Chapter

Introductory Chapter: Contemporary Pediatric Hematology and Oncology

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1. Introduction

Blood diseases are distinctive group of inherited and acquired, benign and malignant, acute and chronic disorders with diverse incidence, etiology, pathogenesis, and prognosis.

In the early days of hematology-oncology practice, hematology dominated and occupied most of the practitioner's time because most patients with cancer had a short life span and limited therapeutic modalities were available [1].

Our understanding of hematologic conditions has advanced considerably with the explosion of molecular biology and the management of most hematologic conditions has kept pace with these scientific advances. It has been a privilege to be a witness and participant in this great evolution over the last years where blood disorders have been studied extensively through many laboratory approaches for example, microscopy, clinical chemistry, immunophenotyping, genetic tests such as conventional cytogenetics, fluorescence in situ hybridization (FISH), and polymerase chain reaction (PCR). Yet we still have a long way to go as current advances are superseded by therapy based upon the application of knowledge garnered from an accurate understanding of the fundamental biology of hematological diseases [2].

Application of these advanced diagnostic tools had clarified the greatest involvement of different molecular mechanisms in the pathological transformation of hematopoietic progenitor cells and disease progression in many hematological diseases. Interestingly, more precise and accurate diagnosis was established, also, patients risk stratification as well as discovery of personalized, tailored therapeutic approach [3].

Aplastic anemia is a disease in which the stem cell fails to maintain bone marrow production. Aplastic anemia may be caused by hereditary disorders that usually present in childhood or in young adults (e.g., Fanconi anemia), or may present as an idiopathic disorder later in life. Many of these "idiopathic" cases may be due to autoimmune attack on the stem cell population. Secondary aplastic anemia can be caused by toxic damage to the marrow by radiation or chemicals (benzene, DDT, chemotherapy drugs, gold, etc.) or secondary to viral infection (e.g., EBV) [4].

Discovery of numerous genes incriminated in pathogenesis of Fanconi anemia and other inherited bone marrow failure syndromes has made great evolution in understanding the mechanism of DNA repair, telomere and telomerase enzyme action as well as many other biology secrets. Also, the relationship between the development of some types of cancers and presence of bone marrow failure syndromes may explains the etiology of these cancers and multiple birth defects [5].

In this disorder, we expect to see declines in all cell counts (pancytopenia) with low reticulocyte counts. Aplastic anemia has been transformed from a near death

sentence to a disease with hope and cure in 90% of patients. Due to the emergence of advanced supportive care, immunosuppressive therapies and hematopoietic stem cell transplantation, this can result in 80% long term survival. In the absence of an HLA-matched sibling, allogeneic BMT can also be performed using an HLA-matched, unrelated donor or stem cells derived from umbilical cord blood [6].

The hemolytic anemias, have multiple causes, and the clinical presentation that can be differ according to the etiology. Many laboratory tests and specialized one can detect the cause of hemolysis, to reach specific diagnosis. With advancement in electrophoretic and other biochemical techniques, hemoglobinopathies are being identified now which were not previously possible. There are differences in the management of various types of hemolytic anemias [7].

Hemoglobinopathies requiring long life transfusion program to maintain a safe hemoglobin level for hemodynamic stability such as in thalassemia major and sickle cell anemia frequently had marked facial characteristics with broad cheekbones along with organ damage and failure, particularly of the heart, liver, beta cells of the pancreas and other tissues due to secondary hemochromatosis because of excessive iron deposition. The clinical findings attributed to extramedullary hematopoiesis are essentially of historic interest because of the development and widespread use of proper transfusion and chelation regimens.

