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ORIGINAL ARTICLE

The clinical and pathological features of patients with hematological neoplasms: A study of hospital-based Cancer Registry from western Turkey

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Summary

Purpose: *To evaluate the frequency and the main features of patients with hematological neoplasms (HNs) who were diagnosed between 1992-2005 at the Izmir Ataturk Education and Research Hospital (IAEAH), affiliated with Izmir Cancer Registry (ICR) database.*

Methods: *A total of 2,424 HNs were recorded with reference to ICD-0-3 according to Surveillance, Epidemiology, and End Results (SEER) data among 20,895 recorded cancer patients from 1993 to 2005. The percentages of male and female patients were 58.5% and 41.5%, respectively. The age ranges were as follows: 15-44 years (37.3%), 45-64 (36%), and > 64 (26.6%). One thousand and nineteen (56%) patients had B cell and 108 (5.9%) patients had T/NK (natural killer) cell lymphoid neoplasms. One hundred and ninety-four (10.7%) patients had lymphoblastic leukemia, 267 (14.7%) had Hodgkin's lymphoma (HL), and 603 (24.9%) had myeloid leukemia. Three hundred and five (16.7%) patients had extranodal involvement (in 1821 regions). The major extranodal location was the stomach.*

Conclusion: *It seems that our data make a contribution to the relevant literature, because the epidemiologic data of Turkey are inadequate, and hematopoietic neoplasms have different geographic distribution.*

Key words: hematological neoplasms, Turkey

Introduction

Hematological malignancies are malignant neoplasms arising from the bone marrow and the lymph nodes. A disease affecting one of these tissues may also affect the other as well. For instance, although lymphoma is simply defined as a disease of lymph nodes, it often spreads to the bone marrow and blood [1,2].

HNs originate from either of the two major blood cell lineages: myeloid and lymphoid cell lines. While the myeloid cell line normally produces granulocytes, erythrocytes, thrombocytes, macrophages and mast cells, the lymphoid cell line produces B-cells, T-cells, NK cells and plasma cells. Therefore lymphomas, lymphocytic leukemias, and multiple myeloma (MM) arise from the lymphoid line, while acute and chronic myelogenous leukemia, myelodysplastic syndromes and myeloproliferative diseases originate from the myeloid cell line [1,2]. Hematological neoplasms including non-Hodgkin's lymphoma (NHL), HL, MM, and acute (ALL) and chronic lymphocytic leukemia (CLL) vary widely according to morphology, immunophenotype, cytogenetic, molecular features and clinical behavior; on the other hand, they are a closely related group of neoplasms [3].

Epidemiological investigations have revealed great variations in the patterns of cancer in the different parts of the world. Specific lymphoid neoplasms occur more frequently in definite geographic areas. For example, follicular lymphomas are rare in Latin America and Asia, whereas Burkitt's lymphoma is seen more frequently in the tropical Africa, and the adult T-cell leukemia/lymphomas are more common in south-east Japan [3,4].

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In this study, we evaluated the frequency and the main features of patients with HNs diagnosed between 1992-2005, at the IAEAH, which is one of the biggest hospitals in the city, and is associated with the ICR database. Izmir and surroundings are located on the west part of Turkey. The ICR, which is the first population-based cancer registry organized in Turkey, is also a member of the European Network of Cancer Registries (ENCR) [5].

In the present study, we also aimed to make a contribution to the epidemiology of hematopoietic neoplasms using the international terminology and the international registration rules of cancer.

Methods

Among 20,895 tumors registered between October 1993 and October 2005 by the ICR, 2,424 patients with histologically confirmed HNs were recorded. The cancer registry has been created by CANREG-3, a software developed by the International Agency of Cancer Registry (IACR). The diagnosis and the histologic and topographic classification of hematopoietic neoplasms were classified according to the 3rd edition of the International Classification of Diseases for Oncology (ICD-O-3) [6]. The subgroups obtained from the histologic and topographic records were reclassified according to Revised European-American Classification of Lymphoid Neoplasms/World Health Organization Classification of Lymphoid Neoplasms (REAL/WHO) [7]. The demographic data were also obtained from the same database.

Statistical analysis

Analysed were the subgroups created from histologic and topographic characteristics and also the incidence of HNs by age and gender.

In statistical analysis, descriptive tests with percents were performed by SPSS 11.0 and Epi-info 6.0 softwares.

