Comment

Across all cancers the most spectacular gains in outcomes over the last few decades have been in the field of childhood cancers. An increase to almost 80% cure rate across all the childhood cancers from about 20% a few decades ago is indeed a laudable achievement. The most contributing factor for this significant success is the integration of care and research in paediatric oncology. To support this view we present the second issue of the "Progress in Medicine" that has been entirely devoted to pediatric oncology and hematology during last few months. Present issue contains 9 original papers, 3 case presentations and 3 review papers.

Dr K. Drabko et al. presented a retrospective analysis of treatment failure in 119 children and adolescence with Ewing sarcoma treated in Polish oncology centers. Most of the treatment failures in children with Ewing's sarcoma (92%) were caused by the underlying disease. According to presented analysis the results of treatment in childhood Ewing sarcoma are still unsatisfactory. Megachemotherapy in patients with high risk factors did not increase the number of deaths due to toxicity and contributed to reducing the number of relapses in these patients.

The value of positron emission tomography (PET) imaging based on the use of *O*-(2-18F-Fluoroethyl)-L-Tyrosine (18F-FET) radiotracer in 22 patients with brain tumors was discussed by authors from Bydgoszcz centre. Increased FET uptake representative for malignant brain tumor was observed in 86% of patients. No FET uptake was observed in three patients. Based on the kinetic analysis of FET uptake we assessed the malignancy degree of suspected tumors finding compliance in 5 of 6 children with confirmed histological diagnosis of gliomas (compliance of 100% in low grade gliomas, 66.7% in high grade gliomas). These preliminary results indicate that FET-PET is a potentially effective method to identify malignant brain lesions, to monitor the disease course and predict the malignancy degree of lesions with unknown histology, based on kinetic analysis of FET uptake.

The other article from the same centre presents assessment of flow cytometry minimal residual disease (MRD) in children with acute lymphoblastic leukemia (ALL) in local laboratory and its validation in a reference laboratory. MRD values obtained locally showed strong correlations with the results from reference laboratory at days 15 and 33 ($p < 0.01$). It was confirmed that MRD values determined in Bydgoszcz were comparable with results in the reference laboratory.

L-asparaginase (L-ASPA) is one of the basic drug in the treatment of the acute lymphoblastic leukemia (ALL) in children. Dr M. Czogała et al. from Cracow analyzed the influence of decrease of L-ASPA activity and allergic reaction on the treatment outcome in children with ALL. Eighty seven patients treated with ALL IC-BFM 2002 Protocol were enrolled to the study. Activity below therapeutic values was noticed in 21% patients and allergic reaction occurred in 49% patients. Disease free survival (DFS) did not differ significantly between the groups with therapeutic and low L-ASPA activity. The authors concluded that decrease in L-ASPA activity in children treated for ALL was not associated with outcome deterioration but was significant risk factor of hypersensitivity to this drug.

The other paper from the same centre is focused on the problems of severe adverse effects in patients treated with high doses of methotrexate despite monitoring of Mtx elimination and administering of calcium folinate. One of the most important enzymes of the folate metabolic pathway affected by Mtx is methylenetetrahydrofolate reductase (MTHFR) which activity depends on genetic polymorphisms. The authors tried to assess occurrence and intensity of Mtx therapy related early toxicities in children with acute lymphoblastic leukemia in correlation to 677C>T MTHFR gene polymorphism. More severe liver toxicities, nausea, stomatitis, and infections were observed in TT homozygotes. Obtained results indicate the possible correlation between the presence of T-allel and high risk of acute toxicities of HD-Mtx therapy in children.

Despite an intensive treatment, therapy results in childhood acute myeloid leukemia are still unsatisfactory. For better understanding the biology of AML the multicenter study was performed to extended genetic diagnostics for detection of *RUNX1(AML1)-RUNX1T1(ETO)*, *PML-RARα*, *CBFβ-MYH11* fusion genes as well as *WT1* gene overexpression in 174 children under the age of 18 with *de novo* diagnosed AML.

Incidence of fusion gene transcript *RUNX1(AML1)-RUNX1T1(ETO)* in the cohort studied was slightly higher, while *CBFβ-MYH11*, *PML-RARα*, overexpression of *WT1* gene and the presence of FLT3/ITD mutation were reported less frequently comparing to other published studies.

