

NON-HODGKIN'S LYMPHOMAS IN SOUTHEASTERN ANATOLIA Güneydoğu Anadolu Bölgesindeki non-Hodgkin Lenfomalar

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Abstract

Purpose: In this study it was aimed to analyse the non-Hodgkin lymphomas of Southeastern Turkey retrospectively.

Material and methods: Between the years 1984 and 1995, 185 patients with non-Hodgkin lymphoma were retrospectively reviewed in The Pathology Department of Dicle University Medical School. All of the cases were classified according to the Working Formulation.

Results: Of all cases, 105 (56.8%) were nodal lymphoma and the remaining 80 (43.2%) were extranodal lymphoma. One hundred thirty-one (70.8%) cases were male and 54 (29.2%) cases were female and the male-to-female ratio was 2.4. Most of the cases were in the fourth decade. The mean age was 36.3. As to distribution according to grade of all cases, 43 (23.2%) were in low grade, 106 (57.3%) were in intermediate grade, 30 (16.2%) were in high grade and 6 (3.2%) were in a miscellaneous group. Of the cases, 23 (12.4%) were follicular lymphomas and 162 (87.6%) were diffuse lymphomas. Fifty-four (29.2%) cases were diffuse large cell lymphomas, which were the most frequent histopathologic subtype.

Conclusion: In conclusion, our values were established to be between the results of developed countries such as Denmark, Hong Kong and USA and developing countries such as China, Gabon and Korea.

Key Words: Non-Hodgkin lymphoma

The malignant lymphoma consists of a diverse group of malignancies that includes Hodgkin's disease and non-Hodgkin's lymphoma (NHL) (1). The classification of NHL is confusing and a universally accepted classification is still not available. Many

Özet

Amaç: Bu çalışmada Güneydoğu Anadolu'da non-Hodgkin lenfomaların retrospektif analizi amaçlandı.

Gereç ve yöntem: 1984-1995 yılları arasında Dicle Üniversitesi Tıp Fakültesi Patoloji Anabilim Dalı'nda non-Hodgkin lenfoma tanısı alan 185 olgu retrospektif olarak incelendi.

Bulgular: Bütün olgular Working Formülasyonu'na göre sınıflandırıldı. Bütün vakaların 105'i (%56.8) nodal ve 80'i (%43.2) ektranodal lenfomaydı. Olguların 131'i (%70.8) erkek, 54'ü (%29.2) kadın ve erkek/kadın oranı 2.4 idi. Olguların çoğu dördüncü dekattaydı ve ortalama yaş 36.3 idi. Vakaların 43'ü (%23.2) düşük dereceli, 106'sı (%57.3) orta dereceli, 30'u (%16.2) yüksek dereceli ve 6'sı (%3.2) karışık gruptaydı. Olguların 23'ü (%12.4) foliküler ve 162'si (%87.6) diffüz lenfomalıydı. Diffüz büyük hücreli lenfoma 54 (%29.2) vaka ile en sık görülen histopatolojik subtipti.

Sonuç: Sonuç olarak verilerimiz gelişmiş ülkeler (Danimarka, Hong Kong ve ABD gibi) ile gelişmekte olan ülkeler (Çin, Gabon ve Kore gibi) arasında tespit edildi.

Anahtar Kelimeler: Hodgkin dışı lenfoma

clinical studies from the early 1970s have demonstrated the clinical relevance of the Rappaport classification of NHL. After 1974, new classifications based upon modern concepts of the T and B-lymphocyte systems have emerged (2). Other classifications are based upon morphologic criteria but challenge the terminology used by Rappaport (3). Recently, The National Cancer Institute (NCI) organized a large-scale international study to compare and evaluate the most prominent classification schemes for malignant non-Hodgkin's

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lymphomas and to attempt formulating a unifying concept. This has resulted in the "New Working Formulation for Clinical Usage" (4). The Rappaport and Kiel systems and the Working Formulation (WF) are the three classifications commonly used (5).

The present study is a retrospective morphologic analysis of 185 cases collected in the Southeast of Turkey. Diyarbakır is situated in The Southeast Anatolia region of Turkey. In this region the population was estimated to be approximately six million. During the period covered by the present study (1984 to 1995), 185 NHL cases from Turkish patients were collected in our department. It focuses on NHL cases classified according to WF (5). The results are compared with those of studies from developed countries such as USA, Denmark and Hong Kong and developing regions such as China, Gabon, Korea and Lebanon to provide some insights into the particular histologic distribution of NHL cases in Southeast Anatolia, specifically Diyarbakır, Turkey.