Results

Among 2,424 patients, 1,821 (75.1%) had lymphoid and 603 (24.9%) had non-lymphoid hematologic malignancies. Four hundred and twenty of the patients (69.6%) with non-lymphoid hematologic neoplasms had AML and 172 (28.5%) CML. Of the patients with lymphoid neoplasms, 1,019 (56%) had B-cell lymphoid neoplasms, 108 (5.9%) T/NK-cell lymphoid neoplasms, 194 (10.7%) had lymphoblastic leukemia/lymphomas, and 267 patients (14.7%) had HL. Diffuse large B-cell lymphoma (DLBCL) was the histological subtype most commonly seen and was recorded in 443 patients (43.4%). The other common subtypes of B-cell neoplasms were CLL/small lymphocytic lymphoma (SLL) (27.3%) and follicular lymphoma (4.0%). Of the patients with HL, mixed cellularity subtype was the most prominent histological type (109 patients, 41.3%). The characteristics of the subgroups of the HNs are summarized in Table 1.

Of all patients with lymphoid neoplasms 305 (16.7%) had extranodal involvement. The majority of those patients had gastrointestinal tract (GI) involvement (36.4%), and the stomach was the most common primary site (28.2%). The other involved sites were as follows: Waldeyer's ring 22.3%, skin 17.1%, and peritoneal/pleural surfaces 6% (Table 2).

The age and gender distribution of all patients is shown in Table 3. Briefly, the incidence of lymphoblastic leukemia/lymphomas (71.7%) was significantly increased in the 15-44 years age group. Also, 65.5% of the patients with HL belonged to the same group. On the other hand, 53.9% of patients with plasma cell neoplasms were in the 45-64 years age group.

Discussion

The incompatibility and the heterogeneity in the definition and the classification of HNs, as well as their different and coding of topography cause many difficulties in the assessment of their subtypes [8,9]. The international formation of tumor registries based on the rules of IARC has greatly aided the diagnosis and analysis of cancer patients [10-14]. Unfortunately, data regarding the real cancer incidence and the survival of cancer patients have never been satisfactory for a defined population in Turkey [14]. This study is an important attempt to investigate hematological malignancies, using hospital-based data of ICR in Turkey, which included the highest patient number among the studies that have been published in the middle and south-east parts of Turkey [15-18].

In 2001, WHO proposed a new system for classifying hematopoietic neoplasms, which combines morphology, immunophenotype, cytogenetic and molecular characteristics, as well as clinical behavior, and some well known aspects of etiology and pathogenesis into the definition of each disease subtype [3,7]. Moreover, WHO classification reveals the interrelation of the different lymphoid neoplasms based on the cell of origin. In the REAL classification, 3 major categories of lym-

Table 1. The incidence of hematopoietic neoplasms by subtype and the ICD-O-3 codes

Hematologic neoplasm subtype	*ICD-O-3 codes**	*n*	*%*	*N (%)*
Lymphoid neoplasms				1821 (75.1)
B-cell lymphoid neoplasms		1019	56	
DLBCL	9680, 9684	443	43.4	
Marginal zone lymphoma	9689, 9699	15	1.5	
Follicular lymphoma	9690-9691, 9695, 9698	41	4	
CLL/SLL	9670, 9823	278	27.3	
Mantle cell lymphoma	9673	7	0.7	
Burkitt's lymphoma/leukemia	9687	5	0.5	
Plasma cell neoplasms		217	21.3	
Multiple myeloma	9732	180	17.7	
Plasma cell leukemia	9733	2	0.2	
Plasmacytoma	9731, 9734	35	3.4	
Hairy cell leukemia	9940	8	0.8	
Lymphoplasmacytic lymphoma	9671	4	0.4	
Waldenström macroglobulinemia	9761	1	0.1	
T/NK-cell lymphoid neoplasms		108	5.9	
Mycosis fungoides/Sezary syndrome	9700	28	25.9	
Peripheral T-cell lymphoma	9702, 9708, 9827	45	41.7	
Angioimmunoblastic lymphoma	9705	2	1.9	
Anaplastic large-cell lymphoma	9714	11	10.2	
T/NK-cell lymphoid neoplasms	9709, 9719, 9717	22	20.4	
Lymphoblastic leukemia/lymphomas		194	10.7	
B-cell lymphoblastic leukemia/lymphoma	9836	1	0.5	
T-cell lymphoblastic leukemia/lymphoma	9729, 9837	4	2.1	
Unknown type lymphoblastic leukemia/lymphoma	9727, 9835	189	97.4	
Prolymphocytic leukemia	9832	2	0.1	
Unknown type lymphoid neoplasms	9590-9591, 9596, 9675, 9820	231	12.7	
Hodgkin's lymphoma		267	14.7	
Classical Hodgkin's lymphoma		264	98.8	
Nodular sclerosis	9663, 9664-9665, 9667	78	29.5	
Lymphocyte predominant	9651	22	8.3	
Mixed cellularity	9652	109	41.3	
Lymphocyte depleted	9653, 9655	16	6.1	
Unknown type classical Hodgkin's lymphoma	9650, 9662	39	14.8	
Nodular lymphocyte predominant Hodgkin's lymphoma	9659	3	1.2	
Nonlymphoid neoplasms	—			603 (24.9)
Myeloid leukemias				
Acute myeloid leukemias	9840, 9861, 9866-9867, 9871, 9872, 9873, 9874, 9891, 9895-9896, 9910, 9931	420	69.7	
Chronic myeloid leukemias	9863, 9875, 9945	172	28.5	
Unknown type myeloid leukemias	9860	7	1.2	
Unknown type leukemias	9800-9801	4	0.6	
Total				2.424 (100)

