Neurological Complications after Stem Cell Transplantation in Children

AKADEMISK AVHANDLING
som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i R 64, Karolinska Universitetssjukhuset, Huddinge

Fredagen den 17 juni 2011, kl 09.30

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Stockholm 2011
ABSTRACT

Allogeneic haematopoietic stem cell transplantation (HSCT) is a well established method used in the treatment of a number of benign and malignant blood diseases, inborn errors of metabolism and severe congenital immunodeficiency syndromes. Around 60 children are transplanted in Sweden every year. Every HSCT carries a risk of different types of complications for the patient. As the success rate and survival after HSCT increases, the prevention of neurological complications and their long-term sequelae has particular significance in the paediatric patient group.

Paper I describes the acute neurological complications after HSCT in 144 paediatric patients transplanted between 1995 and 2002 at the Karolinska University Hospital-Huddinge. The group of 19 patients (13%) who suffered from neurological complications within three months after HSCT had an elevated risk of death within the first year after HSCT. An increasing number of positive herpesvirus serologies and CMV sero-positivity before HSCT as well as electrolyte-disturbances, high blood pressure and elevated bilirubin during the first three months after HSCT increased the risk of neurological complications. The most common complication was seizures and the most frequent causes to these complications were infection and encephalopathy. In several patients the exact aetiology of the complication could not be determined. Intrathecal chemotherapy is given as prophylaxis to high risk patients after HSCT to lower the risk of CNS relapse of malignant disease. The treatment increases the risk for acute and late onset neurological complications. However the need for this treatment is questioned as advances in primary oncologic treatment before HSCT has substantially decreased the risk for CNS relapse. In Paper II and III we retrospectively compared patients who received intrathecal therapy after HSCT to a group who was not given this treatment. The primary aim was to examine if there was a reduction in CNS relapses in the group given intrathecal chemoprophylaxis. In Paper II 120 patients transplanted 1992 to 2005 were included in the study. In Paper III 397 patients transplanted 1992 to 2006 were studied. Neither of the studies could identify a difference in the prevalence of CNS relapses, other types of relapses, mortality or a difference in the prevalence of neurological complications between the two groups. The study results have resulted in a revision of the clinical protocol for intrathecal chemoprophylaxis after HSCT in many centres.

In Paper IV we addressed the fact that infections are a common cause of neurological complications after HSCT and that the exact cause of many complications are unknown. We aimed to study the prevalence and the clinical symptoms of CNS infections by human polyomavirus (HPyV) within a year after HSCT. We analysed retrospectively the CSF of 20 HSCT patients with neurological complications for five different HPyV; JC-, BK-, KI-, WU-, and MCPyV. JC- and BK-PyV are known neurotropic viruses discovered in the 1970’s. KI-, WU- and MCPyV are more recently discovered viruses where the neurotropic ability is not yet known. The PCR analyses of the 20 CSF-samples were negative for all the five viruses. More studies needs to be done to determine the significance of the new HPyV in complications after HSCT.

Conclusion: our studies have contributed with a small piece of knowledge in the struggle to prevent neurological complications after HSCT. Further research is though needed to identify additional risk factors and further improve treatment so that less neurotoxic treatments are needed.