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Non-Hodgkin's Lymphoma: A Histopathologic and Immunohistochemical Study of 79 Cases

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Recently immunophenotyping has become a valuable tool in the diagnostic workup of malignant lymphoma. We classified 79 consecutive cases of non- Hodgkin's lymphoma experienced at our hospital during the last two years according to the Working Formulation and immunologically using MT1, UCHL1 and MB2 monoclonal antibodies. The results of this study are as follows: 1) four cases (5.1%) were low grade, 54 cases (68.4%) were intermediate grade, and 21 cases (23.3%) were high grade. The most common subtype was 'diffuse, mixed' type, 2) fifty cases (63.3%) showed T-cell phenotype and 14 cases (17.7%) showed B-cell phenotype. Immunophenotying was impossible in 15 cases due to either double staining or negative staining. 3) the incidence of extranodal presentation was high (65.8%) and the most common extranodal site was the upper aerodigestive tract (29.1%) followed by the gastrointestinal tract (16.4%), and 4) MT1, UCHL1 and MB2 monoclonal antibodies are valuable markers of T- and B-cells in paraffin embedded tissue, enabling retrospective study. However, because these antibodies are not lineage specific, the results of immunostaining should be interpreted with caution.

Key Words: Non-Hodgkin's lymphoma, immunophenotyping

The classification of malignant lymphoma has evolved over the last 30 years. The histopathologic diagnosis and classification had been entirely dependent on morphologic findings and the Rappaport classification had been the most widely used scheme (Rappaport 1966). In light of the rapid development of immunology in the 1970s, several other classifications of malignant lymphoma, such as Lukes-Collins, BNLI, Kiel, Dorfman, and WHO have been reported (Lukes and Collins 1974; Bennet *et al*: 1974, Gerald *et al*: 1974; Lennert *et al*. 1975; Dorfman 1974; Dorfman 1977; Mathe *et al*. 1976). In 1982, the National Cancer Institute undertook a multi- institutional comparative study that resulted in a classification system called the 'Working Formulation of Non-Hodgkin's Lymphoma for Clinical Usage' (WF) (National Cancer Institute 1982). Since the biologic behavior of malignant lymphoma is known to vary according to its immunologic origin, determination of immunophenotype is clinically important (Grogan *et al*. 1985; Schuurman *et al*. 1988). Immunophenotyping of malignant lymphoma by morphologic features alone is not always reliable in determining immunologic lineage, so immunologic methods should also be employed. Immunophenotyping, especially for T-cells, had been difficult to perform and was limited to fresh tissue. So despite many retrospective studies on malignant lymphoma performed in Korea during recent years, few studies employed immunologic methods (Lee *et al*; Shin *et al*. 1983; Lee *et al*, 1985; Ahn *et al*. 1988). Malignant lymphoma of T-cell origin has been reported with high frequency in Asia, and the incidence of malignant lymphoma showing characteristic morphologic features of peripheral T-cell lymphoma is increasing at our own hospital. The present study is a retrospective analysis of non-Hodgkin's lymphoma based on both histopathologic and imunohistochemical studies using the recently developed MT1, UCHL1 and MB2 monoclonal antibodies in order to reclassify malignant lymphoma according to the cell of origin, clarify the incidence and characteristics of T-cell lymphoma and examine the usefulness of immunohistochemical staining employing MT1, UCHL1 and MB2 in the diagnosis of malignant lymphoma.

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MATERIALS AND METHODS

Materials

Seventy-nine consecutive cases of non-Hodgkin's lymphoma admitted to Severance Hospital from January 1987 to December 1988 were selected.

Methods of Pathologic Examination

Each specimen, fixed in formalin and embedded in paraffin, was cut at 5μ thick sections by a microtome. Sections of each specimen were stained with hematoxylin-eosin.

