Pediatric Oncology and Scientific Investigations in Vulnerable Population

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Oncoología Pediátrica e Investigaciones Científicas em População Vulnerável

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Maria S. Pombo-de-Oliveira

At the population level, pediatric cancers are rare diseases, and as such they have received less attention in public health research seeking to identify causal agents in oncology. The natural history of a malignant neoplasm is strengthened by numerically robust evidence on incidence and mortality and the impact on a population at risk. A classic example is lung cancer, where the scientific research and results in the last three decades have led to major success in treatment and preventive programs. However, unveiling a rare neoplasm is of the utmost importance in studies on carcinogenesis. Examples include acute leukemias in early childhood, retinoblastoma, medulloblastomas, and clear cell vaginal carcinoma, in which the research resulted in major success for cancer treatments in general. Pediatric cancers have been increasingly investigated and unveiled in terms of their cell biology and the consequences of genetic lesions that generate neoplastic clones (leukemic and/or tumoral). The diversity and complexity of each type of leukemia and/or embryonal tumor (e.g., medulloblastoma) increase the current challenges in biotechnology, with endless searches for better understanding of the clinical multiplicity of pediatric cancers. Currently, the knowledge acquired on the cellular and molecular mechanisms that distinguish between subgroups of diseases with the same histopathologic denomination is the target of specific therapeutic interventions.

In epidemiological terms, little is known about pediatric cancers in Brazil. Since low and middle-income countries are in an epidemiological transition in infectious and noncommunicable diseases, treatment of pediatric cancer has become a focus of global interest.1

Acute leukemias are the most common types of childhood cancer. Although with common terms such as “lymphoid” or “myeloid” “leukemia” (lymphoid, ALL, and myeloid, AML), leukemias are highly heterogeneous, with distinct subtypes of morphological (cellular) subtypes and molecular alterations, which determine the treatment, prediction of clinical responses and overall survival, and etiological/pathological risks2-4. Current genomic mapping of tumors has great potential to define targeted therapies for a malignant clone5. Another great stride in cancer treatment has been the rise of immune therapy with the clinical successes obtained, blockade of cell pathways (immune checkpoints), and chimeric antigen receptor T-cell therapies. These successes also highlight the importance of understanding basic tumor immunology for successful clinical translation in the treatment of children with cancer.

This edition of Revista Brasileira de Cancerologia/Brazilian Journal of Oncology (RBC) features studies on pediatric cancer based on different multidisciplinary and clinical approaches resulting from individual experiences in various regions of Brazil. Perhaps the edition’s most important message is that Brazilian researchers are focused on elucidating the natural history of pediatric tumors through scientific studies in referral centers for pediatric oncology. Meanwhile, the edition’s various articles highlight the need to perform multicenter, multidisciplinary, and interdisciplinary studies. Without such characteristics it is more difficult to reach relevant conclusions on the behavior of childhood cancers in Brazil and in developing countries in general. Special emphasis is on population-based cancer registries focused on portraying the problem at the population level. Due to children’s vulnerability, it is also necessary to develop epidemiological studies (on leukemias and embryonal tumors), including genetic-molecular biomarkers associated with environmental factors, the aspects of which are related mainly to parental exposure, as has been done in consortia in international studies.

Although no specific genetic predisposition has been identified in many cases of acute leukemias and embryonal tumors, these diseases are known to have a genetic basis at their origin. Embryonal tumors like neuroblastoma, retinoblastoma, and Wilms’ tumor are associated with germline mutations in TP53, WT1, RB1, and CDKN, or with the presence of congenital anomalies. Acute leukemias in early childhood originate in intrauterine life.5 At any rate,
recurrent genetic alterations are the crux of tumorigenesis and are highly relevant for diagnosis and treatments. Cytogenetic-molecular alterations limited to the neoplastic clone, such as translocations, inversions, deletions, gene amplification, and point mutations are already considered mandatory in the characterization of acute leukemias, lymphomas, and medulloblastoma before any therapeutic intervention. Continuing professional training is thus necessary for professionals in pediatric cancer care. Interdisciplinary teamwork involving a medical specialist, nurse, medical biologist, and molecular biologist is of the utmost importance for successful cancer treatment. Interdisciplinary research is especially important, with greater use of the available biotechnological tools to identify the patients that will benefit from specific treatment with precision medicine, emphasizing that quality medical care and treatment are the most influential factors in the evolution and survival of children and adolescents with pediatric tumors. There are children in poor countries who achieve favorable treatment outcomes, regardless of limited resources, because these countries have developed multi-institutional programs.

The recent formation of research consortia has led to a new generation of consistent information on the different stages of pathogenic mechanisms in cell biology, the genomic-epigenetic relationship, and evolution of the tumor clone, allowing the identification of associations between risks and potential “causal” agents for acute leukemias and some pediatric embryonal tumors. We can be optimistic on the possibility of establishing predictive programs for disease evolution or the development of precise tumor burden markers and even preventive measures for tumors.

This special edition of RBC thus shows that pediatric tumors, regardless of their rarity, have an impact on studies of carcinogenesis, therapeutic approaches, and childhood mortality and quality of life for survivors.

REFERENCES