REVIEW ARTICLE

Pediatric Leukemia- An Overview

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ABSTRACT

Leukemia is characterized by widespread, rapid, and disorderly proliferation of leukocytes. In India, leukemia is the most common childhood cancer with a relative proportion varying between 25% and 40% and continues to be the largest contributor to cancer-related mortality in children. This paper reviews the etiology, risk factors, diagnosis, oral complications, and prognosis of pediatric leukemia.

Keywords: Acute lymphocytic leukemia, Diagnosis, Etiology, India, Oral complications, Pediatric leukemia, Prognosis.

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INTRODUCTION

Leukemia is a malignancy with the disseminated proliferation of immature or blast cells of the bone marrow, which replace the normal marrow elements and tend to accumulate in various tissues of the body.[1] Leukemia was first identified by researchers, Virchow and Bennet in the year 1845.[2] European physicians in the 19th century were the earliest observers of patients who had markedly increased white cell counts. The term "Weisses Blut" or "white blood" emerged as a designation to this disorder. Later, the term leukemia, which is, derived from the Greek word "leukos," meaning "white," and "haima," meaning blood was used to indicate the disease.[3-5] Leukemias are usually classified according to their clinical behavior (acute or chronic) or histogenesis (myeloid or lymphocytic/lymphoblastic). Hence, there are four main types of leukemia, namely chronic lymphocytic leukemia (CLL), chronic myelogenous leukemia (CML), acute lymphocytic leukemia (ALL), and acute myelogenous leukemia (AML). According to the Leukemia and Lymphoma Society, USA, there were approximately 13,410 new cases of AML, 5,200 new cases of ALL, 4,570 cases of CML, and 15,110 cases of CLL diagnosed in the year 2007–2008 in the USA. Again, this society has reported in the year 2010–2011 that blood cancers would account for 9.0% of the 1,529,560 new cancer cases diagnosed in the US this year. Leukemia alone[6] comprises 27.5% of cancers affecting the children aged 0–19 years in the United States. It further states that every 4 min, one person in the United States is diagnosed with blood cancer. Even in Britain, the second largest contributor to mortality from childhood cancer is leukemia.[7] In India, leukemia is the most common childhood cancer with a relative proportion varying between 25% and 40% and continues to be the largest contributor to cancer-related mortality in children.[8]

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ETIOLOGY OF LEUKEMIA

In ALL, chromosomal translocations occur regularly. It is thought that most translocations occur during prenatal development. These translocations cause a rearrangement of genes, which in turn to the transformation of proto-oncogene into an oncogene. The oncogene causes leukemia either by stimulating cell division or by inhibiting the programmed cell death called apoptosis. A translocation can activate a proto-oncogene by two different mechanisms. A more frequent event is a merger of two genes to form a fusion gene that produces abnormal chimeric protein inducing leukemia. As an example, translocation t(1; 19) in ALL creates the fusion of E2A (immunoglobulin enhancer-binding factors E12/E47) and PBX1 (pre-B-cell leukemia transcription factor 1) genes. In the E2A-PBX1 fusion, protein transactivating domains of E2A are joined to the DNA-binding domain of PBX1, which alters the transcriptional properties of the PBX1 transcription factor.[9-16]

RISK FACTORS OF LEUKEMIA

Ethnicity

Indian population being multicultural and multiethnic has conserved their gene pool because of the caste system and intra caste marriage requirement. The records of leukemia comprise 86.5% of Hindus and rest for other religions which are in accordance with their population.[17-26]

Blood Groups

The significant presence of AML has been observed in all types of blood groups but not with other types of leukemias.[27]

Sex Disparities

Males show a higher risk for all forms of leukemia with the overall ratio of 1:8.1. There is no explanation for females to be protected against leukemia.[30] In a study from Haryana by Kumar *et al*., there were 70.2% children and 29.8% adult patients of ALL in which male to female ratio was 2.03:1.[27-31]

Geographic

It has been proposed that T-cell ALL predominates in economically disadvantaged areas, but with urbanization, industrialization, and increasing affluence incidence of ALL have increased. ALL is reported to be the most frequent in the south[32,33] and intermediate in the East, West,[34-36] and central India.[37]

Age

The age distribution of children of ALL in developed countries shows a very marked early peak between 2 and 5 years, followed by a small peak between 11 and 15 years and the median age of 4 years.[37-40] There has been a gradual increase in the incidence of ALL in the past 25 years.[41]

Ionizing Radiation

Ionizing radiation is considered as a known cause of ALL. The risk is also higher for those exposed at an earlier age[42] and secondary leukemias in the individuals treated by radiotherapy. Radiation from nuclear power plants[43] and X-ray examinations of pregnant women may be associated with increased risk of childhood ALL. Postnatal exposure of infants for diagnostic X-ray increased the risk by 60% and was associated with of ALL, specifically B-cell ALL but no AML or T-cell ALL.[44-46]

TREATMENT

Leukemia is usually treated with chemotherapy, irradiation, or bone marrow transplantation. Chemotherapy and radiotherapy are generally cytotoxic for rapidly multiplying malignant cells, but also negatively impact the production of normal hemopoietic and secretary cells as these do not differentiate between normal and malignant cells. This side effect often results in immune suppression and reduced secretions in the body. The systemic sequelae as a result of this medication or radiation can also induce a number of oral and dental complications. The patient with cancer faces an assault on oral health from both the disease and the treatment options. The direct and indirect ill effects to the oral cavity are associated with the development of ulcerative, hemorrhagic, or infectious complications.[47]

ORAL COMPLICATIONS

Various factors increase the potential for developing oral problems in these children. They may include the age of the patient, nutritional status, type of malignancy, pretreatment oral condition, oral care during treatment, and pretreatment neutrophil counts.[47] The oral complications seen in leukemic children can be broadly classified as:

1. Primary complications: Mainly occurring due to the disease itself, that is, resulting from leukemic infiltration in the oral structures such as gingiva and bone, for example, leukemic gingival enlargement.
2. Secondary complications: These are usually associated with a direct effect of the radiation or chemotherapy, such as the ones associated with thrombocytopenia, anemia, and granulocytopenia. These include a tendency to bleeding, susceptibility to infections, and ulcers.
3. Tertiary complications: The tertiary complications are usually due to the complex interplay of therapy itself, its side effect, and a systemic condition arising out of the therapy. They may be ulcerations, mucositis, taste alteration, skin desquamation, candidiasis, gingival bleeding, xerostomia, dysphasia, opportunistic infections, trismus, etc. Sometimes latent and late effects such as some of the vascular lesions, tissue atrophy, permanent taste loss or change, fibrosis, edema, soft tissue necrosis, loss of teeth, salivary flow decrease, carious lesions, osteoradionecrosis, and chondronecrosis are also attributed to tertiary effects.

CONCLUSION

Child health is a priority health issue, and we are progressing toward reducing infection-related childhood deaths. However, childhood cancer is not yet a major area of focus, and it is not acceptable to ignore these children as they have an increasing likelihood of cure with appropriate treatment.

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