*International Classification of Diseases for Oncology (3rd Edn)
DLBCL: diffuse large B cell lymphoma, CLL/SLL: chronic lymphocytic leukemia/small lymphocytic lymphoma

phoid neoplasms are defined with special emphasis on cytology, morphologic grades and clinical behavior [3,7]. Since the etiology of most lymphoid neoplasms is still obscure, the knowledge about their incidence and the behavior of subtypes may clarify the best ways for future etiologic studies, as well as the development of newer therapeutic strategies [3]. We, herein, evaluated 2,424 HN lymphoid neoplasms diagnosed in Izmir using the recent classifications.

NHLs are the 5th most common hematologic malignancies, and the 6th leading cause of death in western countries [19]. In the last decades, the incidence of NHL is increasing; the reasons are unknown. In USA, the incidence of NHL has been increasing at a rate of 3-4% per year [3,20]. Incidence rates vary, with the highest reported in USA, Europe and Australia, and the lowest in Asia [21-25].

The incidence of subtypes show diversity according to the geographic regions and ethnicity [4,20,26,27]. In North America and Europe, 85-95% of the patients

Table 2. Sites of extranodal involvement in lymphoid neoplasms

Extranodal localization *All patients (16.7% of HNs)*	*Patients, n*	*%*
Gastrointestinal involvement	111	
Small bowel	13	11.7
Stomach	86	77.5
Colon and rectum	12	10.8
Waldeyer's ring	68	22.3
Peritoneal/pleural involvement	1	0.3
Central nervous system	20	6.6
Bone	19	6.3
Skin	52	17.1
Testes	5	1.6
Uterine/ovarian	3	1
All other sites	26	8.5
Total	305	100

with NHL have B-cell lymphoma [4,20,26]. On the other hand, higher relative incidence of T-cell NHLs have been demonstrated in Japan, Asia and Africa. The most common NHL types in North America are follicular small cleaved cell lymphoma (20-30%) and DLBCL (30-40%). In the present study, although the ratio of B-cell NHLs was similar to the world ratio (accounted for 78% of the patients), the general characteristics of lymphomas from AEAH in Izmir were found to be similar to the East and different from the West with regard to the lower frequency of follicular lymphomas that constitute 4.1% of B-cell NHLs and 2.2% of all lymphoid neoplasms [3,4,28]. DLBCL, CLL/ SLL, and plasma cell neoplasms were the first 3 most common subtypes of B-cell NHLs (43.4, 27.3 and 21.3%, respectively) and all lymphoid neoplasms (24.3, 15.6 and 11.9%, respectively; Table 1).

In the study by Morton et al., the relative distribution of subtypes of lymphoid neoplasms changed according to race and age. DLBCL accounted for 21% of all lymphoid neoplasms in whites, and CLL/SLL, plasma cell neoplasms, and follicular lymphoma accounted for 16, 15 and 10%, respectively. The most common lymphoid neoplasms' subtypes in Asians were DLBCL (29%), plasma cell neoplasms (17%), and follicular lymphoma, CLL/SLL, and lymphoblastic leukemia/lymphoma each accounting for about 6-7% of the lymphoid neoplasms [3]. The data of our study are similar to those obtained from Asian populations. In the above-mentioned study, the majority of plasma cell neoplasms were MM. Solitary plasmacytoma accounted for ≤ 6% of the cases, and just occasional cases have been diagnosed as plasma cell leukemia [3]. In the present study, the majority of plasma cell neoplasms was MM (21.3%), which is in line with the relevant literature. The reason for the difference of the ratios between south-east Turkey and the present study is the different classification [16].

