RESEARCH COMMUNICATION

Malignant Lymphomas in Pakistan According to WHO Classification of Lymphoid Neoplasms

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Abstract

Objective: To determine the spectrum of malignant lymphoma in our set up, according to the WHO classification. Methods: All the cases diagnosed as malignant lymphoma, during the year 2005, were retrieved from the institution based tumour registry record and classified according to WHO criteria depending on the immunohistochemical results of a panel of lymphoma markers. Results: The male to female ratio was 2.5: 1 for almost all types of malignant lymphomas. The age range was 3 to 80 years. The frequency of Hodgkin's lymphoma, Burkitt's lymphoma and lymphoblastic lymphoma were higher amongst the children, whereas follicular lymphomas, mantle cell lymphoma and CLL/SLL were more frequently reported in 5th, 6th and 7th decades. Of the total cases 62% were nodal and 38% extranodal (majority in the GI tract). Non Hodgkin's lymphoma was more (73%) frequent than Hodgkin's disease. Mixed cellularity and nodular sclerosis were the main histological variants of Hodgkin's disease. Conclusions: Immunohistochemistry is not very frequently used in our set up and that also at very few centres. Therefore, its application should be encouraged to raise the quality of data on lymphoid neoplasms and contribute to their control.

Key Words: Malignant lymphoma, WHO classification, Non Hodgkin lymphoma, Hodgkin's disease

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Introduction

The lymphoid malignancies are quite frequently seen in developing countries and in one of the study these were found to be the most frequent tumours particularly in paediatric age group (Jamal et al., 2006). In most of the histopathological centres of Pakistan, lymphoid malignancies are being reported according to working formulation in past and still classified according to working formulation at many places.

Due to the limited availability of immunohistochemical techniques, WHO (Jaffe et al., 2001) classification of lymphoma is being used at very few centres. Therefore, there is a paucity of data (Muzaffar et al., 1997; Aziz et al., 1999) concerning the pattern of lymphoid malignancies according to WHO classification in our set up. So this study was carried out to find the pattern of lymphoid malignancies

Materials and Methods

The Armed Forces Institute of Pathology (AFIP), Rawalpindi, Pakistan receives specimens from various military hospitals all over Pakistan and civil institutions mainly from part of northern Pakistan. The present study included all the lymphoma cases retrieved from the tumour registry database of AFIP, Rawalpindi between the period of January 2005 to December 2005. The lymphoid neoplasms, which were classified according to WHO classification by employing a panel of antibodies according to morphology, were included. The panel of antibodies were selected from antibodies including CD45 (LCA), CD 45RO,CD 79,CD 20, CD10, CD 23,CD 3,CD5, CD43, CD56, CD 8, CD 4, CD 30,CD 15,CD 34,EMA, Bcl 2,TdT, Ki 67, ALK1, kappa and lambda light chains, as recommended (Kalyan et al., 2006).

Results

Out of 308 cases of malignant lymphomas, 246 cases, classified according to WHO classification were included in this study. The male to female ratio was 2.5:1 for almost all types of malignant Lymphomas. Non-Hodgkin's lymphoma (NHL) was more frequent, 180 cases (73%) than Hodgkin's disease (HD), 66 cases (27%). Malignant lymphomas were reported amongst patients with an age range of 3 to 80 years. The frequency of Hodgkin's lymphoma, Burkitt's lymphoma and lymphoblastic lymphoma was higher amongst the children. In contrast, follicular lymphomas, mantle cell lymphomas and CLL/SLL were more frequently reported in 5th, 6th and 7th decades (Figure 1).

