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Childhood Non-Hodgkin's Lymphoma: An Immunophenotypic Analysis

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Abstract

Objective: To observe the frequency of histological subtypes of childhood non-Hodgkin's lymphoma and its immunohistochemical profile.

Setting: All cases of non-Hodgkin's lymphoma diagnosed in children (<15 years) in the section of histopathology at the Aga Khan University Hospital Karachi during the period of three years.

Methods: These consecutive cases were evaluated on H&E stained sections and then immunohistochemistry analysis of these tumors was performed by employing Peroxidase Anti-Peroxidase (PAP) technique.

Results: The present series included 61 cases of non-Hodgkin's lymphoma. NHL was more common in males as compared to females with male to female ratio of 5.8:1. High grade NHL comprised 87% of childhood lymphoma. The mode of presentation in majority of NHL (57%) was extranodal. Burkitt's lymphoma (33%) was the most prevalent histological subtypes, followed by lymphoblastic (28%), diffuse large cell (15%), diffuse mix small and large cell (13%), small non cleaved Non-Burkitt's (7%) and immunoblastic (4%). Immunophenotypic analysis of the childhood Non-Hodgkin's lymphoma revealed that 67% of the Non-Hodgkin's lymphoma are cell type while 33% are those of T-cell lineage.

Conclusion: NHL was more common in males. Majority of NHL in children were high grade tumors. Burkitt's lymphoma was the most frequent histological subtype. T-cell NHL comprised a significant portion of childhood lymphomas (JPMA 50:89,2000).

Introduction

Non-Hodgkin's lymphoma (NHL) is one of the most common group of malignant solid tumors encountered in children¹⁻⁷. NHL is an extremely heterogeneous group of malignant tumors, which exhibit variability in histological features, growth pattern, antigenic phenotype and biological behavior. Marked geographic and ethnic variation has been observed in the frequency and distribution of histologic subtypes of Non-Hodgkin's lymphoma all over the world⁸. Non-Hodgkin's lymphoma is more prevalent in African countries like Nigeria and Uganda as compared to USA, UK and Japan^{7,8}. The childhood non-Hodgkin's lymphomas are more common in boys than in girls⁸. In children, high grade lymphomas are more frequently encountered and this category includes small non cleaved cell (Burkitt's and Non-Burkitt's) lymphoma, lymphoblastic lymphoma, large cell and immunoblastic lymphoma⁹. NHL is more frequently extranodal in the younger age group while in adults it is more commonly nodal in origin^{8,10}.

Immunohistochemical analysis is not only helpful in the diagnosis of lymphoma but phenotyping has got prognostic significance as well. In Revised European American classification of Lymphoid neoplasm (REAL), the immunophenotyping of the neoplastic lymphoid cells is considered necessary for the characterization and grading of the lymphoma".

Sometime, childhood NHL poses a formidable diagnostic challenge due to the close morphological resemblance to the other small round cell tumors. It becomes very important to differentiate between these tumors because most childhood, NHL tumors respond to the specific chemotherapeutic regimens.

which have improved the survival rates in these cases¹².

The objective of this study was to observe the frequency of histological subtypes of Non-Hodgkin's lymphoma in childhood and its immunohistochemical profile.

Materials and Methods

This study included sixty one consecutive cases of non-Hodgkin's Lymphoma which were diagnosed in children (<15 years) in the section of histopathology at the Aga Khan University Hospital Karachi during the period of three years (1995-97). International working formulation was used for the classification of these tumors. Initially these tumors were evaluated on H&E stained sections and then Immunohistochemical analysis was performed by employing Peroxidase Anti-Peroxidase (PAP) technique. The antibodies used in immunohistochemical staining included Leukocyte Common Antigen (LCA), PAN B (CD20, L26), PAN T (UCHL 1), granulocyte associated antigen ((iAA Leu MI), Ki-1 (CD 30), Desmin, Vimentin, Neuron specific enolase (NSE) and Cytokeratins depending upon the nature of lesion. Special stains such as reticulin, periodic acid schiff(PAS) and periodic acid schiff with diastase (PASD) were performed whenever required. Relevant, clinical details like age, sex and site of lesion were also recorded.