Nowadays hematopoietic stem cell transplantation (HSCT) is an important component of the oncological treatment in children, especially in those with hematological malignancies and the treatment of choice for some congenital and acquired non-malignant disorders.

Professor J. Wachowiak on behalf of 5 Polish peadiatric BMT centres presented a survey of its activity between 1989-2012. A rate of transplants increased from 0.8/10 milion to 201/10 milion between 1989-2012.

Professor J. Styczyński and his team have analysed 369 patients aged < 20 years for PTLD after allo-haematopoietic stem cell transplantation performed in 2 pediatric centres. A total 20 PTLD cases were identified.

Three-fourths of patients with EBV-PTLD survived after rituximab-based treatment. Reduction of immunosuppression was associated with improved outcome while multiorgan disease, acute/chronic GVHD, and increase of EBV-DNA-emia after one week therapy predicted poor outcome.

The same group focused on the incidence of multidrug resistant bacteria in children with malignant diseases undergoing chemo- and/or radiotherapy in oncohematology department and hematopoietic stem cell transplantation. During analyzed 24 months period, the incidence of patients with at least one bacterial microbiologically determined infection reached 33.6% among children undergoing chemo- and/or radiotherapy, and 26.2% among children undergoing hematopoietic stem cell transplantation. Bacterial infections occurred significantly earlier in HSCT patients. Among Gram-negative rods, the incidence of MDR bacteria was 56.1%, including 52.2% in patients undergoing chemo- and/or radiotherapy and 64.5% in transplant patients.

Subsequent 3 papers are dealing with diagnostic and therapeutic problems in individual patients. First publication presents a case of 13- year old girl, who was presented with a localized subcutaneous tumor on the right arm. Biopsy of the lesion revealed a dense, monomorphous infiltration of the skin formed by T-lymphoid cells. Acute lymphoblastic bilinear leukemia was confirmed nearly a year later. Leukemia cutis is observed mostly in patients with myeloid leukemia, especially the myelomonocytic and monocytic types of AML in adolescents and adults. In children similar lesions are very uncommon.

Intra-abdominal bleeding with symptomatic haemorrhagic shock in patients with haemophilia A is a rare clinical condition. A 14-year-old male patient with a mild form of haemophilia A was presented by authors from Lublin. The patient suffered from intra-abdominal haemorrhage. Ultrasound examination and computed tomography (CT) scan revealed the presence of a large retroperitoneal duodenal haematoma with a large amount of free blood in the peritoneal cavity. An emergency laparotomy revealed 2000 ml free blood in the abdominal cavity and a huge intramural duodenal haematoma.

In the next paper multiple complications which affected therapy in a 16-year old girl with mixed phenotype acute leukemia were described. This is an example how multiple complications interfere with chemotherapy. Severe side effects lead to interruption of treatment, prolonged hospitalization, affect the outcome and have negative impact on a child's psyche. In this issue of the "Progress in Medicine" three review article are also included.

The article by Prof. M. Samardakiewicz et al. is devoted to cryopreservation of ovarian cortex as an experimental, but very promising method of preserving fertility especially for young women, also before puberty. In contrast to other methods, it requires no hormonal stimulation prior to collection the tissue so it doesn't delay cancer therapy. After at least 2 years from the end of cancer treatment and exclusion of recurrent disease, ovarian tissue can be transplanted orthotopic or heterotopic.

The paper by K. Pawelec presents the role of telomeres in the pathogenesis and the impact of their length on the results of treatment of patients with SAA. The role of the telomeres in the development of the diseases such as aplastic anemia, pulmonary fibrosis, cirrhosis or neoplasms has been recently taken into consideration.

One of the key elements of supportive therapy in pediatric oncohematology is prophylaxis and therapy of infections. Infectious complications might significantly contribute to mortality in children undergoing chemotherapy or hematopoietic stem cell transplantations. Prof. J. Styczyński presents review of current knowledge on prophylaxis and therapy of viral and fungal infections in children in oncohematology settings, based on ECIL guidelines.

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