Chimerism analysis and graft rejection after allogeneic hematopoietic cell transplantation with nonmyeloablative conditioning

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ABSTRACT

This PhD thesis is based on work performed in The Allogeneic Hematopoietic Cell Transplantation Laboratory, Department of Hematology, and The Tissue Typing Laboratory, Department of Immunology, Rigshospitalet.

Hematopoietic cell transplantation (HCT) is a potential curative treatment modality for several hematological disorders where allogeneic hematopoietic cells are infused into a recipient prepared with a conditioning regimen. This thesis will focus on the novel treatment modality, nonmyeloablative-conditioning HCT (NMC-HCT), where reduced conditioning consisting of low-dose radio-chemotherapy results in less toxicity but an increased risk of graft rejection in comparison to conventional myeloablative conditioning HCT. The curative principle of NMC-HCT is the graft-versus-tumor effect. Measurement of coexisting recipient and donor cells by chimerism analysis is an important tool in the follow-up of these patients.

The aims of the thesis were to implement and evaluate a high-resolution real time quantitative polymerase chain reaction (RQ-PCR) method for chimerism analysis, and to analyze graft rejection episodes after NMC-HCT in a cohort of Danish patients treated for hematological malignancies.

Implementation of RQ-PCR based chimerism analysis with an improved detection limit of 0.1% cells was successful and results were comparable with results by standardized chimerism analysis based on short tandem repeats. Low donor T cell chimerism was confirmed as a risk factor for graft rejection and storage of donor cells at room temperature was identified as a new risk factor. Storage of donor cells is now being performed at 5°C. Retransplantation with NMC-HCT with increased total body irradiation was well-tolerated but with decreased overall- and progression-free survival as compared to patients with successful primary engraftment. There was no effect of pentostatin and donor lymphocyte infusion in patients with imminent graft rejection. Retransplantation as soon as possible seems to be the treatment of choice of graft rejection after NMC-HCT.