ORIGINAL ARTICLE

An Immunohistochemical Study of Nodal Non Hodgkin's Lymphoma to Correlate 2008 WHO Classification and Working Formulation

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ABSTRACT

Introduction: Working Formulation (WF) classification system of nodal Non Hodgkin s Lymphoma (NHL) is followed in Pakistan commonly. NHL has been reclassified by 2008 WHO classification. However, overlapping between newer and older classification systems tend to be confusing. This study was carried out to correlate results of WF and 2008 WHO classification of lymphomas.

Materials and methods: This study was carried out on 60 consecutive diagnosed cases of nodal NHL on routine H&E stain. New sections were cut from retrieved paraffin blocks of these cases and stained with panel of immunohistochemical stains. These immunostained sections were diagnosed and correlated with H&E based diagnosis.

Results: The results revealed that small lymphocytic lymphoma (SLL) according to WF has been classified into (WHO) lymphoplasmacytic lymphoma and unclassifiable, Diffuse Large cell lymphoma(WF) into Diffuse large B cell NOS, Peripheral T cell NOS, Anaplastic large cell lymphoma and Angioimmunoblastic lymphoma(WHO) and Lymphoblastic (WF) into B lymphoblastic and T lymphoblastic lymphoma (WHO). The small cleaved, mixed and large subtypes of follicular lymphoma (WF) have been unified as follicular lymphoma (WHO). Small cleaved cell lymphoma (WF) has been renamed as mantle cell lymphoma (WHO). Diffuse large B cell lymphoma NOS (WHO) encompasses immunoblastic lymphoma (WF), diffuse mixed (WF), and some cases (15 out of 27 in our study) of diffuse large cell lymphoma (WF).

Conclusion: Classification of lymphomas is a confusing domain. However, unification of various classification systems will enhance understanding in this field.

Key words: Lymphoma, Anaplastic, Immunoblastic, Lymphoblastic

INTRODUCTION

WHO classification of lymphomas 2008 is a revised version of 2001 classification which followed similar guidelines of REAL classification introduced in 1994[1]. REAL classification was an initiative in providing a comprehensive and composite version of different classifications of lymphomas. It gave an opportunity to identify new clinicopathological variants in classification of lymphomas[2]. This classification updates the entities of modified Kiel classification. It was recommended by International Lymphoma Study Group that for any advance classification of lymphomas, it is necessary to segregate lymphoid neoplasms into B and T cell subtypes. A variation in occurrence of various types of lymphomas exists in different parts of the world. Immunological techniques are uncommon in public and private sector laboratories in our country. WF classification for NHL is commonly used in Pakistan. In WHO classification of lymphoma 2008, lymphoma entities are sub classified according to immunological and genetic characteristics. In Pakistan, a lot of work regarding immunohistochemistry of lymphoid neoplasms needs to be done. A limited number of studies have been done on this topic. This study was conducted to carry out immunophenotyping of lymphomas and its categorization according to WHO 2008 classification and correlation of WHO classification 2008 with WF.

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MATERIALS & METHODS

This was a retrospective study carried out at Armed Forces Institute of Pathology (AFIP) Rawalpindi from September 01, 2008 to December 20, 2008. During this period, immunophenotyping of sixty consecutive cases of NHL was done. The cases belonged to age groups ranging from 6 t0 78 years in both sexes. Only nodal NHL cases were included. Diagnosed cases of lymphoma receiving therapy and cases with inadequate biopsy material were excluded. H&E sections and paraffin blocks of the cases were retrieved from laboratory record. Sections of each case were cut and dried in air. Immunophenotyping was done by using the B cell markers including CD

20,CD 74, CD w 75 , Kappa and Lambda light chains, T cell markers including CD 2, CD 3, CD 5, NK cell markers and other markers including CD30, CD15,CD68, K1-67, BCL-2,EAM . Both positive and negative control slides were used to assure the specificity of positive staining reaction. Positive cases revealed dark brown color. Histological diagnosis in all these was made by simultaneous examination of positive and negative control slides along with immunohistochemically stained sections and correlated with H&E diagnosed cases of NHL.

