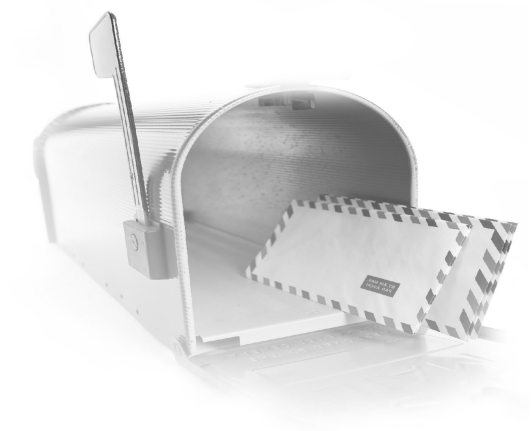

DOI: 10.5045/kjh.2011.46.2.143
The Korean Journal of Hematology
Volume 46 · Number 2 · June 2011

Letter to the Editor

What should we consider in mixed chimerism after hematopoietic stem cell transplantation?

TO THE EDITOR: Mixed chimerism (MC) was initially thought to indicate impending relapse; however, it has become clear that it is an important parameter for estimating immunologic balance after hematopoietic stem cell transplantation (HSCT). Moreover, the emergence of more tailored HSCT procedures, including reduced-intensity stem cell transplantation (RIST), depletion of the donor's T cells from bone marrow graft, and donor lymphocyte infusion (DLI), makes it even more important to estimate the exact chimeric status after HSCT.

Recently, Goh et al. reported MC results in 24 myeloablative HSCT patients. MC in nucleated cells (NCs) was significantly correlated with relapse, and MC in NCs, T cells, and NK cells was correlated with mortality. Furthermore, MC in all cell types was uncorrelated with the incidence of acute and chronic graft-versus-host disease (GVHD). These data were analyzed in limited cases, but individual diseases and HSCT strategy were not considered [1].

Myeloablative HSCT without T cell depletion often results in GVHD but is associated with less frequent relapse. T cells in the graft lead to full donor complete chimerism (CC), although early CC indicates GVHD. However, T cell-depleted (TCD) myeloablative HSCT is commonly found to give rise to MC, and is therefore used to avoid GVHD. In the case of RICT, all cases typically experience MC. Therefore, MC has to be precisely evaluated. Low donor T cell and NK cell chimerism levels around the second week after HSCT are associated with high probabilities of graft rejection, whereas early establishment of donor NK cell chimerism is associated with better progression-free survival [2]. In contrast to NK cell chimerism, early establishment of donor T cell chimerism is associated with the development of acute GVHD [3]. In recent interesting reports on lineage-specific chimerism, monitoring of leukemia lineage-specific chimerism has been shown to be important for DLI response in the case of relapse after HSCT [4]. Further, a low donor T cell chimerism of $<60\%$ at day 30 may be associated with a poor prognosis in HSCT when using a busulfan-containing reduced-intensity conditioning regimen [5]. Although MC is an important indicator of disease relapse, graft rejection, or GVHD post HSCT, it should be taken into consideration that the recipient cells in MC could be normal hematopoietic cells or leukemic cells. Therefore, it is important to identify those patients who develop an increasing or progressive MC of recipient cells by monitoring serial chimerism levels. Additionally, with respect to accurate analysis of chimerism, it should be recognized that variation in the degree of MC is influenced by a number of factors, including the sensitivity of the method used, the timing of the assay, the disease indication for HSCT, the stage of disease at the time of HSCT, and the choice of conditioning regimen.

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