FURTHER EVIDENCE FOR TRANSFORMATION OF GENETIC MARKERS IN RECIPIENTS AFTER BMT

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INTRODUCTION

The HLA compatibility has been somewhat overemphasized, even to the point of ignoring other important marker genes, including the ABO system, an essential consideration for blood transfusion. A study of the genetic makers of the bone marrow recipient after bone marrow transplantation (BMT) reveals an alteration of the genetic makers to the donor type.

Blume et al. have discussed the transformation in the MN, Rh, Kidd, and gammagroblin marker (Gm) systems as representative of the genetic marker transformation from the recipient to the donor type. Dijk et al., Wolpl et al., and Ikemoto et al. reported the transformation of genetic markers in red cells, serum protein, and red cell enzymes accompanying BMT. Mori et al. studied the red cell antigens of a recipient with an ABO incompatibility. Despite being unable to detect a transferase, these authors found ABO antigens of the donor type. The antibodies to the donor type also declined rapidly. Yam et al. concluded that deoxyribonucleic acid (DNA) restriction fragment length polymorphism (RFLP) are powerful and practical genetic markers in bone marrow transplantation studies and that further studies of mixes hematopoiëtec chimerism are warranted. Kitano et al. reported observations of the behavior of red cell membrane antigens of donors and recipients as an index for early recognition of transplanted bone marrow engraftment.

The following report describes that transformation of genetic markers on 17 pairs of donor and recipient with bone marrow transplantation.

MATERIAL AND METHODS

The present examine are on 17 pairs samples were obtained from the blood transfusion service of the Jichi Medical School Hospital and Tottori Central Hospital. A broad range of gene markers at 41 loci, including red blood cell markers (ABO, MNSs, Lewis, P, Rh, Duffy, Kidd, Lutheran, Kell-Cellano, Diego, and Xg), HLA systems (HLA-A, -B, -C, -DR, and -DQ), serum protein markers (Gc, Tf, Hp, Gm, Km, PLG, Bf, C2, C6, C7, C8-1, and FXIII-B), red cell enzyme markers [esterase D (EsD), acid phosphatase (ACP), glyoxalase (GLO), phosphogluconate dehydrogenase (6PGD), and phosphoglucomutase (PGM)], and salivary markers (Se, Pa, Pb, Pr, PmF, Db, PIF, Amy1) were evaluated before and after BMT over about 2 months. Blood grouping and HLA typing were used. The serum protein and red cell enzyme types were analyzed according to experimental methods described by Tamaki et al., salivary typing was determined by methods described Ikemoto et al., and flow cytometry techniques were carried out using methods described by Hashimoto et al.

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RESULTS AND DISCUSSION

Results of the transformation in genetic markers before and after BMT in recipients with different phenotypes from the donor follows. The red cell antigens transformed as follows; type O to type A, type O to type B, type AB to type A and type A to type O (the pre-BMT recipient type to the post-BMT donor type), MN/ss to M/ss, MN/ss to N/ss, NSs to Nss, CcDEe to CCDee, CcDee to CCDee, CCDee to CcDEe, CcDEe to ccDEE, P1(+) to P1(-), P1(-) to P1(+), Jk(a+b+) to Jk(a+b-), Jk(a+b+) to Jk(a-b+), Jk(a-b+) to Jk(a+b+), Jk(a+b-) to Jk(a+b+), Fy(a+b+) to Fy(a+b-), Xg(a+) to Xg(a-), Xg(a-) to Xg(a+). The red cell enzyme types transformed as follows; EsD2-1 to EsD1-1, EsD1-2 to EsD1-1, PGM2-1 to PGM1-1, PGM1(1+1-) to PGM 2-1(2+1+), PGM1-1(2-1+) to PGM1-1(1-1-), ACP A to ACP AB. Some genetic markers which did not transform when the donor phenotypes differed from the recipient phenotypes include the Lewis, Hp, Tf, FXIII-B, Se, Pa, Pr, Db, and PmF markers. Other genetic markers, including the Lutheran, Kell-Cellano, Xg, HLA, Gc, Gm, Km, Bf, PLG, GLO, 6PGD, Pb, PIF, Amy_1, and various complementing systems could not be evaluated because the donor and recipient phenotypes were identical.

Many transformations in genetic markers which accompany BMT illustrate the relationship between gene products and the bone marrow. Various antigens from red cell membrane substances of the glycolipid and glycophorin systems are produced primarily in the bone marrow. However, production of the Lewis antigen, blood-group-related substances secreted in saliva, and salivary polymorphic protein appear to take place in the bone marrow.

Changes in the red blood cell agglutinin appear to be related to antibody production under gene control and are presumably produced by the transformed Gm system (immunoglobulin allotype) rather then being the result of serum antibody absorption by antigens, which leaves only nonself antibodies. The transformation of the red cell enzyme EsD, PGM, ACP, PGD markers provides a useful clue for therapy for enzyme defects. RFLP analysis using DPβ, DQβ, and DRβ cDNA as a probe was carried out in a case which showed the high MLC activity although Class I and Class II on HLA typing were coincident each other. The recipient showed some specific bands which were not observed in the donor and her patients, that suggested the relationship between the specific bands and high MLC activity.

BMT between family members may lead to transformation in the gene markers, but within a pattern compatible with family inheritance patterns, and no genetic paradox will be found in later surveys of familial genetic relationships. However, in a personal identification system in forensic medicine using genetic markers as an index, the appearance of a phenotype incompatible with a blood relationship is possible after BMT from a donor who is not a blood relative. This result is similar to the inheritance pattern observed after artificial insemination by a donor, a more complete out-of-family cross.

As development of immune suppressants such as cyclosporins improves, BMT will be performed more frequently based upon HLA histocompatibility alone. Care will be required to track the transformation in personal identification and paternity testing based on genetic makers.

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