Dynamics of Bone Marrow Cellularity in Paediatric Acute Lymphoblastic Leukemia: Automatic Approach

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Introduction. Bone marrow cellularity (BMC) is related to hemopoiesis activation, suppression and infiltration. It is reported by histology or cytology, evaluation is subjective and prone to sampling and technical artefacts. Using automated leukocyte count is a logical solution, but scarce data on the results have been published. Acute lymphoblastic leukemia (ALL) is a primary BM tumour. It is a good model for BMC studies, since BM is sampled during treatment at defined time points (at diagnosis, on the 15th, 33rd, 78th day of therapy and before reinduction).

Aim, Material and Methods. The aim of the study was to retrospectively evaluate and to follow-up BMC of paediatric ALL patients, using automated hematology counts. BM was routinely analysed by Advia 2120i (2011–October 2014) and Sysmex XN 1000 at the Children's Clinical University Hospital. 216 analyses were available (40 at diagnosis, 47 at day 15, 47 at day 33, 43 at day 78 and 39 before reinduction). BMC of reactive BM (100 tests, N1 group) and samples from N1 group with BMC cytologically evaluated as normal (37 tests, N2 group) were used for reference. MS Excel and IBM SPSS v.21. were used for statistical analysis.

Results. 48 primary ALL cases diagnosed in 2011–2015 and treated according to BFM protocol at the Children's Clinical University Hospital Hematooncology Department were included in the study. Median BMC at diagnosis was 79.6 E9/L, at day 15 – 10.5 E9/L, at day 33 – 11.9 E9/L, at day 78 – 53.7 E9/L and before reinduction – 55.8 E9/L. Median BMC in the N1 reference group was 67.6 E9/L and in N2 group – 54.8 E9/L. Difference between BMC at diagnosis and N1 was non-significant by Mann–Whitney U test; nevertheless, it was significantly higher than N2 ($p = 0.030$). BMC at day 15 and at day 30 was highly significantly lower than both N1 and N2 ($p < 0.001$ in all tests). BMC at day 78 and before reinduction was not significantly different from both N1 and N2. BMC at therapy day 15 was highly significantly lower than at diagnosis ($p < 0.001$) by the related samples Wilcoxon test, at day 33 significantly higher than at day 15 ($p = 0.025$), at day 78 highly significantly higher than at day 33 ($p < 0.001$), and there was no difference between day 78 and before reinduction. BMC at diagnosis did not correlate with further BMC levels during therapy by Spearman test, the only significant correlation found was between day 15 and day 33 ($p = 0.011$).

Conclusions. BMC of ALL patients during treatment follow the general cytological experience: sharp decrease during the initial treatment followed by mild regeneration at day 33, then return to normal levels. The study provided an objective basis for the trend and demonstrated the utility of the automatic hematological analysis for evaluating BMC. Use of reactive BM for reference seems to be a workable approach. The study supports the notion of only minimal difference in BMC between reactive BM and initial ALL infiltration in children. A larger patient cohort would be necessary to define reference values of BMC for standard time points, the study prolongation to BM status during maintenance therapy and at the end of treatment may be of interest. Particular attention should be paid to technical artefacts like hemodilution and clotting that significantly influence leukocyte counts.