Sickle cell disease (SCD) is one of the most frequent inherited genetic blood disorders in the world. It predominantly affects people of African ancestry (about 80% of sickle cell disease cases are believed to occur in Sub-Saharan Africa) as well as people with Hispanic background and individuals from the Middle East, India, and Mediterranean regions [8]. The disease was first described in the medical literature by the American physician James B. Herrick in 1910 [9]. Sickle cell disease is an autosomal-recessive disease caused by a point mutation in the hemoglobin beta gene found on chromosome 11p15.5, Several subtypes exist, depending on the exact mutation in each hemoglobin gene, and results in a number of health problems, for example, attacks of pain "sickle cell crisis," feet, anemia, bacterial infection, acute chest syndrome, pulmonary hypertension, stroke, cardiac, CNS, gastrointestinal involvement and nephropathy which is not only a chronic comorbidity but is also one of the leading causes of mortality. Significant advances in prophylactics and therapy achieved improved survival among children with sickle cell disease, with the majority of children attaining adulthood [10]. However, The average life expectancy in the developed world is 40–60 years with only 35.0% surviving beyond age 35 years was reported by the Centers for Disease Control (CDC).

Problems in sickle cell disease typically begin around 5–6 months of age. Knowledge of the natural progression of the disease, as well as identification of persons at risk, allows for timely intervention and improved outcomes. The search for biomarkers for the early diagnosis of the disorder and its outcomes is an area of intense contemporary research [11]. Our understanding of the basic science of molecular biology, oncology, genetics, and the management of several oncologic conditions made a huge evolution in the field of pediatric oncology. The previous decade was almost associated with fatal outcomes have changed a lot and replaced by an era in which most childhood cancers are cured.

This has been made possible not only because of advances in chemotherapeutic regimen but also, because of the parallel development of radiodiagnosis, radiotherapy, surgery as well as supportive care such as the pre-emptive use of antibiotics and blood product therapy.

There is greatest variation in childhood cancer incidence internationally, when comparing developed countries to developing ones. It is estimated that childhood cancer has an incidence of more than 175,000 per year, and a mortality rate of approximately 96,000 per year. In developed countries, childhood cancer has a

mortality of approximately 20% of cases. In low income countries, on the other hand, mortality ranges from 80–90%. This may attributed to different modalities in cancer diagnosis, differences in risk factors among different ethnic population subgroups as well as differences in reporting. In children aged 0–14 years incidence rates range from less than 100 per million in areas of sub-Saharan Africa and India to more than 150 per million in some populations of North America and Europe [12].

Familial and genetic factors are identified in 5–15% of childhood cancer cases. Many epidemiological studies have reported the effects of cancer genetics, family pedigrees and penetrance, and identified subtypes of certain cancers and their implications for treatment and prognosis. In addition, the study of certain genetic diseases that increase the risk of malignancy in childhood has led to understanding the genetics of cancer [13].

Survival from childhood cancer is no longer rare, and people who have been cured of cancer during childhood should be accepted as normal members of society. The overall survival rate for children's cancer has increased from 10% to nearly 80% today, and it is considered one of the major success stories of medicine in the twenty-first century. Improvements in the survival rates of leukemias, Hodgkin lymphoma, gonadal, and renal tumors have been notable successes. On the other hand, Overall mortality has decreased by 50% between 1975 and 2010 [14, 15].

Improvements in survival rate has led to the new challenge of caring for a growing number of cancer survivors. The most ominous late effect of pediatric cancer treatment is a second malignancy, for example, the risk of a second malignancy appears 15–20 years after an initial diagnosis of acute lymphoblastic leukemia is approximately 10% [16]. Many risk factors such as environmental factors, treatment and hereditary factors have been incriminated in second cancer. For example, the risk of acute myeloid leukemia in subject with the 9:11 translocation is approximately 3–6% within 5 years of chemotherapy that includes alkylating agent therapy or high-dose etoposide according to the dose and type of in addition to exposure to diagnostic radiation in utero has been associated with an increased risk of childhood cancer [17].

Contemporary Pediatric Hematology and Oncology covers many aspects of research and patient management within the area of blood disorders and malignant diseases in children. Of interest are clinical studies as well as basic and translational research reports regarding pathogenesis, genetics, molecular diagnostics, pharmacology, molecular targeting, standard and novel therapies for the most common blood disorders and childhood cancer. This book intends to provide the reader with a comprehensive overview on today's practices and tomorrow possibilities about the most important pediatric hematological and oncological diseases.

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