Monosomy 7 in donor cell-derived leukemia after bone marrow transplantation for severe aplastic anemia: Report of a new case and review of the literature

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Abstract

Monosomy 7 arises as a recurrent chromosome aberration in donor cell leukemia after hematopoietic stem cell transplantation. We report a new case of donor cell leukemia with monosomy 7 following HLA-identical allogenic bone marrow transplantation for severe aplastic anemia (SAA). The male patient received a bone marrow graft from his sister, and monosomy 7 was detected only in the XX donor cells, 34 months after transplantation. The patient’s bone marrow microenvironment may have played a role in the leukemic transformation of the donor hematopoietic cells.

Key words: monosomy 7, donor cell leukemia, bone marrow transplantation, severe aplastic anemia.

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2010, the patient underwent a second transplantation with G-CSF-mobilized peripheral blood cells from the same donor. The engraftment occurred on day 10. However, 15 days after the transplantation, the patient died due to refractory septic shock.

Literature reports on chromosome abnormalities resulting in hematological malignancies in donor cells after BMT are rare. Only a few cases of DCL have been reported after BMT for SAA. In the current case, we detected monosomy 7 in donor cells at day 1029 after BMT. Immuno-phenotype and morphological analysis confirmed the acute myeloid leukemia M4/M5 diagnosis at that time. Monosomy 7 in DCL after BMT for SAA was previously described by Lang et al. (2004). In their case, the donor cells were identified by microsatellite marker analysis, since patient and donor were both females. In our case, a male patient received a graft from his sister, and monosomy 7 was detected only in the XX donor cells. Monosomy 7 was also reported in one case of transient donor cell-derived myelodysplastic syndrome (Sevilla et al., 2006) and in one case of donor cell-derived acute monoblastic leukemia (Hamaki et al., 2008), after unrelated cord blood transplantation. In a recent study, Wang et al. (2011) described 10 cases of DCL, of which six had monosomy 7/del(7q). Thus, monosomy 7 arises as a recurrent chromosome aberration in donor cell leukemia after hematopoietic stem cell transplantation. In general, monosomy 7 represents one of the most common chromosomal abnormalities in myelodysplastic syndromes, being present in approximately 50% of therapy-related cases (Flactif et al., 1994). It probably arises at the level of myeloid progenitor cells and is usually associated with a very poor prognosis ( Gerritsen et al., 1992). To investigate the possibility of occult leukemia cells in the donor, we performed conventional cytogenetic and FISH analysis, but no monosomy 7 was detected in the donor bone marrow sample. The mechanisms underlying the development of chromosomal abnormalities in donor cells are not fully understood so far. The microenvironment of our patient’s bone marrow may have played a role in the development of monosomy 7 in the normal donor cells. This possibility was also suggested by Lang et al. (2004). We further believe that the impact of post-BMT immunosuppression, G-CSF utilization and local viral infection cannot be precisely assessed. A significantly increased incidence of MDS/AML was reported by the European Group for Blood and Marrow Transplantation in SAA patients receiving immunosuppressive therapy and G-CSF compared to those not receiving G-CSF (Socie et al., 2007). Some authors hypothesized that treatment with G-CSF might have played a role in the transformation of SAA into AML with monosomy 7 (Hashino et al., 1996). Another Japanese study demonstrated a substantial risk in children with SAA receiving G-CSF, and a high frequency of deletion of the long arm of chromosome 7 and monosomy 7, was identified by FISH (Kojima et al., 2002). Notwithstanding, in a more recent study, Avalos et al. (2011) argued that the available clinical data do not provide evidence that G-CSF can transform donor normal hematopoietic stem cells in the absence of predisposing factors. The host microenvironment could play a role in the leukemic transformation. Our patient received G-CSF support 32 months after BMT, and monosomy 7 was detected two months after starting its use.

Our case highlights the fact that donor cell leukemia is an important entity in understanding the leukemogeneic process.

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