

Herpesvirus infections in transplant recipients

Akademisk avhandling

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Avhandlingen baseras på följande delarbeten:

- I. Lindahl J, Woxenius S, Brune M, Andersson R. Cytomegalovirus DNAemia and treatment following allogeneic stem cell transplantation with focus on long-term outcome. *Scandinavian Journal of Infectious Diseases* 2010; 42(9): 691-698.
- II. Lindahl J, Woxenius S, Brune M, Andersson, R. Human herpesvirus type 6 DNAemia and infection following allogeneic stem cell transplantation with focus on long-term outcome. *Scandinavian Journal of Infectious Diseases* 2013, 45(7): 557-61.
- III. Lindahl J, Friman V, Westphal Ladfors S, Hansson S, Andersson R, Jertborn M, Woxenius S. Long-term study showed that vaccination protected paediatric renal transplant recipients from life-threatening varicella zoster virus. *Acta Paediatrica* 2018, Dec;107(12):2185-2192. Doi: 10/1111/apa.14375. Epub 2018 May 25.
- IV. *Westphal Ladfors S, *Lindahl J, Hansson S, Brandström P, Andersson R, Jertborn M, Lindh M, Woxenius S, Friman V. Long lasting chronic high load carriage of Epstein-Barr virus is more common in young pediatric renal transplant recipients. Submitted.
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**SAHLGRENKA AKADEMIN
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Abstract

Herpesvirus infections are common and can cause serious and life-threatening conditions in transplanted individuals. In this thesis, consisting of 4 papers (**I-IV**), we investigated primary infection and reactivation of Cytomegalovirus (CMV), Human Herpesvirus type 6 (HHV-6), Varicella Zoster Virus (VZV) and Epstein-Barr Virus (EBV) in transplant patients. The overall aim was to expand our knowledge on the incidence, prophylaxis, management and long-term effects of herpesvirus infections after transplantation. The studies were all retrospective. Results from serum and whole blood analyses by quantitative polymerase chain reaction (PCR) for CMV and HHV-6 in a cohort of 97 adult allo-SCT patients (papers **I** and **II**) and CMV and EBV in 58 renal transplanted children (paper **IV**) were compiled. VZV antibodies were analyzed using ELISA assays and immunofluorescence from blood samples of 85 renal transplanted children (paper **III**).

In paper **I**, patients with CMV DNAemia had improved survival compared to CMV negative patients. There was an increased risk of CMV DNAemia with a seronegative donor to a seropositive recipient. CMV disease with debut more than 110 days after transplantation was related to steroid treatment for Graft versus Host Disease (GVHD). The morbidity associated with HHV-6 DNAemia following allo-SCT was in most cases mild. The overall one-year survival among the patients with HHV-6 DNAemia was not significantly different from the HHV-6 negative patients (paper **II**). At renal transplantation, protective VZV antibody-levels were less frequent and of lower magnitude in varicella-vaccinated children than in those with previous varicella. Vaccinated patients then lost their seropositivity to a greater extent than previously infected individuals. Herpes zoster was only seen in previously infected children (paper **III**). Long-lasting chronic high EBV load carriage (CHL) was seen in 24% of the renal transplant patients despite reduced immunosuppression. CHL carriage mainly developed in younger children. None developed post-transplant lymphoproliferative disorder (PTLD) during the median follow up of almost 8 years (paper **IV**). To conclude, the incidence of herpesvirus DNAemia is high after transplantation. VZV-vaccination and antiviral prophylaxis against CMV and VZV as well as pre-emptive CMV treatment and surveillance of EBV DNA are life-saving and reduces the long-term effects of herpesvirus infections.

Keywords: Allogeneic stem cell transplantation, Cytomegalovirus, Epstein-Barr virus, Human Herpesvirus type 6, Renal transplantation, Varicella zoster virus.