Immunohistochemical Staining

Immunohistochemical staining of the paraffin sections was done by 3 step sandwich immunoperoxidase methods using PAP system kit purchased from BioGenex Laboratories (San Ramon, CA, U.S.A). Sections were dewaxed in xylol for 20 minutes, hydrated through graded alcohols for 5minutes and immersed in distilled water for 30 minutes. Endogenous peroxidase activity was blocked with 0.03% hydrogen peroxide for 30 minutes. Trypsinization was not performed. All sections were then washed in water and then immersed in Tris-Buffer for 20 minutes. The sections were immersed in normal goat serum for 20 minutes followed by incubation with moncolonal antibodies overnight 4°C. The MT1 and MB2 antibodies were purchased from Biotest Diagnostics (W.Germany) and the dilution was 1:5. The UCHL1 was purchased from Dakopatts (Copenhagen, Denmark) and the dilution was 1:100. After washing in Tris-Buffer for 10 minutes, the sections were incubated with link antibody for 30 minutes. After 10 minutes wash, labelling antibody was applied for 30 minutes. After another wash the sections were stained with substrate solution containing aminocarbazole. Nuclear counterstaining was performed with Harris hematoxylin.

Table 1. Classification of NHL according to WF

Grade	Type	Number (%)
Low	Small lymphocytic	4 (5.1)
	Follicular, small cleaved	– (–)
	Follicular, mixed	– (–)
Intermediate	Follicular, large	– (–)
	Diffuse, small cleaved	2 (2.5)
	Diffuse, mixed	45 (57.0)
	Diffuse, large	7 (8.9)
High	Large cell, immunoblastic	11 (13.9)
	Lymphoblastic	7 (8.9)
	Small noncleaved	3 (3.8)
Total		79 (100.0)

Clinical Data

The medical records of all patients were reviewed. Pertinent clinical observations, such as primary site of origin, age and sex were selected for correlation with pathologic findings.

RESULTS

Classification of non-Hodgkin's lymphoma according to WF

Of the 79 cases studied, the most common were intermediate grade lymphomas (54 cases, 68.4%) followed by high grade (21 cases, 23.3%) and then low grade (4 cases, 5.1%). All low grade lymphomas were 'small lymphocytic' type and there were no cases of follicular lymphoma. Of the 54 cases of intermediate grade, the most common one was 'diffuse, mixed' type (45 cases, 57.0%) followed by 'diffuse, large' type (7 cases, 8.9%) and 'diffuse, small cleaved' type (2 cases, 2.5%). Within high grade lymphomas, there were 11 cases (13.9%) of 'large cell, immunoblastic' type, 7 cases (8.9%) of 'lymphoblastic' type and 3 cases (3.8%) of 'small noncleaved' type (Table 1).

Age and Sex Distribution

The peak incidence of malignant lymphoma was in the third decade (15 cases, 19.0%) followed by the fifth decade (14 cases, 17.7%), and the second decade (11 cases, 13.9%). Of the 4 cases of 'small lymphocytic' type, 3 cases affected elderly patients over 70 and 9 out of the 11 cases of 'large cell, immunoblastic' type occurred in patients over 40 years of age. 'diffuse, mixed' type occurred with a relatively even distribution in all age groups. Five out of the 7 cases of 'lymphoblastic' type and all 3 cases of 'small noncleaved' type affected patients below 20 years. The incidence of malignant lymphoma was about 2 times greater in men than in women (Table 2).

Distribution of the Primary Site of Mallignant Lymphoma

Extranodal lymphomas were more common than

Table 2. Histologic type and age distribution

WF	Results of stain	Age								
		-10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90
Low	Small lymphocytic	–	–	–	–	–	–	–	3	–
	Follicular, small cleaved	–	–	–	–	–	–	–	–	–
	Follicular, mixed	–	–	–	–	–	–	–	–	–
Intermediate	Follicular, large	–	–	–	–	–	–	–	–	–
	Diffuse, small cleaved	–	–	–	–	–	–	–	–	–
	Diffuse, mixed	2	4	12	1	7	5	10	4	–
	Diffuse, large	–	–	1	1	2	1	1	1	–
High	Large cell, immunoblastic	–	–	1	1	4	1	3	–	1
	Lymphoblastic	1	4	–	2	–	–	–	–	–
	Small noncleaved	1	2	–	–	–	–	–	–	–
	Total	4	11	15	5	14	7	14	8	1
	(%)	(5.1)	(13.9)	(19.0)	(6.3)	(17.7)	(8.9)	(17.7)	(10.1)	(1.3)

