**GT-1401-004**

Hemopoiesis morphology after transplantation of allogenic bone marrow in myelodysplastic syndromes


Hematology Research Center, Moscow, Russia

**Summary.** The morphology of hemopoiesis was studied in patients with myelodysplastic syndromes (MDS) during different periods after transplantation of allogenic hemopoietic stem cell (allo-HSC) with conditioning of low intensity. Bone marrow aspirate specimens (n = 98) and bone marrow biopsy specimens (n = 94) were studied in 10 patents with primary MDS. Morphologic studies of hemopoietic tissue were carried out directly before allo-HSC transplantation with low intense conditioning and during different periods after transplantation. Rapid replacement of the host hemopoiesis and hemopoiesis recovery were observed in MDS patients after allo-HSC transplantation due to healing of the donor transplant. Despite conditioning in the low intensity mode, hemopoietic tissue hypoplasia was detected during the early and late periods after transplantation, presumably because of stromal microenvironment damage, this limiting complete recovery of hemopoietic tissue. Good reparation of the erythroid and granulocytic hemopoiesis stems was observed after allo-HSC transplantation. The recovery of megakaryocytic stem was incomplete. Dysplastic changes in hemopoietic cells reduced significantly. Slight reversible secondary dysplastic changes were however found in erythrokaryocytes. In megakaryocytes the dysplastic changes were more stubborn and detected during the early and late stages after allo-HSC transplantation. Comparative analysis of bone marrow aspirate and biopsy specimens indicated that hemopoietic tissue recovery after allo-HSC transplantation in MDS patients developed during about the same periods as in other hematological malignancies. Hemopoietic tissue hypoplasia after allo-HSC transplantation was observed in the majority of patients over the entire period of observation. Morphologic studies of the signs of dysplasia of various hemopoietic stems in MDS showed significant reduction of dysmyelopoiesis after allo-HSC transplantation.

**Key words:** myelodysplastic syndromes; allo-HSC transplantation; cytology; histology.

**GT-1401-011**

FEATURES OF PLATELET AGGREGATION IN PATIENTS WITH JAK2 GENE MUTATION: GENDER DIFFERENCES AND ASPIRIN EFFECT

I.A. Olkhovsky¹, ², M.A. Stolyar¹

¹ Krasnoyarsk Affiliated Department of Hematology Research Center, Krasnoyarsk, Russia; ² Krasnoyarsk Research Center, Krasnoyarsk, Russia

**Summary.** The effects of acetylsalicylic acid (ASA) on platelet aggregation were studied in 44 patients with V617F mutation in JAK2 gene and in 7 patients with chronic myeloproliferative diseases (CMPD) without this mutation. The study was carried out by adenosine diphosphate-induced impedance aggregometry of whole blood. Aggregometry values in the majority of CMPD patients receiving low-dose ASA did not differ from the values in the patients receiving no ASA. In some cases the aggregation amplitude was sharply reduced. In these patients restriction of antiplatelet therapy was required. Platelet aggregation in women was significantly higher than in men, both in health and CMPD. The degree of gender-associated differences in the aggregation amplitudes depended on the presence of JAK2 gene mutation and ASA effect. Individual evaluation of the platelet functional activity by whole blood incubation with ASA could be recommended for disaggregation therapy monitoring.

**Key words:** impedance aggregometry; chronic myeloproliferative diseases; JAK2 gene V617F mutation; aspirin resistance; acetylsalicylic acid; gender differences.

**GT-1401-015**

Residual risks of transfusion transmissive transfer of HIV infection and viral hepatitis C in the Moscow region in laboratory screening of donor blood by NAT technologies

V.V. Belyakova¹, I.A. Gukasyan¹, O.V. Donskaya¹, N.V. Ivanova¹, O.A. Maiorova¹, N.G. Dashkova², A.A. Ragimov²

¹Blood Transfusion Station, Moscow, Russia; ²Blood Center, Clinical Center, I.M.Setchenov First Moscow State Medical University, Moscow, Russia

**Summary.** Serological and NAT-methods used for blood screening have a limit of detection, that does not eliminate the risk of blood transfusion transmitted infections (TTIs). The residual risk of TTIs allows evaluating the effectiveness of new blood screening methods. The residual risk of TTIs was calculated with a math model “incidence rate/window period” and was 3.2 for HIV and 13.35 for hepatitis C virus (HCV) per 1 million of donations. This study was performed on a small sample (412028 donations), so the results can be extrapolated only to the Moscow region, and are not representative for other regions of Russia. The rate of residual risk of HIV and HCV is higher than in other countries because of donor infection. Obligatory NAT
testing of blood samples of all donations by highly sensitive test systems is expected to reduce the risk of TTI.

Key words: donor blood; NAT testing; residual risk of infection.

