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The Relationship Between NK Cell Function and Non-KIR Receptor Levels with GVHD in Patients Undergoing Allogeneic Stem Cell Transplantation

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Abstract

Objective: Hematopoietic stem cell transplantation (HSCT) is a curative treatment for hematological malignancies; however, graft-versus-host disease (GVHD) remains a major complication. While donor T cells are central to GVHD pathogenesis, natural killer (NK) cells, via activating and inhibitory receptors, may also influence disease course. This study evaluated post-transplant changes in non-KIR receptor expression on NK cells and their association with GVHD.

Materials and Methods: Twenty patients (M:3, F:13) who underwent allogeneic HSCT at Hacettepe University (2021–2024) were included. The mean age was 50, with a median follow-up of 26.1 months. Eleven patients received fully matched and nine haploidentical transplants; GVHD developed in 10 patients. Peripheral blood samples were collected at day 0 and on days 30, 100, and 180. Patients were followed for at least 6 months. Mononuclear cells were isolated, and non-KIR receptor expression in NK subsets was analyzed by flow cytometry. NK cells from days 0 and 30 were co-cultured with the K562 cell line to assess CD107a, perforin, and granzyme expression.

Results: Eight AML, six ALL, four MDS, and two lymphoma patients were included. NKG2A and NKG2D decreased significantly (p=0.0001; p=0.0049). NKG2C declined until day 30, then increased. NKp30, NKp44, and NKp46 decreased. ILT-2 and ILT-4 also showed significant reductions (p=0.004; p=0.0001). Cytotoxicity analysis showed increased granzyme and decreased perforin and CD107a, with only perforin reduction significant (p=0.025). Increased NKp46 and NKp30 expression was associated with reduced GVHD risk (AUC: 0.819; 95% CI: 0.576–1.000).

Conclusion: Allogeneic HSCT is associated with reduced NK cell non-KIR receptor and perforin expression. Although no significant relationship was found between GVHD development and receptor profile, changes in expression levels suggest that NK cells are affected by chronic inflammation. Higher NKp46 and NKp30 expression may indicate reduced GVHD risk, supporting their potential as biomarkers and the need for larger studies.

Keywords: Graft-versus-host disease (GVHD), Hematopoietic Stem Cell Transplantation (HSCT), non-KIR receptor, NK cell

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