CHIMERISM MONITORING OF POSTALLOGENEIC HSCT PATIENTS: EXPERIENCE OF TIMIŞOARA

S. Arghirescu[1], C. Jinca[1], A. Bălan[1], A. Oprisoni[1], O. Ciocarlie[1], A. Isac[1], V. Ordodi[1], M. Baica[2], E. Gai[3], A. Pascalau[2], M. Şerban[1]
1 - "Victor Babes" University of Medicine and Pharmacy Timişoara
2 – "Louis Turcanu" Emergency Hospital for Children Timişoara
3 – Emergency County Hospital Timişoara

Background. The precise assessing and monitoring of allogeneic hematopoietic stem cell transplantation (allo-HSCT) chimerism is of utmost interest. Complete donor chimerism, mixed or split chimerism and their dynamics are suggestive prognostic markers with potential predictive value for the outcome of the transplanted patients.

Material and methods. Seventy investigations of hematopoietic chimerism have been performed in 28 allo- transplanted and followed-up patients (matched sibling donor-25, matched unrelated donor-3) in Timisoara, both children (n=17) and adults (n=11), with the following diseases: malignant hemopathies – 20 consisting of acute leukemia - 19 (lymphoblastic-10 and myeloblastic – 9), non-Hodgkin lymphoma-1 and non-malignant hemopathies-8 represented by aplastic anaemia - 4, chronic granulomatous disease – 2 and beta thalassemia-2. Eighty sixth percent of the patients received a myeloablative conditiniong regimen while in 14% the conditiong regimen applied was a reduced intensity one. Chimerism was monitored not on a regular basis; the first determination was performed at about 45 days post-transplant followed by retesting with a periodicity of 45-60 days. In all patients chimerism was assessed in peripheral blood, either unfractioned (n=29) or cell –sorted (n=41). PCR based method – polymorphism analysis of short tandem repeats (STRs) has been used in 44 cases while cytogenetic FISH analysis in 26. Type of chimerism and its behaviour have been focused in correlation with the age of patients, their patology, type of conditioning regimen, frequency of GvHD, graft failure or rejection and outcome.

Results. At first chimerism determination we have assessed complete donor chimerism in 5 patients and mixed chimerism in 23 cases. The dynamics has been stable in 8 cases and transient in other 15 with conversion to complete donor chimerism (n=7) or progressive mixed chimerism (n=8). Acute GvHD was registered in 8 patients (28,57%) with either complete donor chimerism (n=4) or mixed chimerism (n=4). Seven patients (25%) relapsed after allo-HSCT, 4 of them with progressive mixed chimerism at the last analysis. Graft rejection occurred in one patient (3,57%) with serial chimerism detections revealing a decreasing pattern of all donor-derived cell lineages. Three years overall survival of the entire cohort was 64,28% with the following distribution: non-malignant hemopathies - 62,5% and malignant hemopathies – 65%. In patients who have achieved complete donor chimerism, 1y OS was significantly higher than in cases with stable or progressive mixed chimerism (83,33% vs 75%), while analysis of 3 yOS showed no statistically significant difference between the two groups (66.66% vs 62,5%).

Conclusions. The small number of investigated patients, the diversity of their pathological background and of their conditioning regimen make difficult to draw some reliable conclusions. The proportion of acute GvHD was similar in both groups with or without complete donor chimerism. On the other way, relapse after allo-HSCT was strongly connected with the pretransplant disease status of the patients (multiple relapses or partial remissions). Therefore, analysis of chimerism in the posttransplant period remains an indispensable diagnostic tool for the control of the quality of engrafment, for the detection of the graft rejection risk and for a timely alert for an imminent disease relapse.