Malignant Lymphomas

Clinicopathological analysis of malignant lymphoma in Taiwan, defined according to the World Health Organization classification

We report the distribution and clinicopathological characteristics of malignant lymphomas in Taiwan, defined according to the WHO classification. Data including age and gender of the patients, clinical staging and disease courses were collected for 598 cases of malignant lymphomas. The results showed that the epidemiological characteristics of malignant lymphomas in Taiwan are similar to those in other Asian countries except for a lower incidence rate of T/NK cell lymphoma.

haematologica 2005; 90:1703-1705
(*http://www.haematologica.org/journal/2005/12/1703.html*)

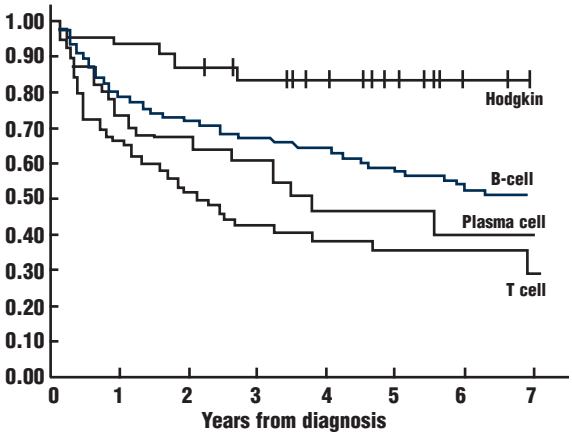

Figure 1. Overall survival curve of 598 patients with malignant lymphomas.

Malignant lymphomas are a varied group of malignancies with many different clinical presentations, histological subtypes and biological behaviors. Compared with Western regions, Asian countries have been reported to have higher rates of T/NK cell lymphoma (TCL) and a low incidence of Hodgkin's lymphoma. To assess the clinical characteristics of lymphoma in Taiwan, we retrospectively analyzed 598 malignant lymphomas in Taiwan, defined according to the WHO classification.[1] We also compared our observations with previously reported data from other Asian countries. We found 482 cases (80.6%) of B-cell lymphoma, 74 (12.4%) of TCL and 42 (7%) of Hodgkin's lymphoma during the period from 1995-2002, including 234 cases (39%) from consultation files sent from all over the island. The primary sites at presentation were lymph node (42.1%), an extra-nodal site (48.2%), bone marrow (8.9%) and spleen (0.8%). The incidence of TCL was relatively low compared with that reported in other Asian countries (18.9-23.6%)(Table 1).[2-6]

The commonest subtype in B-cell lymphoma was diffuse large B-cell lymphoma, followed by follicular lymphoma, plasma cell neoplasm, extranodal marginal zone lymphoma of the mucosa-associated lymphoid tissue (MALT) type, and mantle cell lymphoma. The distribution of the different subtypes was similar to that in other Asian countries, except for a higher incidence of follicular lym-

Table 1. Incidence rates of Hodgkin's and non Hodgkin's lymphoma: a comparison in Asian countries.

