1238 POSTER

New trends in the epidemiology of paediatric cancer in Romania

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Purpose: Taking into account some of our epidemiological features (high prevalence of HIV,HBV,EBV and HTLV I infection in children), we analysed the dimension, profile and dynamics of paediatric cancer in a period of two decades.

Methods: We used the data proceeded from the paediatric cancer registry and from the records of the registered patients between 1980 -2000, analysing the incidence of malignancies, the proportion of different anathomo-clinical forms, the EFS at 3 and 5 years of the different types of cancer and the frequency of non-compliance.

Results: The incidence of cancer in our area was assessed at 12,7-14,8/100.000/year, with an overall increase of 35,47% in the second decade. The distribution of the different types of malignancies was as follows: leukaemia 38,05% vs 41,3%, lymphoma and reticuloendothelial neoplasms 26,92% vs 20,82%, central nervous system and miscellaneous intracranial and intraspinal neoplasms 1,7% vs 3,15%, sympathetic nervous system tumours 2,56% vs 5,04%, retinoblastoma 1,7% vs 2,83%, renal tumours 7,26% vs 5,36%, hepatic tumours 1,28% vs 0,63%, malignant bone tumours 2,13% vs 5,04%, soft tissue sarcomas 7,69% vs 14,8%, germ cell, trophoblastic and other gonadal neoplasms 0,42% vs 0,31%, carcinoma and other malignant epithelial neoplasms 1,28% vs 0,94% respectively. The increased incidence of cancer in the second decade, was due to leukemia, NHL presenting an equally high prevalence. In the same period, impressive was the rise of the frequency of soft tissue sarcomas (7,65% vs 14,8%) and the confrontation with new types of cancer: 3 Kaposi sarcomas and 6 cases of AIDS related NHL. The hepatoblastomas, with a similar incidence in the two decades, were associated in 3 cases with HBV and in 2 cases with HCV infection. We observed a decreasing dynamic of Langerhans histiocytosis (2,99% vs 0,94%. The use of the internationally validated therapeutical protocols permitted an improvement of the overall 3 and 5 years EFS from 33,48% to 59,04% and from 28,05% to 51,92% respectively, and a decrease of non-compliance from 18,8% to 8,09%.

Conclusions: The new trends in the epidemiology of paediatric cancer, dominated by the increase of lymphoproliferative diseases and of soft tissue sarcomas and by the occurrence of new types are only partially justified by HIV, HTLV I and HBV/HCV infection. The prognostical improvements are due to the efforts of setting the therapy in concordance to the international standards.

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Identification of genetic polymorphisms at the glutathione S-transferase pi locus and association with susceptibility to childhood neoplasms

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Two variant glutathione S-transferas cDNAs have been described at the GSTP1 locus, which differ by a single base pair (A-G) substitution at nucleotide 313 of GSTP1 gene. This change represents an amino acid substitution from isoleucine to valine at codon 105 which reduce enzyme activity. Since GSTP1 is a major enzyme involved in the inactivation of xenobiotics we were interested to determine whether this polymorphism was related to childhood malignancy.

The study comprised 31 children (12 girls and 19 boys; mean age 8.5 ±4.5 years), with various types of neoplasms (15 with lympho- myeloproliferative diseases and 15 with solid germinal tumours). Using polymerase chain reaction followed by restriction fragment length polymorphism (PCR-RFLP) on peripheral white blood cell DNA, we identified the GSTP1a and GSTP1 b alleles.

In all studied children, the frequencies of the GSTP1a and GSTP1b alleles were 0.5 and 0.5 respectively. A total of 32.25% of children were homozygous for the low activity allele GSTP1b and 35.5% had halotype GSTP1a/GSTP1b. Comparing to population studies from healthy volunteers (Watson M et al. Carcinogenesis 1998, 19, 227) in our children with neoplasm a highly increase in the frequency of GSTP1b/GSTP1b genotype was observed. We should like to emphasise the need for a large study of children with neoplasms in order to substantiate this preliminary results.

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Life after childhood cancer

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Purpose: Since the advent of paediatric chemotherapy in the 1970s survival has increased dramatically (currently around 70%). Long-term effects have begun to appear in these survivors, the result of either the disease itself or of the treatment. It is now imperative to study these effects, in order to benefit future generations of patients.

At this hospital, patients have been followed up indefinitely in order to investigate the incidence and nature of any long-term physical or intellectual effects of the disease or its treatment and also to assess certain social aspects of the patients' lives.

Methods: A database has been established of patients who are alive 5 years from diagnosis, 3 years off treatment and who are still attending follow-up clinics. Full treatment details (surgery and exact chemotherapy/radiotherapy dosages) are abstracted from casenotes and detailed coding of long-term effects is updated after every clinic attendance, together with information on education, employment and social/family life.

Results: Of the 826 patients on the database, 679 are still attending clinics. 51 have died and 96 have been transferred to adult services, other regions or postal follow-up. Of the 679 12% are brain/CNS tumour survivors, 23% leukaemias and 64% other solid tumours. Their ages range from 5 to 36 years (median 17 years) and almost 40% are over 20.

16% of the survivors have no problems at all. Effects are classified into 6 sections: Organs/systems (35%); cosmetic (34%); endocrine (32%); special senses (23%); intellectual/psychological (20%) and neurological/orthopaedic (19%).

However, positive results include 20% University attendance (2 PhDs), many are married and have healthy offspring, others have achieved sporting success, etc.

Conclusions: This is an ongoing study, from which the results of analyses of disease and treatment-related effects will be of benefit to future patients. Workload studies will be enabled to plan the transition from paediatric to adult oncology follow-up care for these survivors.

Paediatric lymphoma/leukemia

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Correlation between neurocognitive dysfunction and MRI findings after central nervous system prophylaxis for childhood leukemia

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Purpose: Aim of this study was to evaluate a cohort of long term survivors of acute lymphoblastic leucemia in childhood with regard to assessment of intellectual function and MRI lesions after central nervous system (CNS) prophylaxis depending on modality of treatment and age.

Methods: 35 long term survivors were treated from 1981 to 1986 according to the ALL-BMFT 81 and 83 protocol, respectively. In 13 patients CNS prophylaxis consisted of MTX alone and in the other 22 patients it was combined with whole brain irradiation (WBI) (12 - 18 Gy). MRI was performed in order to measure volume of brain and ventricular system by using a computer assisted programme. Changes of white matter were assessed by using an Inter-rater-reliability test. Validated psychometric tests were performed to evaluate cognitive function. Cognitive function was correlated with imaging findings, treatment modality and age of the child at time of treatment (< 5 Y. or > 5 Y.).

Results: 2 Children had evidence of pathologic white matter lesions in MRI, uncertain lesions could be seen mainly in younger and irradiated children. All patients reached normal range full scale IQ values in relation to age, but the IQ of children with WBI were significantly lower than those of non-irradiated children. Independent of treatment younger children had lower IQ values than older children. No correlation was found between neurocognitive dysfunction, brain atrophy and white matter lesions.

Conclusion: White matter changes, neurocognitive disorders and brain atrophy are regarded as typical late effects after CNS prophylaxis in childhood. In our study these findings are more frequent after WBI combined