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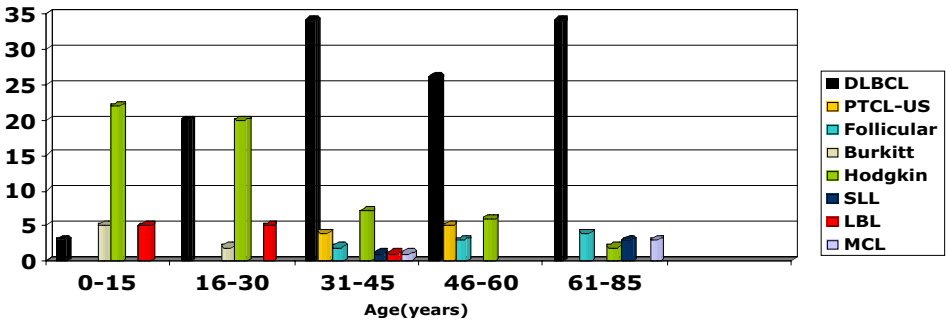

Figure 1. Various Subtypes of Lymphoma in the Different Age Groups

Sixty six cases (27%) of Hodgkin's disease (HD) were found.The mixed cellularity was the most frequent (17% of total 27% of HD) followed by nodular sclerosis (10%). There were no cases of lymphocytic depletion and lymphocyte rich Hodgkin lymphomas (Table 1).

The extra nodal presentation was observed in 38 % cases. Stomach followed by the skin was the commonest site of extra nodal presentation. Nodal presentations were about 62%. Cervical lymph nodes followed by the inguinal lymph nodes, were the commonest lymph node groups involved.

In the Non-Hodgkin lymphomas group, B cell lymphomas were 86% (n= 156) and T cell lymphomas (n =24) were 14%. Amongst the B cell lymphomas, 119 cases were diagnosed as Diffuse large B cell lymphoma (76%), followed by follicular lymphoma 6% (n=9) and 7 cases (4% each) of Burkett's lymphoma and Lymphoblastic lymphoma. Extra nodal marginal zone lymphoma, Mantle Cell lymphoma and CLL/SLL each had four cases reported (Table 1). Of the diffuse large B cell lymphoma, one case each of anaplastic large cell lymphoma and T cell rich B cell lymphoma were reported.

Table 1. Numbers of Cases of Different Subtypes of Lymphoma in Both Sexes (n=246)

	Total	Male	Female
B- Cell Lymphoid Neoplasms	147	118	64
DLBCL	119	75	44
Extra nodal Marginal zone	4	1	3
Follicular lymphoma	9	7	2
CLL/SLL	4	3	1
Mantle cell	4	3	1
Burkitt's	7	5	2
Lymphoplasmacytic	0	0	0
T/NK Lymphoid Neoplasms	22	16	6
Cutaneous T cell	5	2	3
CD 30 + Cutaneous T cell	3	3	0
Angioimmunoblastic	0	0	0
Anaplastic large cell	4	2	2
Peripheral T cell, unspec	10	6	4
T/NK cell	0	0	0
Lymphoblastic Lymphoma	11	7	4
B – cell	9	6	3
T – cell	2	1	1
Hodgkin's Lymphoma	66	49	17
Nodular Sclerosis	22	17	5
Mixed Cellularity	44	32	12
Lymphocyte depleted	0	0	0
Lymphocyte rich	0	0	0

The T cell lymphomas were rare (14%). With 10 cases, Peripheral T cell lymphomas were the commonest followed by cutaneous T cell lymphomas (n=5). Four cases of anaplastic large cell lymphoma were reported and there were 2 cases of lymphoblastic lymphoma. Three cases of CD 30+ cutaneous T cell lymphomas were also reported (table)

Malignant lymphoma of paediatric age group (<15 years) was seen in 32 patients where Hodgkin's disease (19 cases) was most frequent, followed by 05 cases of Lymphoblastic (03 cases of B and 2 of T cell type) and Burkitt's lymphoma each.