GT-1401-019
Additional criteria for evaluating the health status of donors for plateletapheresis
S.V. Varlamova, N.N. Kalinin, M.O. Egorova, I.V. Gribkova, E.S. Shurkhina, D.A. Shmarov, E.A. Vatagina, V.N. Miganov, V.M. Gorodetsky
Hematology Research Center, Moscow, Russia
Summary. Search for additional criteria for evaluating the health status of donors for plateletapheresis (PA) was carried out. The effects of PA on blood biochemistry, erythropoiesis, and rheology were carried out by Density-specific distribution of erythrocytes (DSDE) method and the clotting system status was evaluated by endogenous thrombin potential (ETP) registration. Platelet donors exhibited folic acid deficit, associated with increase of homocysteine level, associated with liability to thrombophilia. Studies of blood rheology by ETP registration showed that repeated PA procedures did not impair the barrier characteristics of erythrocyte membrane. Studies of hemostasis with ETP evaluation showed no appreciable shifts, while the detected trend to hypocoagulation (5.7% decrease) after PA was caused by the anticoagulant. Studies of platelet reduction after PA detected the reserve potentials of donors (platelet counts reduced to 184.7 ± 7.7 • 10^9/l). Conclusion. Substantial inspection of donors for repeated PA for identification latent anemias and a thrombophilia is necessary.

Key words: donors; platelet pheresis; erythropoiesis; homocysteine.

GT-1401-025
Detection of latent karyotype abnormalities in myelodysplastic syndrome
A.V. Kokhno, M.A. Pimenova, E.N. Parovichnikova, E.V. Domracheva, V.G. Savchenko
Hematology Research Center, Moscow, Russia
Summary. Clonal disorders of karyotype are detected in half of patients with the myelodysplastic syndrome (MDS. Bone marrow cell karyotype is an independent prognostic factor for risk stratification and choice of treatment strategy. Conventional cytogenetic analysis (CCA) do not always give complete information about chromosome abnormalities in MDS patients. The efficiency of fluorescent in situ hybridization (FISH) in addition to CCA, detecting latent abnormalities of karyotype in MDS, is demonstrated. A clinical case is presented: a female patient with 5q deletion, which could not be detected by CCA.

Key words: myelodysplastic syndrome; latent karyotype abnormalities; standard cytogenetic studies; fluorescent in situ hybridization (FISH) myelodysplastic syndrome with isolated del(5q).

GT-1401-029
Detection of MLL genomic breakpoints in infant acute leukemia
G.A. Tsaur1, 2, C. Meyer3, A.M. Popov1, 2, O.M.Plekhanova1, A.M.Kustanovich4, E.V.Volochnik4, T.O.Riger1, 2, A.S.Demina1, 2, A.E.Druy1, 2, 5, E.W.Fleischman4, O.I. Sokova6, Yu.V. Olshanskaya7, O.V. Streneva1, 2, E.V. Shorikov1, 2, L.I. Saveliev1, 2, 5, R.Marschalek8, S.I.Kutsev1, 2, L.I. Saveliev1, 2, 5, S.V. Tsvirenko1, 2, L.G. Fechina1, 2
1Regional Pediatric Clinical Hospital N1, Ekaterinburg, Russia; 2Institute of Medical Cell Technologies, Ekaterinburg, Russia; 3Diagnostic Center of Acute Leukemia, Institute of Pharmaceutical Biology/ZAFES, Goethe-University of Frankfurt, Frankfurt-on-Main, Germany; 4Republican Center for Pediatric Oncology, Hematology and Immunology, Minsk, Belarus; 5Ural State Medical University, Ekaterinburg, Russia; 6N.N. Blokkin Russian Cancer Research Center, Moscow, Russia; 7D. Rogachev Federal Institute of Pediatric Hematology, Oncology, and Immunology, Moscow, Russia, 8Research Centre for Medical Genetics RAMS, Moscow, Russia; 9N.I. Pirogov Russian National Medical Research University, Moscow, Russia
Summary. The mechanisms of chimeric gene formation with MLL gene involvement in infants aged under 1 year, suffering from acute leukemia, are described. Rearrangement of MLL gene in DNA was detected in the patients by long inverted polymerase chain reaction (LI-PCR). The study was carried out in 72 patients aged 1 day to 11 months, 52 of these with acute lymphoblastic leukemia (ALL), 19 with acute myeloid leukemia (AML), and 1 with acute undifferentiated leukemia. The most incident (53.8%) chimeric gene in ALL was MLL-AF4; other ones were more rare: MLL-MLLT1 (23.1%), MLL-MLLT3 (13.5%), MLL-EPS15 (7.7%), and MLL-AFF3 (1.9%). In AML the most incident (36.8%) chimeric gene was MLL-MLLT3; other chimeric genes were MLL-MLLT10 (26.3%), MLL-MLLT1 and MLL-MYO1F (10.5% each), MLL-AF4, MLL-SEPT6, and MLL-SEPT9 (5.3% each). The most frequent aberration zone in MLL gene DNA was intron 11 (48.1% cases) in ALL and intron 9 (42.1%) in AML. Patients with ALL with the rupture site in intron 11 were the youngest (p = 0.025). No relationship between the location of rupture sites and patient's gender, initial leukemia level, and partner gene type was detected. The aberration zones in MLL partner genes most often involved one or two introns, except AF4 and MLLT10 genes, in which the aberration zones were longer. The most incident
mechanism of chimeric gene formation with MLL participation was reciprocal translocation (73.6%), trans-splicing or insertions were significantly more rare (15.3 and 11.1%, respectively). Rare MLL partner genes were found by Li-PCR: AFF3, MYO1F, SEPT6, SEPT9, as well as atypical locations of ruptures in the presence of MLL-AF4: MLL gene intron 7 and AF4 gene intron 10, not detected by the standard reverse transcription PCR. Hence, we characterized in detail the structure of chimeric genes with MLL participation in a large group of infants aged under 1 year, suffering from acute leukemia.

