 9.0.

Clinical blood analysis (09.12.2010): Hb 69g/L, RBC 2.5x410^{12}/L, Plt 33 thous., WBC 1x10^{9}/L, band 5%, segm 11%, lymph. 20%, mon. 14%.

Thus, the patient is resistant to the major chemotherapeutic drugs (cytosar, anthracyclines), including the high dose. Since mid-July there is agranulocytosis, thrombocytopenia, and profound anemia (red blood cell transfusions are carried out, is adapted to the level of H_B more than 60g/l). Infectious complications are stopped to 25.10.10, antibacterial and antifungal therapy is completed on 31.10.10. Currently, the patient is medically safe; no clinical problems.

Conclusion: Due to the resistance to chemotherapy it is necessary to consider the possibility of conducting allogeneic bone marrow transplantation on vital indications from an unrelated matched donor. HLA typing was carried out, the results are attached (4 sheets). Due to ineffectiveness of chemotherapy and progress of aplasia after treatment, bone marrow transplantation from an unrelated donor is the treatment of choice.