Results

A total of 366 cases of malignant tumors were diagnosed in children which included 61(16.7%) cases of Non-Hodgkin's lymphoma (NHL) and 40 (10.9%) cases of Hodgkin's disease. The age ranged from 7 months to 14 years with mean and median of 8.7 years and 9 years respectively. NI-IL was more common in males as compared to females with male to female ratio of 5.8: 1. High grade NHL comprised 87% of childhood lymphoma followed by intermediate grade (13%). In most of the cases of NHL (57%), the mode of presentation was extranodal. Amongst the extranodal sites, gut was the most frequent site for these malignant tumors. Burkitt's lymphoma (33%) was the most common histological subtype, followed by lymphoblastic (28%), diffuse large cell (15%) and diffuse mix small and large cell (13%). Less frequent histological types included small non-cleaved Non-Burkitt's (7%) and immunoblastic (4%). The results are summarized in Table.

Table. Histological types of non-Hodgkin's lymphoma in children.

Histological type	No. of cases	%
Burkitt's lymphoma	20	33
Lymphoblastic	17	28
Diffuse large cell	9	15
Diffuse mix small and large cell	8	13
Small non cleaved (non Burkitt's)	4	6
Immunoblastic	3	5
Total	61	100

Burkitt's lymphomas were mostly extranodal (abdominal) while lymphoblastic was nodal in origin. Immunophenotypic analysis of the childhood Non-Hodgkin's lymphoma revealed that 67% of the Non-Hodgkin's lymphomas were B-cell type while 33% were those of T-cell lineage.

Discussion

Considerable variation in the prevalence of NHL has been observed along with distribution of its histological types and immunophenotypic pattern in the different regions of the world^{8,13,14}. In equatorial Africa, Burkitt's lymphoma comprised about half of all tumors in children⁸. Lymphomas were the most common solid tumour in children in the present study. Higher prevalence of lymphoma in children has been reported in different series from various centres of Pakistan¹⁵⁻¹⁷. According to the Western literature, Non-Hodgkin's lymphoma is more prevalent than Hodgkin's disease and its Non-Hodgkin's lymphomas (90%) in children are those of high grade¹⁸. Similar findings were observed comprising 60% of all childhood lymphomas⁷. Majority of in the present study. In our series, Non-Hodgkin's lymphoma constituted 56.1% of childhood lymphoma. Majority of the cases of NHL (87%) were those of high grade. Non-Hodgkin's lymphoma and Hodgkin's disease were more frequent in males as compared to females. Similar observation was reported in other series^{8,16,17,19}. In the present series, Burkitt's lymphoma was the most frequent histological subtype (33%) of Non-Hodgkin's lymphoma, which correlates well with the figure of 34% reported in the Western series¹⁸. A relatively high frequency of Burkitt's lymphoma (43%) has been reported in a series from Armed Forces Institute of Pathology (AFIP) Rawalpindi²⁰. In the present series, Burkitt's lymphomas were predominantly presented in extranodal location and in 46% cases the mode of presentation was abdominal mass. A similar observation was made in a series from AFIP, Rawalpindi²¹. Sporadic cases of Burkitt's lymphoma usually involve the abdominal region while endemic cases predominantly arise in the jaw⁸. Lymphoblastic lymphoma comprised 28% of all NHL. In the other series, lymphoblastic lymphoma constituted 29-33% of all cases of NHL¹⁸⁻²⁰, Diffuse large cell lymphoma constituted 15% of all NHL, which compares well with the figure of 16.6% from AFIP, Rawalpindi²⁰. But it was significantly low from the figure of 27% reported in the Western literature¹⁸. In the present series, the extra-nodal NHL comprised 57% of all cases which is quite high as compared to the figure of 36% from AFIP, Rawalpindi²⁰. It might be because of the geographical variation as our department receives biopsy material mainly from the Southern part of the country while AFIP, Rawalpindi covers most of the Northern part of the Pakistan. Immunohistochemical analysis of NHL revealed that 67% of NHL were of B-cell phenotype while 33% were of T-Cell lineage. T-Cell lymphoma exhibit significant clinical and prognostic differences from B-cell lymphoma. T-cell immunophenotype in diffuse large cell sub-group is associated with poor prognosis²². The application of immunohistochemical technique has gained paramount importance for the diagnosis and evaluation of the prognosis of non-Hodgkin's lymphoma.

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