Second Malignant Neoplasms after Treatment of Childhood Cancer in 2000–2016 in Latvia

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Introduction. Second malignant neoplasm (SMN) is one of the major late effects of antitumor therapy. The number of long-term cancer survivors is growing worldwide as treatment options for primary tumors improve. The problem has not been studied in Latvia neither in total population, nor in children. Department of Children Oncology and Haematology is the only Latvian Institution where all 0–18 year-old paediatric patients with malignant diseases are registered, treated and followed up. Transition to adult oncology occurs after 18 years.

Aim, Materials and Methods. The aim of the study is to find and characterize SMN in paediatric haematooncological cohort.

738 patients younger than 18 years at diagnosis of the first malignancy who had been registered in the department between 2000 and 2016 were retrospectively analyzed. The cohort included leukemias, CNS tumors, non-Hodgkin lymphomas and Hodgkin lymphomas, neuroblastoma, soft tissue tumors, Ewing sarcoma, osteogenic tumors, nephroblastoma, retinoblastoma, germ cell tumors, other rare malignancies. Follow up time was available until patients reached 18 years. SMN were defined as tumors that were not directly spread or metastases of primary neoplasm and were of different histological type.

Results. 9 cases of SMN in 8 patients (3 girls and 5 boys) were identified in the cohort. Median age at the diagnosis of the first malignancy was 52.5 months. Primary tumors were 2 NHL, 2 ALL, 2 CNS malignancies, 1 neuroblastoma, 1 hereditary bilateral retinoblastoma. In 4 cases radiotherapy was part of primary treatment, in 1 case SMN developed within the irradiated field. The types of SMN were 3 NHL, 2 leukemias, 2 MDS, 1 glioma, 1 hemangiopericitoma. Time from diagnosis to SMN occurrence was 10–129 months (median 43 months). The shortest intervals were observed in two cases with underlying cancer predisposition (a boy with hereditary bilateral retinoblastoma and proven RB1 mutation diagnosed at the age of 2 months, who developed acute myeloid leukemia in 10 months; and a girl with Fanconi anemia who developed 3 consecutive tumors: primary CNS tumor at 6 years followed in 22 months by non-Hodgkin lymphoma and in another 32 months by myelodisplastic syndrome).

SMN treatment was challenging and depended on type of malignancy, previous therapy and cumulative dosages, aggressiveness of disease, toxicity during treatment and other factors. Survival after SMN varied: 4 patients are currently alive (follow up time 9–57 months, median 18 months); 4 patients died (2 days to 38 months from SMN occurrence, median time to death 13 months); 2 patients with NHL are alive, one of them underwent allogenic BMT. Both patients with leukemia did poorly due to aggressive and resistant diseases, one died in two days due to AML, and second boy with ALL – in 6 months. One patient with MDS was transplanted, one patient with MDS (third malignancy) died due to fatal sepsis. Patient with secondary high-grade glioma died in 4 months, parents refused treatment. Patient with splenic hemangiopericitoma underwent splenectomy and remains in remission.

Conclusions. The results indicate that the risk of developing SMN for survivors of paediatric tumors in Latvia is slightly above 1 % until the age of 18. A more comprehensive evaluation, including cumulative risk in long-time survivors and SMN outcome, would be possible in cooperation with adult oncology registry. The prognosis of SMN is variable and depends on the tumor type; half of the cases responded to therapy, thus proving that SMN are potentially curable. Our small experience with BMT demonstrated that it could be a good option for some patients with SMN.