RESULTS

This study included a total of 60 cases of Non-Hodgkin's lymphoma. The ages of the patients ranged from 6-78years (mean age 49years±16.5). 37 cases (61.66%) were males and 23 cases (38.33%) were females with male to female ratio1.6: 1. After immunohistochemical staining, 45 cases (75%) were of B cell type, 13 cases (21.67%) T cell type and 2 cases (3.33%) remained unclassifiable. Correlation between Working Formulation and WHO Classification 2008 is given below in Table

Table : Correlation between Working Formulation and WHO Classification 2008

Working Formulation		WHO Classification	
Small Lymphocytic Lymphoma (Low Grade)	12	SLL (B Type)	7 (58.33%)
		Lymphoplasmacytic Lymphoma	3 (25%)
		Unclassified	2 (16.67%)
Follicular Lymphoma Small Cleaved Lymphoma (3) (Low Grade) Mixed Lymphoma (3) (Low Grade) Large Cell Lymphoma (4) (Intermediate Grade)	10	Follicular Lymphoma	10 (100%)
Small Cleaved Cell Lymphoma (High Grade)	1	Mantle Cell Lymphoma	1 (100%)
Diffuse Mixed Lymphoma (Intermediate Grade)	2	Diffuse Large B Cell Lymphoma – NOS	2 (100%)
Diffuse Large Cell Lymphoma (Intermediate Grade and High Grade)	27	Diffuse Large B Cell Lymphoma – NOS	15 (55.55%)
		Peripheral T Cell Lymphoma – NOS	5 (18.52%)
		Anaplastic Large T Cell Lymphoma	4 (14.81%)
		Angioimmunoblastic T Cell Lymphoma	3 (11.11%)
Burkitt's Lymphoma (High Grade)	1	Burkitt's Lymphoma	1 (100%)
Lymphoblastic Lymphoma (High Grade)	6	B Lymphoblastic Lymphoma	5 (83.33%)
		T Lymphoblastic Lymphoma	1 (16.67%)
Immunoblastic Lymphoma (High Grade)	1	Diffuse Large B cell Lymphoma – NOS	1 (100%)

DISCUSSION

In Pakistan, cases of NHL are diagnosed and categorized according to WF. This classification is based upon morphological features and clinical behavior (grading). This is simple and is easily followed by the physicians and oncologists. This study included a total number of 60 cases of nodal lymphomas in age groups ranging from 6 – 78years with mean age 49years. On phenotyping, 45 cases (75%) were of B cell type. This percentage is slightly less when compared with studies in western countries where B cell lymphomas constitute 80-85% of lymphomas[3]. Other studies conducted by Khan MA and Khan MS in AFIP Rawalpindi, found B cell lineage in NHL cases to be 85.5% and 72.5% respectively[4&5]. 27 cases (45%) of diffuse large B cell lymphoma were diagnosed according to WF. It was the most common type of B cell lymphoma in present series. Rittaluga S et al[6] found 32% of lymphomas were of diffuse large B cell type in one of studies. The next common B cell lymphomas were follicular lymphomas comprising 10 cases (20%) of this series. 12 cases of small lymphocytic lymphoma(SLL) on immunophenotyping revealed 7 cases(58.33%) of SLL(B), 3 cases(25%) of lymphoplasmacytic lymphoma(B) and 2 cases (16.67%) remained unclassifiable. 3cases of lymphoplasmacytic lymphoma were separated from B-SLL by showing negative staining with CD5. 2 cases were labeled as unclassified as these revealed negative staining with B cell, T cell, CD30(Ki-I), CD68 and CD 57 markers. T cell lineage was seen in 13 out of 60 cases (21.67%) of NHL. In western countries 30% of NHL cases are of T cell type shown in one of the studies[7]. The difference between occurrence of T cell and B cell type NHL cases in this study and other studied in Asian and European countries can be due to small sample size in this study. 5 cases (18.52%) of peripheral T cell lymphoma NOS were diagnosed as diffuse large cell in WF. There were 4 cases (14.81%) of Ki-1 lymphoma and all these cases revealed T cell phenotype. Among 6 cases of lymphoblastic lymphoma, 5 cases (83.33%) proved to be of B cell and 1 case (16.67%) T cell type lymphoblastic lymphoma. According to WF, one case of small cleaved cell lymphoma was diagnosed mantle cell lymphoma on immunophenotyping.

CONCLUSION

WHO classification of lymphomas 2008 is more acceptable to clinicians and oncologists because it explains the complexity of disease and addition of new disease entities. Diagnosis of NHL cases according to WF is still recommended as this classification is based upon clinical behavior and morphological features of lymphomas. Immunophenotyping of lymphoma poses problems in its easy adaptation as it is not cost effective and its limited availability in most of the diagnostic centers in our country.

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