	Taiwan		Japan		Korea		Thailand	
	No.	%	No.	%	No.	%	No.	%
Total	598	100.0	2956	100.0	1548	100.0	425	100.0
Non-Hodgkin's lymphoma	556	93.0	2787	94.3	1463	94.5	389	91.5
B-cell neoplasm	482	80.6	2189	74.1	1097	70.9	255	60.0
T/NK cell neoplasm	74	12.4	558	18.9	366	23.6	88	20.7
NHL undefined	–	–	40	1.4	–	–	46	10.8
Unclassified and others	–	–	28	0.95	3	0.2	–	–
Hodgkin's lymphoma	42	7.0	141	4.8	82	5.3	36	8.5
B-cell neoplasms								
Precursor B-cell lymphoblastic lymphoma	4	0.7	75	2.5	8	0.5	–	–
B-cell chronic lymphocytic lymphoma	11	1.8	42	1.4	33	2.1	24	5.6
B-cell prolymphocytic lymphoma	0	0.0	2	0.07	–	–	–	–
Lymphoplasmacytic lymphoma	6	1.0	22	0.7	11	0.7	–	–
Mantle cell lymphoma	24	4.0	89	3.0	22	1.4	–	–
Follicular lymphoma	98	16.4	214	7.2	91	5.9	35	8.2
Marginal zone B cell lymphoma of MALT	34	5.7	270	9.1	243	15.7	–	–
Nodal marginal zone lymphoma	6	1.0	32	1.1	9	0.6	–	–
Splenic marginal zone B-cell lymphoma	1	0.2	4	0.14	–	–	–	–
Hairy cell lymphoma	0	0.0	5	0.17	–	–	1	0.2
Diffuse large B cell lymphoma	233	39.0	1065	36.0	641	41.4	114	26.8
NOS	221	37.0	1052	35.6	634	41.0	–	–
Mediastinal	12	2.0	8	0.3	7	0.5	–	–
Intravascular	0	0	3	0.1	–	–	–	–
Primary effusion	1	0.2	2	0.07	–	–	–	–
Burkitt's lymphoma	12	2.0	32	1.1	16	1.0	12	2.8
Unclassified	7	1.2	45	1.5	6	0.4	65	15.3
Plasmacytoma	4	0.7	35	1.2	–	–	4	0.9
Plasma cell myeloma	42	7.0	257	8.7	17	1.1	–	–
T/NK-cell neoplasms								
Precursor T-cell lymphoblastic lymphoma	9	1.5	55	1.9	42	2.7	10	2.4
T-cell prolymphocytic lymphoma	0	0.0	2	0.07	1	0.06	8	1.9
T-cell large granular lymphocytic leukemia	0	0.0	2	0.07	3	0.2	-	–
Aggressive natural killer cell leukemia	0	0.0	6	0.2	–	-	-	–
T/NK cell lymphoma, nasal and nasal-type	17	2.8	83	2.8	129	8.3	-	–
Mycosis fungoides/Sèzary syndrome	2	0.3	37	1.3	5	0.3	6	1.4
Angioimmunoblastic T-cell lymphoma	3	0.5	77	2.6	15	1.0	-	–
Peripheral T-cell lymphoma, unspecified	23	3.8	213	7.2	138	8.9	42	9.8
Adult T-cell lymphoma/leukemia (HTLV-1)	0	0.0	- *	-	1	0.06	-	-
Anaplastic large cell lymphoma	8	1.3	49	1.7	23	1.4	15	3.5
Primary cutaneous CD30 (+) T-cell lymphoma	2	0.3	8	0.3	–	-	–	–
Subcutaneous panniculitis-like T-cell lymphoma	3	0.5	2	0.07	11	0.7	–	–
Enteropathy-type intestinal T-cell lymphoma	6	1.0	8	0.3	1	0.06	–	–
Hepatosplenic γ/δ T-cell lymphoma	1	0.2	2	0.07	0	0	–	–
Unclassified	–	–	14	0.5	–	–	7	1.6
Hodgkin's lymphoma								
Nodular lymphocyte predominant	3	0.5	5	0.2	–	–	–	–
Lymphocyte rich	2	0.3	8	0.3	8	0.5	1	0.2
Nodular sclerosing	29	4.8	57	1.9	26	1.7	13	3.0
Mixed cellularity	2	0.3	52	1.8	38	2.5	16	3.8
Lymphocyte depletion	0	0.0	8	0.3	6	0.4	6	1.4
Unclassified	6	1.0	11	0.4	4	0.3	–	–

**Note: 238 cases of endemic adult T-cell lymphoma/leukemia in Kyushu were xcluded.*

phoma and a lower rate of extranodal marginal zone lymphoma of MALT type in our series. The low frequency of follicular lymphoma may be overlooked as diffuse lymphoma in other Asian studies. Some subtypes, such as hairy cell leukemia and T-cell large granular lymphocytic leukemia, were not observed in the current study. Perhaps these subtypes are very rare in Taiwan and the sample size may not have been large enough to detect any cases. The overall survival rate of patients with B-cell lymphoma was 72.3% and 58.9% at 2 and 5 years, respectively (Figure 1). Histological subtype and clinical stage were significant prognostic factors (p<0.0001).

