Graft-versus-Host Disease

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

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Fredagen den 3 juni, klockan 13.00

av Julia Cromvik

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Avhandlingen baseras på följande delarbeten:


Graft-versus-Host Disease

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