**Key words:** acute lymphoblastic leukemia; infants; MLL rearrangements; PCR.

**GT-1401-038**

*Long remission of patient with chronic myeloid leukemia with mixed chymerism after allogenic bone marrow transplantation*


Hematology Research Center, Moscow, Russia

**Summary.** Donor lymphocyte transfusions and cytokine therapy are used for the treatment and prevention of hematological malignancy relapses after allogenic bone marrow transplantation (allo-BMT). The efficiency of these methods is explained by induction of the transplant vs. leukemia reaction. This clinical report presents an observation of a long remission of patient with chronic myeloid leukemia (CML) with mixed hemopoietic chymerism after allo-BMT, persisting during 78 months, which was confirmed by the results of molecular genetic studies by fluorescent in situ hybridization (FISH) with studies of DNA probes to X/Y chromosome centromeric sites. Donor lymphocyte transfusion followed by IL-2 treatment did not lead to complete recovery of donor hemopoietis, but constant IFN-α therapy maintained the CML remission for a long time.

**Key words:** allogenic bone marrow transplantation; mixed chymerism; donor lymphocyte transfusion; interleukin-2; interferon-α; chronic myeloid leukemia.

**GT-1401-042**

*Allogenic bone marrow transplantation without pretreatment conditioning and tolerance induction by cyclophosphamide and mesenchymal stromal cells*


Hematology Research Center, Moscow, Russia

**Summary.** Case report of a patient developed deep neutropenia and severe infectious complications after chemotherapy is presented. Lasting aplasia after a course of chemotherapy, life-threatening infectious complications did not allow pretransplantation conditioning with standard immunosuppression because of extremely high risk of a lethal outcome. Allogenic bone marrow transplantation from a related donor was carried out. Immunosuppression was carried out only with cyclophosphamide (50 mg/kg on day 3 after transplantation) and mesenchymal stromal cells. Transplant healing (WBC >1 • 10⁹/l) was diagnosed on day 19. The patient was discharged 3 months after transplantation. 12 months after bone marrow transplantation a 100% donor chimera persists. This case report is the first report about effective bone marrow transplantation without pretransplantation conditioning in a patient with acute leukemia and lasting aplasia after chemotherapy.

**Key words:** allogenic bone marrow transplantation; cyclophosphamide; mesenchymal stromal cells; tolerance, no conditioning.

**GT-1401-047**

*Intensive care for gastrointestinal hemorrhages in patients with Glanzman’s thrombasthenia*

O.K. Levchenko, E.M. Shulutko, V.M. Gorodetsky

Hematology Research Center, Moscow, Russia

**Summary.** Published data on Glanzman’s thrombasthenia are reviewed, diagnostic criteria are presented, and two clinical cases with severe gastrointestinal hemorrhages in patients with Glanzman’s thrombasthenia are described.

**Key words:** Glanzman’s thrombasthenia, platelet resistance; activated recombinant factor VII (rFVIIa); plasmapheresis.

**GT-1401-051**

*Blood service in the Netherlands*

S.R. Madzaev¹, T.V. Gaponova², E.B. Zhiburt³

¹N.I.Pirogov National Medical Surgical Center, Moscow, Russia; ²Hematology Research Center, Moscow, Russia

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**GT-1401-038**

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Hematology Research Center, Moscow, Russia

**Summary.** Donor lymphocyte transfusions and cytokine therapy are used for the treatment and prevention of hematological malignancy relapses after allogenic bone marrow transplantation (allo-BMT). The efficiency of these methods is explained by induction of the transplant vs. leukemia reaction. This clinical report presents an observation of a long remission of patient with chronic myeloid leukemia (CML) with mixed hemopoietic chymerism after allo-BMT, persisting during 78 months, which was confirmed by the results of molecular genetic studies by fluorescent in situ hybridization (FISH) with studies of DNA probes to X/Y chromosome centromeric sites. Donor lymphocyte transfusion followed by IL-2 treatment did not lead to complete recovery of donor hemopoietis, but constant IFN-α therapy maintained the CML remission for a long time.

**Key words:** allogenic bone marrow transplantation; mixed chymerism; donor lymphocyte transfusion; interleukin-2; interferon-α; chronic myeloid leukemia.
Summary. The experience gained by the blood service of the Netherlands and its structure, organization of blood donation and blood components preparation and storage, research activity, economy, and staff management are described. Recommendations are offered which would be useful for the Russian blood service.

Key words: blood; blood donor; blood harvesting; examination of donors.