MICROBIOLOGY AND IMMUNOLOGY

Transformation of Blood Groups B (III) and A (II) into AB (IV) after Bone Marrow Transplantation from HLA Identical Sibs with Groups A (II) and B (III)

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After HLA-identical transplantation of bone marrow to two patients with leukemia with erythrocytic phenotype B (III) Rh+ and A (II) Rh+ from two donor sibs with opposite blood groups A (II) Rh- and B (III) Rh+, 10-15% erythrocytes of phenotype AB were produced for several months in both recipients, which may be due to the formation of hybrid hemopoietic cells.

Key Words: *HLA-identical sibs; hybrid cells; antigenic phenotype; blood chimera*

Effective transplantation of allogenic bone marrow (BM) involves taking in of transplanted cells, as seen from the appearance of a blood chimera in the recipient, which was identified by the donor-recipient differences in human antigenic AB0 system, rhesus, etc. [1-3,7]. The outcome for blood chimeras is different. In some cases the recipient's erythrocytes are completely replaced by donor's antigenic phenotype, involving the alteration of recipient's blood group. In other cases both autologous erythrocytes and the donor phenotype erythrocytes circulate in the organism [1,5].

We observed the formation of the chimera: appearance of the donor phenotype erythrocytes in the recipient after transplantation of BM from donors differing from the recipient by AB0 A and B antigens.

MATERIALS AND METHODS

Erythrocytes of two hematological patients to whom allogenic HLA-identical BM was transplanted from donor sibs with opposite AB0 blood groups were studied.

Male patient G. (age 24 years) with acute myeloblastic leukemia, blood group B (III) Rh+, phenotype HLA — A1, 2, B 5, 15 received the bone marrow from an HLA-identical sister with an opposite blood group A (II) Rh- April 12, 1996. Before the operation the patient was treated by cyclophosphamide in a total dose of 120 mg/kg and fractionated total irradiation in a total dose of 12 Gy. For decreasing the titer of natural α-isohemagglutinins (initial titer 1:16), one plasma substitution was carried out.

Female patient I. (age 34 years) with chronic myeloleukemia, blood group A (II) Rh+, phenotype HLA — A2, 19, B13, Bw4, was given the bone marrow from an HLA-identical brother with blood group B (III) Rh+ May 14, 1998. Before the operation the patient was treated by myelosan in a total dose of 16 mg/kg and cyclophosphamide in a total dose of 120 mg/kg. Patients' and donors' lymphocytes were not reactive in the lymphocyte blastogenesis test.

Investigation of blood chimera included counting of nonagglutinated recipient's and donor's erytrocytes

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TABLE 1. Dynamic Quantitation of Blood Chimera in Patients I. and G

Test reagent	Erythrocyte %	Patient I.						Patient G.				
		time after bone marrow transplantation, days										
		0	31	35	45	50	60	0	18	55	65	72
Anti-A	Nonagglutinated	0	7.2	13.7	16.9	35.4	33.9	0	84.0	70.2	68.2	81.0
	Agglutinated	100	92.8	86.3	83.1	64.6	66.1	0	16.0	29.8	31.8	19.0
Anti-B	Nonagglutinated	0	80.0	70.0	67.4	55.9	54.0	0	10.7	17.3	21.8	12.4
	Agglutinated	0	20.0	30.0	32.0	47.8	45.8	100	89.3	82.7	78.2	87.6
	Phenotype A	100	80.0	70.0	67.0	52.2	54.0	0	10.7	17.3	21.8	12.4
	Phenotype B	0	7.2	13.7	16.9	35.4	33.9	100	84.0	70.2	68.2	81.0
	Mixed AB phenotype	0	12.8	16.3	15.7	12.4	11.9	0	5.3	12.8	10.0	6.4

after incubation with monoclonal anti-A and anti-B antibodies or hyperimmune sera of appropriate specificity. The erythrocytes agglutinated by anti-A and anti-B antibodies were counted and the percentage of erythrocytes of each phenotype in the studied suspension was calculated. The sum of erythrocytes of groups A (II) and B (III) was taken as 100%. Higher percentage of erythrocytes reacting with test reagents was regarded as an indicator of the presence of AB erythrocytes in the suspension.

RESULTS

Blood chimera was detected on day 18 after transplantation in patient G. and on day 31 in patient I. On days 18 and 55 after transplantation, the count of patient's G. erythrocytes with antigen A and group antigen B was higher than expected (Table 1). This can be explained only by the presence of erythrocytes with antigen A (donor phenotype) and with mixed phenotype AB in the blood, along with recipient's B erythrocytes.

In patient I. the count of agglutinated erythrocytes decreased after reaction with anti-A antibodies and increased after reaction with anti-B antibodies (Table 1). This could occur only in the presence of erythrocytes with both group A (recipient) and group B (donor) phenotypes, which were produced by transplanted cells, and of AB erythrocytes, but no more than 20%. In both cases AB erythrocytes circulated in recipient's blood for a long time. In patient I. they were detected for more than 2 months and in patient G. for 5 months after transplantation. Circulation of AB erythrocytes in recipients indicates that transplantation of allogenic BM results in redistribution of the genetic material between donor and recipient hemopoietic cells. We mean a specific form of transgenation (transgenism) associated with the formation of hybrid cells producing erythrocytes bearing both A and B antigens. The number of these hybrid cells is low. They produce no more than 15-20% erythrocytes with mixed phenotype. This process is stable, and AB erythrocytes circulate for several months. Hybrid cells may be responsible for rapid production of cells with the initial phenotype of the recipient in some urgent situations [6]. Some authors have observed this process under experimental conditions when leukocytes were transfused from an opposite sex donor [4].

Our results show that allogenic transplantation of a closely related bone marrow after cytostatic therapy and total irradiation creates unique conditions for the formation of hybrid hemopoietic cells capable of producing erythrocytes with a mixed antigenic phenotype.

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