Plasma cell myeloma was analyzed separately because its staging system and clinical presentation differ from those of non-plasma cell B-cell lymphoma. The 2- and 5-year overall survival for this disease was 66.3% and 45.5% (Figure 1). The 5-year overall survival of 17 cases with poor renal function type B (serum creatinine >2 mg/dL) was worse than that of patients with type A (serum creatinine <2 mg/dL) (11.4% vs 64.4%) indicating that renal insufficiency is a significant prognostic factor (p=0.003). Our patients had higher clinical stages (81%) and more frequently by had associated renal insufficiency (40%), explaining the poorer prognosis in the current study.

The frequently of TCL, in our study was relatively lower rate than that reported for other Eastern countries, including Hong Kong, Japan, Korea, Thailand and southern Taiwan, and more similar to that in Western regions.[7-9] Ko *et al*. reported that the incidence of TCL in Korea decreased in six years from 35.2% to 25%.[2-3] A similar trend was found in Japan. These changes in the rate of TCL might represent a true decrease in this disease in the Far East, although previous Asian studies may have overestimated the frequency of this lymphoma due to case selection bias or small numbers of cases. The prevalent histologic subtype of TCL was unspecified peripheral T cell lymphoma, followed by nasal type T/NK cell lymphoma, T-cell lymphoblastic lymphoma and anaplastic large cell lymphoma. The distribution of TCL subtypes was similar to that in other Asian countries. The low frequency of mycosis fungoides/Sézary syndrome may be a consequence of referral status and the relatively lower number of skin biopsy specimens in our center. There was an unusually high incidence of enteropathy-typed intestinal T-cell lymphoma (ETCL)(8.1%) in Taiwan, compared with other studies (0.3-1.4%).[2,4,7-8] This may suggest a possible geographic or ethnic role for ETCL in Taiwan. The overall survival of patients with TCL was 51.4% and 34.7% at 2 and 5 years, respectively (Figure 1). The 5-year overall survival of patients with TCL was significantly lower than that of patients with B-cell lymphoma (34.7% vs. 58.9%) in our study, resembling results of international lymphoma study group (41% vs. 53%).[9] Thus, T-cell immunophenotype is an independent and significant prognostic factor. Histological subtype and clinical stage were also significant prognostic factors (p<0.05). It was noteworthy that all six patients with ETCL died within 25 months of diagnosis.

Hodgkin's lymphoma accounts for 20-45% of malignant lymphomas in Western countries, but it is much less common in Asians with incidence rates ranging from 4.4% to 18%[2,4,6,10] comprising the 7% in this study. The most prevalent histologic subtype of Hodgkin's lymphoma was nodular sclerosis (69%). There was low incidence of mixed cellularity subtype in the current study. The 2- and 5-year overall survival was 86.9% and 83.5%, respectively (Figure 1). Two rare cases of primary bone marrow Hodgkin's lymphoma (5%) both died within one month of diagnosis, indicating that this form of lymphoma is a very aggressive variant. Patients with stage IV disease with bone marrow involvement had a poorer prognosis, compared to those with stage I- III disease without marrow involvement.

In conclusion, we believe that the current data represent the incidence rates and distribution of histologic types of malignant lymphoma in Taiwan. There are relatively lower incidence rates of TCL and Hodgkin's lymphoma. The immunophenotypes, histological subtypes and clinical stages are significant prognostic parameters. The WHO classification gives important prognostic information, reflecting the clinical outcome.

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Key words: malignant lymphoma, Taiwan, WHO classification.

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