Discussion

By using WHO classification with the help of immunohistochemical techniques, various subtypes of Hodgkin and non- Hodgkin lymphoma are easily classified (Turner et al., 2004). Lymphoid malignancies in which morphology is enough to support a diagnosis, immunohistochemical techniques can act as ancillary tests. In most of the cases reported here, the results of the immunohistochemistry supported the morphological diagnosis and in only a small percentage did the results vary. There are small percentages of lymphoid malignancies where morphology alone is so deceptive, that it is difficult to determine the cases to be, Hodgkin or Non-Hodgkin lymphoma on morphology alone (Hartge et al., 1994). In such cases, immunohistochemistry comes to the pathologist and oncologists as a great aid. Classifying lymphomas alone as B and T cell type, has very significant prognostic information provided to oncologists (Akpek et al., 2000). Approaching any lymphoid malignancies by using WHO classification helps us to classify lymphomas into B and T cell types and recognizing specific entities (Turner et al., 2004; Shivarov et al 2005).

The present series found that frequency of Hodgkin's lymphoma has not changed much when compared to our previous analysis (Ahmed et al., 1993). Most of the developing countries have higher frequency of Hodgkin lymphoma (Kalyan et al., 2006; Tumwine, 2004), and same was observed here. This may be attributed to its association with Epstein Barr Virus infection which is quite frequent in developing countries.

The frequency of B and T cell Non-Hodgkin lymphomas was same as observed in the previous

Pakistani studies. In Pakistan, though T cell lymphomas have been reported more as compared to western studies (Khan et al., 1993; Khan et al., 1995; Muzaffar et al., 1997; Aziz et al., 1999) but overall T cell lymphomas are less frequent all over the world except the Far East Asian countries for unknown reasons. Nevertheless recognizing and diagnosing various subtype of T cell lymphomas according to WHO classification gives vital prognostic information. As generally the prognosis of T cell lymphomas is poorer than B cell lymphomas (Lee et al., 2005).

Amongst the B cell lymphomas, diffuse large B cell lymphoma is the commonest malignant lymphoma all over the world (Chiu and Weisenburger, 2003; Fisher and Fisher, 2004), and the same was observed in the present series. The results when compared to the percentages of large cell lymphomas (according to working formulation) in studies conducted previously in Pakistan were not much different. The next commonest lymphoma in this series was follicular lymphoma followed by small lymphocytic lymphoma, which were the other way round previously as well as reported in an earlier study in Karachi (Ahmed et al., 1993; Khan et al., 1993; Aftab et al., 2006). In an American study although the incidence of small lymphocytic lymphoma was reported more than follicular lymphomas, but it was reported that the incidence of follicular lymphoma was more amongst the Asian Americans (Morton et al., 2006). WHO/Real classification helped us diagnose Mantle cell lymphoma by employing Cyclin D1, which was previously not identified and as a result there is no data regarding its frequency in previous epidemiological studies of Non – Hodgkin lymphoma in Pakistan (Aftab et al., 2006). Autoimmune aetiology is thought to be involved in Extra nodal marginal Zone lymphomas and these are reported to be more common in far East Asian countries like Japan and china than in Pakistan (Anonymous, 2000; Zhang et al., 2005).

Peripheral T cell lymphomas – unspecified were more common than anaplastic large cell lymphomas in this study which was in concordance to western studies. Primary cutaneous CD 30 + anaplastic large cell lymphomas were also identified with the help of morphology and immunohistochemistry. Such cases previously were used to remain undiagnosed. Separating systemic anaplastic large cell lymphoma from primary cutaneous CD 30 + anaplastic large cell lymphoma is important, as the latter has much better prognosis (Savage et al., 2004). No cases of angioimmunoblastic lymphomas or Natural killer/T cell lymphoma were reported.

Over all lymphoblastic lymphoma was found to be more frequent than Burkitt's lymphoma but in paediatric age group 5 cases of each were seen which was contrary to what was found in another study of Pakistan where Burkitt's lymphoma was more common in children (Shah et al., 2000).

In the end it can be concluded that by using WHO classification, immunohistochemistry helps us to classify lymphoid neoplasm into B and T cell types & subtypes and to identify newer entities for more precise diagnosis and proper management of patients.

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