Male: 52 cases Female: 27 cases

Table 3. Distribution of the primary site of NHL

Site	Number (%)	Site	Number (%)
Lymph node	27 (43.1)	Tonsil	9 (11.4)
Neck	21 (26.6)	Nasal cavity	8 (10.1)
Mesentery	2 (1.3)	Skin	3 (3.8)
Axillary	1 (1.3)	Oral cavity	4 (5.1)
Inguinal	1 (1.3)	Brain	3 (3.8)
Paraaortic	1 (1.3)	Nasopharynx	2 (2.5)
Retroperitoneum	1 (1.3)	Epididymis	1 (1.3)
G-I tract	13 (16.6)	Ovary	1 (1.3)
Soft tissue	7 (8.9)	Breast	1 (1.3)

nodal lymphomas. Of the 79 cases studied, 27 cases (34.1%) occurred in lymph nodes and 52 cases (65.8%) occurred in extranodal sites. Of the 27 cases with nodal primaries, 20 cases occurred in the cervical lymph nodes. The distribution of extranodal lymphomas was as follows: upper aerodigestive tract (23 cases), gastrointestinal tract (13 cases), soft tissue (7 cases), skin (3 cases) and and central nervous system (3 cases) (Table 3).

Results of Immunohistochemical Staining

In control sections of reactive hyperplastic lymph nodes, MT1 and UCHL 1 antibodies showed strong membrane staining of T-lymphoctyes located predominantly in the paracortical areas (Fig. 1). However, macrophages and some cells in the germinal centers were also reactive. MB2 antibody showed cytoplasmic staining of the B-lymphocytes situated in the mantle zone and germinal centers with occasional staining of some cells located at the parafollicular areas (Fig.2) (Table 4).

Forty-one cases of malignant lymphomas showed positive membrane staining to MT1 and UCHL1 with negative staining to MB2, 6 cases showed positive membrane staining to only MT1, and 3 cases showed positive reaction to only UCHL1 (Fig. 3). So the total number of malignant lymphomas showing T-cell phenotype was 50 cases (63.3%) out of the 79 cases studied. There were 13 cases (16.5%) of malignant lymphoma with B-cell phenotype showing positive cytoplasmic staining only to MB2 antibody (Fig. 4). Four cases showed positive staining to both MT1 and MB2, 1 case showed positive staining to all three antibodies

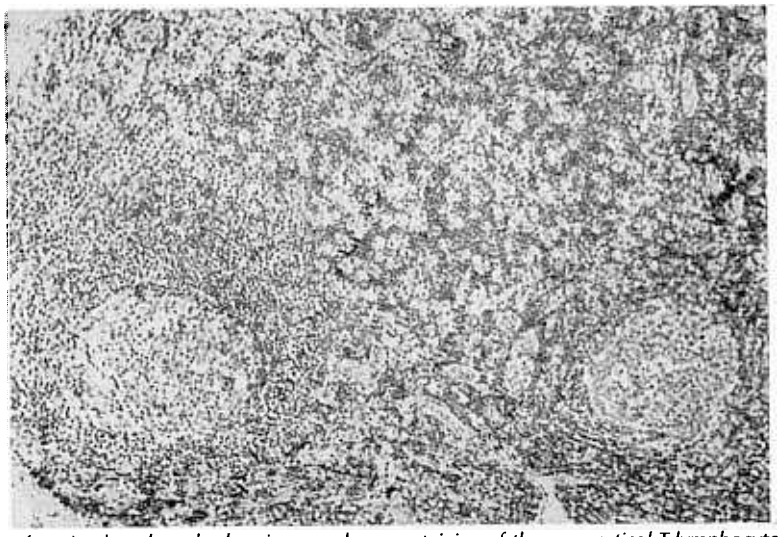

Fig. 1. *MT1 staining of reative lymph node showing memberane staining of the paracortical T-lymphocytes (PAP method with hematoxylin counter stain. ×100).*