MATERIALS AND METHODS

In this retrospective study, 185 consecutive cases of NHL were diagnosed between the years 1984 and 1995 in The Department of Pathology at Dicle University Medical School in Diyarbakır, Turkey. In all cases, Hematoxylin-eosin stained sections and paraffin blocks were available. Sections and imprint preparations of NHLs have been re-examined and PAS, Methyl Green Pyronin (MGP), Giemsa and Reticulin stains have been applied to slides where applicable. The cases of NHLs have been classified histologically according to the guidelines of WF (5). Descriptive statistics of all and each type of NHLs such as mean and range of age were determined. Relative rates of the types of NHLs have been compared with the data from other reports.

RESULTS

A total of 185 cases of NHL were diagnosed over an 11-year period (1984 to 1995) at our Department. Of these, 105 cases (56.8%) were nodal and 80 cases (43.2%) extranodal in origin. The data regarding all the cases of NHLs are summarized in Table I. More than half of the cases (70.8%) were males and the male-to-female ratio was 2.4. Males had a mean age of 36.4 while females had 34.7 years (Table I).

When charted by decades (Fig. 1) most cases showed an accumulation in the fourth decade. The ages of 185 patients ranged from three to 75 years and the mean age was 36.3 (Fig 1).

The histological distribution of 185 NHL cases according to the classification of the Working Formulation is in Table II. As shown in Table II, the major group was intermediate grade lymphomas with 106 cases (57.4%). As to distribution according to grade of all cases, 43 (23.2%) were in low grade, 106 (57.4%) were in intermediate grade, 30 (16.2%) were in high grade and six (3.2%) were in miscellaneous group. Of the cases, 23 (12.4%) were follicular lymphomas and 162 (87.6%) were diffuse lymphomas. Fifty-four (29.2%) cases were diffuse large cell lymphomas, which were the most frequent histopathologic subtype. Follicular mixed cell lymphoma was the histopathological subtype that appeared the least common. Follicular large cell lymphoma was not established. There was a male predominance in all histologic types except for the follicular small cleaved cell and small noncleaved cell lymphomas. Small noncleaved cell and lymphoblastic type were the two histopathologic subtypes having the lowest mean age with 16.3 and 20.7 years, respectively (Table II).

Table I. Summarization of the data NHL cases

Location	Male		Female		Total		M/F	Mean	Age
	Cases	%	Cases	%	Cases	%		Male	Female
Extranodal	54	67.5	26	32.5	80	43.2	2.1	33.9	18.7
Nodal	77	73.3	28	26.7	105	56.8	2.7	39.0	20.4
Total	131	70.8	54	29.2	185	100	2.4	36.4	19.6

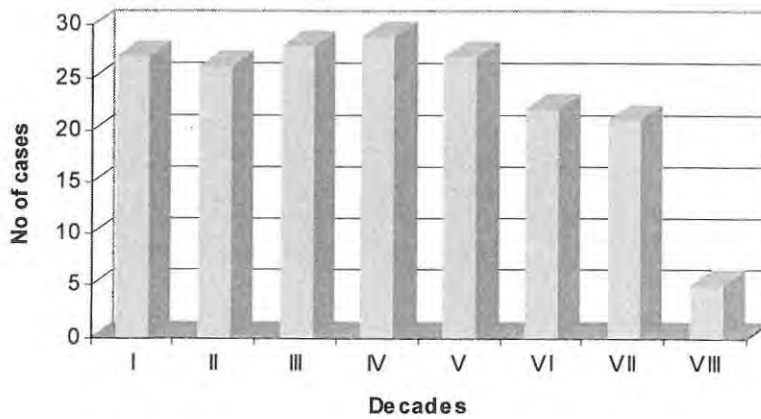


Figure 1. Distribution of cases according to decades

Table II. Age and sex distribution by histologic types

Histologic Type	Cases	%	M/F	Mean age	Age range
LOW GRADE	43	23.2	2.3	29.718.9	3-75
Small lymphocytic	20	10.8	9	28.618.6	6-65
Follicular small cleaved cell	20	10.8	1	32.619.8	8-75
Follicular mixed cell	3	1.6	2	18.016.1	3-35
INTERMEDIATE GRADE	106	57.4	2.6	40.118.9	5-75
Follicular large cell	0	0	0	0	0
Diffuse small cleaved cell	27	14.6	2.3	41.119.8	5-70
Diffuse mixed cell	25	13.6	3.2	36.020.9	5-72
Diffuse large cell	54	29.2	2.4	41.517.5	7-75
HIGH GRADE	30	16.2	2.8	28.523.7	4-70
Immunoblastic	12	6.5	3	42.521.9	12-70
Lymphoblastic	12	6.5	5	20.720.7	4-65
Small noncleaved cell	6	3.2	1	16.321.7	4-58
OTHER	6	3.2	2	54.018.9	23-73
TOTAL	185	100	2.4	36.320.5	3-75

