Göteborg, 2016

Graft-versus-Host Disease

Eosinophils, Chimerism and Clinical Features in Patients Undergoing

Allogeneic Hematopoietic Stem Cell or Multivisceral Transplantation

Akademisk avhandling som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Mikrobiologens föreläsningssal, våning 3, Guldhedsgatan 10A, Göteborg

Fredagen den 3 juni, klockan 13.00

av **Julia Cromvik**

Fakultetsopponent**: Jonas Mattson**, Professor och överläkare, Institutionen för onkologi-patologi, Karolinska institutet, Stockholm, Sverige

Avhandlingen baseras på följande delarbeten:

I. **Eosinophils from hematopoietic stem cell recipients suppress allogeneic T cell proliferation.** Andersson J*, Cromvik J*, Ingelsten M, Lingblom C, Andersson K, Johansson JE, Wennerås C. *shared first authorship *Biol Blood Marrow Transplant. 2014 Dec;20(12):1891-8.*

II. **Eosinophils in the blood of hematopoietic stem cell transplanted patients are activated and have different molecular marker profiles in acute and chronic graft-versus-host disease.** Cromvik J, Johnsson M, Vaht K, Johansson JE, Wennerås C. *Immun Inflamm Dis. 2014;2(2):99-113*

III. **Graft-versus-host disease after intestinal or multivisceral transplantation: A Scandinavian single-center experience.** Cromvik J*, Varkey J*, Herlenius G, Johansson JE, Wennerås C. *shared first authorship *Transplant Proc. 2016;48(1):185-90*

IV. **T cell chimerism after allogeneic hematopoietic stem cell transplantation: impact on graft-versus-host disease and tapering of immunosuppression**. Cromvik J, Wennerås C, Johansson JE. *In manuscript.*

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Eosinophils, Chimerism and Clinical Features in Patients Undergoing Allogeneic Hematopoietic Stem Cell or Multivisceral Transplantation

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Abstract

Graft-versus-host disease (GVHD) is a potentially severe complication that may develop after allogeneic hematopoietic stem cell transplantation (HSCT). It can also occur after transplantation with isolated intestinal grafts or after multivisceral transplantation (MVTX). GVHD is difficult to diagnose. The aims of this thesis were to 1) investigate the potential of the eosinophilic granulocyte as an immunoregulatory cell and biomarker in GVHD, 2) determine the incidence, risk factors and clinical features of GVHD in MVTX, 3) evaluate the utility of lymphocyte chimerism analyses to predict overall survival and risk of GVHD after HSCT. In paper I, we used an *in vitro* model of GVHD to see if eosinophils could inhibit allogeneic T cell proliferation. In paper II, flow cytometry was used to examine patterns of surface receptors on blood eosinophils from transplanted patients +/- GVHD and +/- systemic glucocorticoids. Paper III is a retrospective epidemiological study of patients with acute GVHD after MVTX. In paper IV, the predictive capacity of chimerism analyses and impact of chimerism status on the duration of immunosuppression was evaluated. It was found that eosinophils can inhibit allogeneic T cell proliferation *in vitro* and that eosinophils in patients with acute and chronic GVHD have an activated phenotype, which is altered by systemic steroid therapy. Our conclusion is that the blood eosinophils are activated and have immunoregulatory capacity in GVHD, and might serve as a biomarker of GVHD. In MVTX, it was seen that a tumor diagnosis or neoadjuvant chemotherapy were possible risk factors for GVHD. Finally, chimerism analyses could not predict relapse, survival or GVHD after HSCT. However, patients with mixed chimerism or chronic GVHD had longer treatment time with cyclosporine A.

Keywords: graft-versus-host disease, eosinophilic granulocyte, intestinal transplantation, multivisceral transplantation, chimerism analysis

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