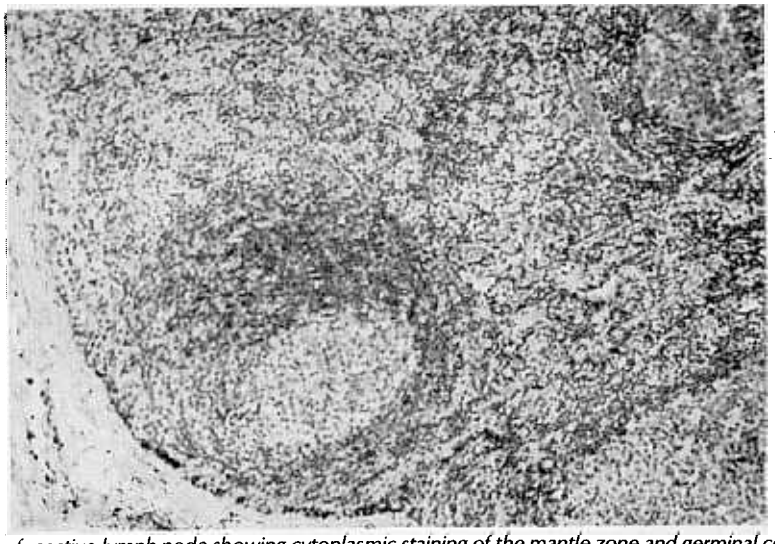

Fig. 2. *MB2 staining of reactive lymph node showing cytoplasmic staining of the mantle zone and germinal center B-lymphocytes (PAP method with hematoxylin counterstain. ×100).*

Table 4. Reactivity of MT1, UCHL1, MB2 within reactive lymph nodes

Cell type	MT1	UCHL1	MB2
T-lymphocyte			
Paracortical lymphocyte	+	+	−
B-lymphocyte			
Germinal center cell	−	−	+
Mantle zone cell	−	−	+
Plasma cell	−	−	−
Histiocyte	+	+	−

and 10 cases showed negative staining to all three antibodies. One out of the 4 cases of 'small lymphocytic' type, 36 out of the 45 cases of 'diffuse, mixed' type and 8 out of the 11 'large cell, immunoblastic type' showed T-cell phenotypes. In contrast 3 out of the 4 cases of 'small lymphocytic' type, 5 out of the 7 cases of 'Diffuse, large cell' type, 1 out of the 2 cases of diffuse, small cleaved' type, 1 out of the 3 cases of 'small noncleaved cell' type, and 2 out of the 11 cases of 'large cell, immunoblastic' type showed B-cell phenotypes (Table 5).

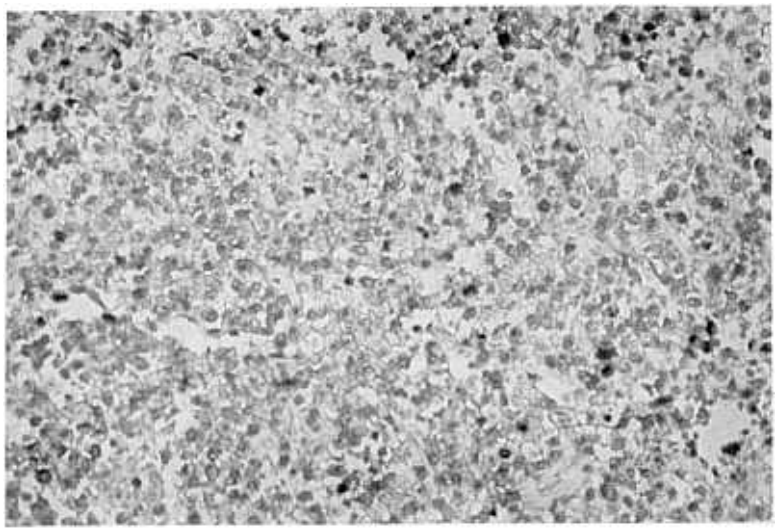

Fig. 3. MT1 staining of peripheral T-cell lymphoma showing strong membrane staining of the tumor cells (PAP method with hematoxylin counterstain. ×200).