NHL is primarily a disease of older age, with a median age at diagnosis of 65 years [29] and a peak at the age of 80-84 years in white Americans [20]. In African-American patients, the peak age is about 55-64 years [30]. In some studies performed in Asia, the peak age was 40-50 years [20,26]. In the present study, apart from the lymphoblastic leukemia/lymphomas and HL groups, the majority of patients were 45-64 year-old (Table 3), similar to the peak age of African-American patients [29,30].

It is well known that HL has a bimodal incidence curve: the first one includes young adulthood patients (15-35 years) and the second one includes individuals over 45 years of age [31]. In developing countries, the incidence of HL increases in patients younger than 15 years, and the peak is not significant in adolescent and young adults as in developed countries [32]. In the pres-

Table 3. The incidence of hematologic neoplasms by age and gender

Hematologic neoplasm subtype		*Gender*	*Age (years)*		
		M/F	*15-44*	*45-64*	*> 64*
	n	*n (%) / n (%)*	*n (%)*	*n (%)*	*n (%)*
Lymphoid neoplasms	1821	1082 (59.4) / 739 (40.6)	665 (36.5)	662 (36.6)	494 (27.1)
B-cell lymphoid neoplasms	1019	593 (58.2) / 426 (41.8)	232 (22.8)	430 (42.2)	357 (35.0)
Plasma cell neoplasms	217	129 (59.4) / 88 (40.6)	34 (15.7)	117 (53.9)	66 (30.4)
T/NK-cell lymphoid neoplasms	108	65 (60.2) / 43 (39.8)	38 (35.2)	42 (38.9)	28 (25.9)
Lymphoblastic leukemia/lymphomas	194	108 (55.7) / 86 (44.3)	139 (71.7)	42 (21.7)	13 (6.7)
Hodgkin's lymphoma	267	173 (64.8) / 94 (35.2)	175 (65.5)	59 (22.1)	33 (12.4)
Extranodal involvement of lymphoid neoplasms	305	163 (53.4) / 142 (46.6)	96 (31.5)	119 (39.0)	90 (29.5)
Nonlymphoid neoplasms	603	336 (55.7) / 267 (44.3)	238 (39.5)	214 (35.5)	151 (25.0)
Acute myeloid leukemias	420	241 (57.4) / 179 (42.6)	173 (41.2)	147 (35)	100 (23.8)
Chronic myeloid leukemias	172	90 (52.3) / 82 (47.7)	61 (35.5)	64 (37.2)	47 (27.3)
Total	2424	1418 (58.5) / 1006 (41.5)	903 (37.3)	876 (36.1)	645 (26.6)

M: males, F: females

ent study 65.5% of the patients with HL were in 15-44 years age group.

In an international analysis of 1,546 patients with HL an increased risk for EBV-associated HL was demonstrated in Hispanics (vs. whites), in patients who had mixed cellularity histologic subtype (vs. nodular sclerosis), in children who came from less developed regions (vs. more developed), and in young adult men (vs. women) [33]. Nodular sclerosis is the most common (58%) histologic subtype in USA and the other developed countries [34]. In the present study, 14.7% of all patients had HL, and 98% of them had classical HL. Being the most common subtype, 41.3% of patients with classical HL were classified as mixed cellularity subtype, and nodular sclerosis was the second most common subtype (29.2%). Mixed cellularity HL was reported more frequently in studies from eastern countries [35].

In our study, 305 patients had extralymphatic involvement, and the primary site was the G.I. tract in 36.4% of them (Table 2) with stomach being the most common site (77.5% of patients with G.I. involvement) as in previously published studies in Turkey [17,18]. Waldeyer's ring was the second most commonly affected site (22.3%). In the study performed in southeast Turkey, G.I. tract involvement was similar to our results, whereas the rate of Waldeyer's ring involvement was lower [16]. Our results are also in concordance with the results of studies performed in Japan and Australia (gastric involvement 70 and 75%, respectively) [36,37]. However, the above-presented rates may not reflect the real frequency of G.I. involvement, because endoscopy is usually performed only in patients who have G.I. symptoms [38].

As a heterogeneous group of malignancies, HNs constitute the 5th most common group of cancers in western countries. The incidence and several clinicopathological features of these neoplasms vary among several geographical regions. Therefore, there is a strong need to perform multicenter, population-based studies showing the true incidence of HNs in developing countries including Turkey, where the data regarding this field are inadequate. The organisation and adaptation of these efforts with a National Cancer Registry program may contribute to the development of more effective and specific treatment algorithm for hematological malignancies.

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