Table III. Male to female ratio and mean age in the various series

	Current series	Walter et al(8)	Sarpel et al(6)	Liang et al(9)	Raemaekers et al(10)	Salem et al(11)	Lieberman et al(12)
Male-to-female ratio	2.4	2.5	1.7	1.2	1.5	1.5	1.5
Mean age	36.3	44	43	54	56	45	56

Table IV. Comparisons of histologic grades in various countries

Region- COUNTRY	LOW GRADE		INTERMEDIATE GRADE		HIGH GRADE		TOTAL CASES
	n	%	n	%	n	%	
Diyarbakır-TURKEY	43	23.2	106	57.3	30	16.2	185
NCI (5)	389	33.8	427	37.1	198	17.2	1175
Adana-TURKEY (6)	45	25.0	101	58.0	30	17.0	185
GABON (8)	7	10.4	21	31.3	28	41.9	67
Beurit-LEBANON (11)	72	17.5	170	40.5	145	35.0	417
KOREA (14)	4	5.1	54	68.4	21	23.3	79
CHINA (15)	41	16.5	58	21.2	150	62.5	249
Copenhagen-DENMARK (16)	178	27.0	181	27.5	243	36.9	658
Guangzhou-CHINA (1)	24	12.4	75	39.1	83	43.3	192
Nebraska-USA (1)	94	18.8	269	53.9	131	26.5	498
Hong Kong (9)	122	14.5	420	49.7	134	16.0	840
NewYork-USA (12)	142	29.5	257	53.3	57	11.8	482

Table V. Paired comparisons by types of NHLs with various series of different countries

Region		SL	FSC	FM	FL	DSC	DM	DL	IBL	LBL	SNC	Other	Total
Diyarbakır	Cases	20	20	3	0	27	25	54	12	12	6	6	185
	%	10.8	10.8	1.6	0	14.6	13.6	29.2	6.5	6.5	3.2	3.2	
Adana (6)	Cases	39	6	0	0	58	8	35	15	13	2	3	185
	%	22.0	3.0	0	0	33.0	4.0	20.0	9.0	7.0	1.0	1.0	
Gabon (8)	Cases	7	0	0	1	0	5	15	9	2	17	11	67
	%	10.4	0	0	1.5	0	7.5	22.4	13.4	3.0	25.4	16.4	
Beurit (11)	Cases	29	37	6	8	29	19	114	88	33	24	30	417
	%	7.0	9.0	1.5	2.0	7.0	4.5	27.0	21.0	8.0	6.0	7.0	
Copenhagen (16)	Cases	51	93	34	23	32	50	76	146	66	31	56	658
	%	7.7	14.1	5.1	3.5	4.9	7.6	11.5	22.2	10	4.7	8.5	
Hong Kong (9)	Cases	32	52	38	13	52	94	261	61	48	19	164	840
	%	3.8	6.2	4.5	1.5	6.2	11.0	31.0	8.0	5.7	2.3	19.4	
Nebraska (1)	Cases	40	16	38	42	29	39	117	108	13	10	46	498
	%	8.0	3.2	7.6	8.4	5.8	7.8	23.5	21.8	2.6	2.1	9.2	
NCI (5)	Cases	41	259	89	44	79	77	227	91	49	58	161	1175
	%	3.6	22.5	7.7	3.8	6.9	6.7	19.7	7.9	4.2	5.0	11.8	
New York (12)	Cases	42	78	22	15	67	10	165	28	18	11	26	482
	%	3.7	16.2	4.6	3.1	13.9	2.1	34.2	5.8	3.7	2.3	5.4	

Table VI. Frequency in the various series follicular lymphoma

	Diyarbakır	Adana	Gabon	Beurit	Copenhagen	Hong Kong	Nebraska	NCI	NewYork
Cases	23	6	1	51	150	103	96	392	115
%	12.4	3.0	1.5	12.5	22.7	12.2	19.2	34.0	23.9

DISCUSSION

The incidence of non-Hodgkin's lymphoma varies considerably worldwide. Epidemiologic studies of specific geographic areas have been hampered in the past by the lack of a uniform classification scheme, which made meaningful comparisons between studies difficult (1). In this study, we classified the NHLs from Diyarbakır (Turkey) according to the Working Formulation scheme, which permitted a statistical comparison of clinical and histologic data with National Cancer Institute (NCI) data.