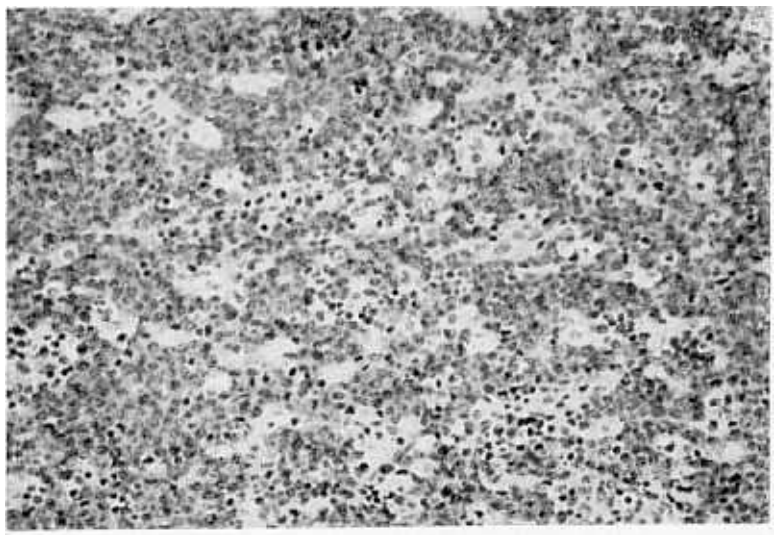

Fig. 4. MB2 staining of Burkitt's lymphoma showing cytoplasmic staining of tumor cells (PAP method with hematoxylin counterstain. ×100).

Distribution of T-cell Lymphoma According to Histologic Types by WF and Suchi's Classification

We classified 50 cases of malignant lymphoma of T-cell origin confirmed by immunostaining according to Suchi's classification. Within 36 cases of 'diffuse, mixed' type by WF, 22 cases belonged to 'pleomorphic medium and large cell' type, 13 cases belonged to 'pleomorphic small cell' type and 1 case was 'lymphoepithelial' type according to Suchi's Classification. Within 8 cases of 'large cell, immunoblastic' type by WF, 3 cases belonged to 'AILD- like T-cell lymphoma and 5 cases belonged to 'immunoblastic' type by Suchi's Classification (Table 6).

Table 5. Results of immunohistochemical staining with MT1, UCHL1 and MB2 in NHL

WF	Results of stain	T-phenotype			B-phenotype	Unclassified			
		MT1+ UCHL1+ MB2−	MT1+ UCHL1− MB2−	MT1− UCHL1+ MB2−	MT1− UCHL1+ MB2+	MT1+ UCHL1− MB2+	MT1− UCHL1+ MB2+	MT1+ UCHL1+ MB2+	MT1− UCHL1− MB2−
Low	Small lymphocytic	1	–	–	3	–	–	–	–
	Follicular, small cleaved	–	–	–	–	–	–	–	–
	Follicular, mixed	–	–	–	–	–	–	–	–
Intermediate	Follicular, large	–	–	–	–	–	–	–	–
	Diffuse, small cleaved	–	–	–	1	–	–	–	1
	Diffuse, mixed	29	5	2	1	1	1	–	6
	Diffuse, large	–	–	–	5	–	–	1	1
High	Large cell, immunoblastic	8	–	–	2	–	–	–	1
	Lymphoblastic	3	1	1	–	1	–	–	1
	Small noncleaved	–	–	–	1	2	–	–	–
	Total	41	6	3	13	4	1	1	10
	(%)	(51.9)	(7.6)	(3.8)	(16.5)	(5.0)	(1.3)	(1.3)	(12.7)

Table 6. Distribution of T-cell lymphoma according to histologic type by WF and Suchi's classification

WF	Low			Intermediate			High			
Suchi's classification	Small lympho-cytic	Follicular small	Follicular mixed	Follicular large	Diffuse small cleaved	Diffuse mixed	Diffuse large	Large cell, immunoblastic	Lympho-blastic	Small noncleaved
A. Prethymic and thymic T-cell lymphoma Lymphoblastic	–	–	–	–	–	–	–	–	5	–
B. Peripheral T-cell lymphoma										
Low grade										
CLL	1	–	–	–	–	–	–	–	–	–
MF/Sezary syndrome	–	–	–	–	–	–	–	–	–	–
Lymphoepithelial	–	–	–	–	–	1	–	–	–	–
AILD	–	–	–	–	–	–	–	3	–	–
T-zone	–	–	–	–	–	–	–	–	–	–
Pleomorphic small	–	–	–	–	–	13	–	–	–	–
High grade										
Pleomorphic medium and large	–	–	–	–	–	22	–	–	–	–
Immunoblastic	–	–	–	–	–	–	–	5	–	–
Large cell, anaplastic	–	–	–	–	–	–	–	–	–	–

Diatribution of the Primary Sites of T-cell Lymphoma

Of the 50 cases immunologically proven as T-cell lymphoma, 18 cases occurred in the lymph nodes and 32 cases occurred primarily in extranodal sites. Peripheral T-cell lymphomas showed a high frequen-

