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POSTER ABSTRACTS

721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Analysis of Laboratory Parameters before the Occurrence of Hepatic Sinusoidal Obstruction Syndrome in Pediatric Patients after Hematopoietic Stem Cell Transplantation

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Introduction: Hepatic sinusoidal obstruction syndrome (SOS), also known as veno-occlusive disease of the liver, is a serious complication following hematopoietic stem cell transplantation (HSCT). Early diagnosis and treatment with defibrotide can improve patient outcome. The pathogenesis is not fully understood, but it is obvious that some laboratory parameters are already changed before the onset of SOS. The aim of our retrospective study was to detect laboratory parameters following HSCT that can predict the occurrence of SOS.

Methods: We analyzed 182 children with a median age of 7.2 years who underwent allogeneic or autologous HSCT for the first time and without defibrotide prophylaxis. Our study population consisted of 126 patients who received allogeneic HSCT (69.2%) and 56 patients who underwent autologous HSCT (30.8%). The stem cell sources were peripheral blood stem cells (50.5%) or bone marrow (49.5%) and the most frequent underlying diseases were solid tumors (34.1%), genetic diseases (19.2%), acute lymphoblastic leukemia (18.1%), and acute myeloid leukemia (13.7%). The diagnosis of SOS was based on the pediatric criteria of European Society for Blood and Marrow Transplantation. We investigated the following 15 laboratory parameters after HSCT before the onset of SOS: international normalized ratio (INR), activated partial thromboplastin time (aPTT), reptilase time, factor VIII, factor XIII, von Willebrand factor (vWF), von Willebrand factor activity (vWF activity), fibrinogen, antithrombin III, protein C, protein S, D-dimer, alanine aminotransferase (ALT), bilirubin, and ferritin. The last laboratory values within one week before the onset of SOS were analyzed in the SOS patient group. In the non-SOS patient group, we investigated the parameters for four weeks after transplantation and calculated the median. We selected cut-off values for the continuous parameters based on receiver operating characteristic curves analyses and existing reference values. We performed Mann-Whitney *U* test, univariate and multivariate analyses to find significant ($P < .05$) associations between the values of laboratory parameters and the occurrence of SOS. The probability of developing SOS was calculated using the significant independent variables.

Results: The overall incidence of SOS was 14.8% at a median time of 13 days after HSCT. SOS developed in 24 of 126 allogeneic (19.1%) and in 3 of 56 autologous (5.4%) HSCT patients. Only 3 out of 27 patients (11.1%) who suffered from very severe SOS died within 100 days after HSCT. In the univariate analysis, we found significant associations between the onset of SOS and the following parameters: INR $\geq$ 1.3, aPTT $\geq$ 40 sec, reptilase time $\geq$ 18.3 sec, factor VIII $\leq$ 80%, antithrombin III $\leq$ 75%, protein C $\leq$ 48%, D-dimer $\geq$ 315 µg/L, bilirubin $\geq$ 9 µmol/L, and ferritin $\geq$ 3100 µg/L. In multivariate analysis, we confirmed INR $\geq$ 1.3 [odds ratio (OR) = 8.104, $P = .006$], aPTT $\geq$ 40 sec (OR = 10.174, $P = .001$), protein C $\leq$ 48% (OR = 5.215, $P = .014$), and ferritin $\geq$ 3100 µg/L (OR = 7.472, $P = .004$) as independent risk factors after HSCT before SOS. If three of the four significant cut-off values were present, the probability of developing SOS was more than 70%. The probability of SOS was 96%, if all four laboratory parameters were changed according to the cut-off values. The values of factor XIII, vWF, vWF activity, protein S, fibrinogen, and ALT were not relevant for the occurrence of SOS.

Conclusions: In summary, the laboratory parameters INR, aPTT, protein C, and ferritin were very useful to predict the occurrence of SOS. These four parameters can enable earlier diagnosis and treatment leading to an improved outcome. In addition, this is the first report on a significant association between SOS and high values of INR and aPTT after HSCT before SOS.

Disclosures No relevant conflicts of interest to declare.

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