Clinical presentation, histologic condition and natural history of NHL show differences according to the geographic location of the disease (6). NHL constitutes 3.0% of all malignancies in Western countries, whereas the relative frequency rate increases to 8.0% in Turkey, and to 12.0% in the Middle East countries (Lebanon, 12.0%; Saudi Arabia, 10.3%; Egypt, 11.8%; and this study, 6.8%) (7).

Male to female ratio and mean age in our series and various series are shown in Table III. There was a male predominance in all series. In our series according to other series mean age is the lowest age (Table III).

The nodal disease is mainly present in Western countries and the extranodal disease constitutes approximately 10.0% to 24.0% of all of the cases (13). In the developing countries, extranodal presentation could account for more than 40.0% of all NHL cases (Jordan, 43.3%; Lebanon 44.0%; and the current group 43.2%) (11). One reason for this high incidence of extranodal lymphomas in the Middle East is the increased frequency of the gastrointestinal NHL in the same region. The histologic condition of NHL also shows a difference between the Western and developing countries (6) (Table IV).

Our data regarding the rates of low, intermediate and high grade lymphomas is shown in Table IV along with the data from various studies conducted in

different countries and regions of the world. Our distribution according to grades of lymphomas shows striking parallelism with that from the series of Adana (6) (Turkey) and similar relatively in many ways to the series from Nebraska (1), Hong Kong (9) and New York (12). Data from The National Cancer Institute (5) (USA), Gabon (8), Beirut (11), Korea (14), China (15), and Guangzhou (1), however, is markedly different from ours. When compared with the results of the series from several developing countries such as China (15), Gabon (8) and Korea (14) significant differences can be seen. In summary, our distribution of lymphoma types exhibits an intermediate position between the developed and developing countries. Similar comparisons with other reports according to the histologic types have been made in Table V.

The disparity in incidence rates and the differences in the relative frequencies of various histologic types of lymphoma among different populations are well recognized (9). The fact that we have prominently lower rates of follicular lymphomas in comparison to the ones from the NCI (5), Nebraska (1), New York (12) and Copenhagen (16) series is a striking finding. Another important finding is that small lymphocytic lymphoma has a significantly higher rate in our cases than all other reports excluding the NCI (5), Hong Kong (9) and New York (12) series. As far as the high grade lymphomas, lymphoblastic lymphoma has significantly a higher rate than USA-based studies while with all other studies there seems to be no difference in this respect.

Small noncleaved cell and lymphoblastic subtypes are the two most common histopathologic types in children. Diffuse large cell and diffuse mixt subtypes formed the two most important groups in adults. In the present series as well as in developing countries the incidences were slightly more frequent in developing countries compared with other histologic subtypes of NHL (Table V).

The most remarkable feature of NHL seen in the present series was the very low relative frequency of follicular or nodular lymphoma (12.4%). Table VI

shows the frequencies of follicular NHL from series reported from developed and developing countries. Follicular lymphoma represents approximately one third of NHLs in developed countries and 1.5 % to 12.5 % in developing countries (Table VI). Similar low frequencies for follicular lymphoma were reported from Egypt (3.6% of 484 NHLs) and Saudi Arabia (5.0% of 136 NHLs) (8).

The deficit of follicular lymphoma in developing countries remains unexplained, but different possibilities can be considered. First, it is well known that malignant lymphomas can change their morphologic appearance during the evolution of the disease. Low grade NHLs may undergo transformation to a more aggressive histologic subtype: Progression from follicular to the diffuse pattern has been observed in serial biopsy specimens or at autopsy (17, 18). These changes in architectura pattern may or may not be associated with a transformation of the original neoplastic cell population. As NHL transformation occurs generally after several years of the illness, this event may be of importance in developing countries where patients usually search for medical care late after the onset of the disease. Second, the geographic variation of the frequency of follicular lymphoma correlates with socioeconomic status and suggests a dependence on life standarts and/or environmental factors (8).

It is known that environmental factors play a role in the pathogenesis of NHLs along with genetic ones. Japan has a high incidence of adult T cell lymphoma/ leukemia, which is endemic to certain areas (19, 20). The United States shows a logarithmic rise with increasing age, which is preceded by a peak before adolescence and a drop in the late-teenage years (21). An increased risk for non-Hodgkin's lymphoma has been associated with farming (22). In Nebraska, persons living in countries with heavy fertilizer use have an increased risk for non-Hodgkin's lymphoma (23). Pesticide use has also been implicated in the etiology of non-Hodgkin's lymphoma (24). In Nebraska, environmental factors associated with intense agricultural activity may also play an important role

in the etiology of non-Hodgkin's lymphoma (22, 23). We conclude that our values were found as between the results of developed countries such as Denmark, Hong Kong and USA, and developing countries such as China, Gabon and Korea.

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