Table 7. Distribution of the primary site of T-cell lymphoma

Type	Site	Lymph node	Tonsil Nasal cavity Oral cavity Nasopharynx	G-I tract	Soft tissue	Skin	Brain	Ovary	Breast
A. Prethymic and thymic T-cell lymphoma									
Lymphoblastic		5	–	–	–	–	–	–	–
B. Peripheral T-cell lymphoma									
Low grade									
CLL		–	–	1	–	–	–	–	–
MF/Sezary syndrome		–	–	–	–	–	–	–	–
Lymphoeithelial		1	–	–	–	–	–	–	–
AILD		3	–	–	–	–	–	–	–
T-zone		–	–	–	–	–	–	–	–
Pleomorphic small		2	8	1	–	2	–	–	–
High grade									
Pleomorphic medium and large		6	5	3	4	1	1	–	1
Immunoblastic		1	1	2	1	–	–	–	–
Large cell, anaplastic		–	–	–	–	–	–	–	–
Total		18	14	7	5	3	1	1	1
(Toal No. studied)		(27)	(23)	(13)	(7)	(3)	(3)	(1)	(1)

cy of extranodal presentation (32 out of the 45 cases). All three cases of skin primary, 14 of the 23 cases of the upper aerodigestive tract primary, 7 of the 13 cases occurring in the gastrointestinal tract and 1 of the 3 cases occuring in the central nervous system showed T-cell phenotype (Table 7).

DISCUSSION

Since the first description of a malignant tumor occurring in absorbent glands by Thomas Hodgkin in 1832, malignant lymphoma was discussed under different names, such as lymphosarcoma, reticulum cell sarcoma and giant follicular lymphoma until 1966 when Rappaport's classification of malignant lymphoma and Lukes-Butler's classification of Hodgkin's disease were reported (Hodgkin 1832; Virchow 1863; Roulet 1930; Hurst and Meyer 1961; Lukes and Butler 1966). Rappaport's classification was used widely because of its simplicity and good clinicopathologic correlation and its modified form has been applied until recently (Nathwani *et al.* 1976; Jaffe and Berard 1978). However, as a result of the development of immunology in the 1970s, shortcomings in Rappaport's classification were noted and several other classifications of malignant lymphoma have been reported and used independently (Lukes and Collins 1974; Bennet *et al.* 1975; Gerard *et al.* 1974; Dorfman 1974; Lennert *et al.* 1975; Mather *et al.* 1976; Dorfman 1977). In 1982, a National Cancer Institute sponsored study proposed the 'Working Formulation of Non-Hodgkin's Lymphoma for Clinical Usage' as a form of universal translator enabling therapeutic trials using different classifications to be compared directly after examining the clinical relevance and reproducibility of 6 main classifications (National Cancer Institute 1982). WF delineated 3 prognostic groups according to the survival rate and relapse free interval (low, intermediate, high grade) and 10 histologic subgroups. In this study, we classified our 79 cases according to WF. Low grade lymphoma encompassed 5.1% of the total cases, approaching the 7.6% reported by Lee (1985) and 10.6% reported by Shin (1983). However, this percentage was strikingly low in comparison to the 33.8% and 33.3% reported respectively by Nathwani and Winberg (1983) and Newell (1983) and this discrepancy was due to the fact that follicular lymphomas which are common in western countries rarely occur in Asian countries (Lee *et al.* 1973; Jung *et al.* 1982; Gu 1982; Shin *et al.* 1982; Masaki *et al*; Lee *et al.* 1985; Liang *et al.* 1985; Su *et al.* 1985; Ahn *et al.* 1988). The incidence of high grade lymphoma was 25.3% and this is in approximation to the 28.2%, 21.2% and 17.0% reported by Lee (1985). Ahn (1988) and Nathwani and Winberg (1983) respectively. Intermediate grade lymphoma showed

the highest frequency of 64.8% and in particular 'diffuse, mixed' type (57%). The high frequency of 'diffuse, mixed' type in contrast to the reported incidence of the 17% by Lee (1985) and 12.0% by Nathwani and Winberg (1983), is due to the high incidence of peripheral T-cell lymphoma, the majority of which belong to this type by WF.

Malignant lymphoma shows age predilection according to the histologic subtypes, 'lymphoblastic' and ' Burkitt' type occur mainly in children (Nathwani *et al.* 1976; Jaffe et Berard 1976; Hausner *et al. 1977; Wilson et al.* 1984). Our results showed that 5 out of the 7 cases of 'lymphoblastic' type and all 3 cases of 'Burkitt' type occured below 20 years of age. In contrast, 3 out of the 4 cases of 'small lymphocytic' type occurred in patients over 60 years of age, showing a predilection for the elderly and 'diffuse, mixed' type showed an even distribution in all age groups.

Because WF does not attempt immunologic classification of lymphoma, it includes T-cell and B-cell lymphomas in the same groups despite their different biologic behaviors (Nathwani and Winberg 1983). In has been considered possible to predict the immunologic origin of malignant lymphomas by histologic features (Lukes and Collins 1974). The 'plasmacytoid' subtype of 'large cell, immunoblastic' type in WF shows B- cell phenotype and 'clear cell', 'polymorphous cell' and 'epitheliod' subtypes mainly express T-cell Phenotype (Nathwani and Winberg 1983). Peripheral T-cell lymphoma has been known to show rather characteristic morphologic features such as clear cytoplasm of tumor cells, polymorphism of tumor cell size and shape, fine intercellular fibrosis, proliferation of high endothelial cell lined venules and infiltration of reactive inflammatory cells (Waldron *et al.* 1977; Brisbane *et al.* 1983; Weiss *et al.* 1985; Weis *et al.* 1986; Suchi *et al.* 1987). However, it has been proven that immunophenotyping by morphologic features alone has an accuracy rate of only 61% and in consideration of the recently reported 'plasmacytoid T-cell immunoblastic lymphoma', 'T-immunoblastic lymphoma mimicking B-immunoblastic lymphoma' and 'multilobated B-cell lymphoma', immunophenotyping of malignant lymphomas should be done by immunologic methods (Jaffe *et al.* 1982; Prasthofer *et al.* 1985; Swanson *et al.* 1987; Chan *et al.* 1986). In the 1970s, immunofluorescent staining for cell surface immunoglobulin and a sheep red cell rosetting technique were done to confirm B and T-cell phenotype (Jondal *et al.* 1975; Whiteside and Rowlands 1977). But recently immunohistoohemical staining using various monoclonal antibodies to cell surface antigens has been performed for immunophenotyping (Brudaker *et al.* 1979; Li and Harrison 1978; Doggett *et al.* 1984; Knowles 1985; Nash 1986; Picker *et al.* 1987). Immunohistochemical staining to cell surface antigens, particularly to T- cell antigens, required fresh tissue so it was impossible to perform retrospective studies and frozen section artifacts also hindered accurate interpretation. To resolve these difficulties periodate-lysine- paraformaldehyde fixation with low temperature embedding and freeze-drying techniques were developed, but these were hard to perform and resulted in suboptimal morphology in comparison to paraffin embedded tissue (Collings *et al.* 1984; Stein *et al.* 1985). Recently, moncolonal antibodies (MT, MB, UCHL, LN) have been developed enabling immunohistochemical staining for B-and T-cells in routinely fixed and paraffin embedded tissue (Poppema *et al.* 1987; Smith *et al.* 1986; Epstein *et al.* 1984). MT1, UCHL1 and MB2 used in this study are monoclonal antibodies of IgG class produced in the BALB/C mouse. MT1 and UCHL1 were known to react with T-cells and histicoytes while MB2 was known to react with B-cells (Poppema *et al.* 1987; Smith *et al.* 1986). In each staining procedure, we used lymph node sections showing reactive hyperplastic change as a positive control. In reactive lymph nodes, MT1 and UCHL1 showed strong membrane staining of T-cells located in the paracortex, some lymphocytes of germinal center and the mantle zone and sinus histiocytes. MB2 showed cytoplasmic staining of B-cells located in the mantle zone and germinal centers. It has been shown that these antibodies are not lineage specific, but it is possible to determine the immunophenotypes of malignant lymphomas when they are used in combination (Norton *et a;*. 1986; Hall *et al.* 1986; West *et al.* 1986; Poppeoma *et al.* 1987; Dobson *et al.* 1987; Norton and Isaacson 1987).

Immunohistochemical studies applied to 79 cases of malignant lymphoma using MT1, UCHL1 and MB2 showed 50 cases of T-cell phenotype and 14 cases of B-cell phenoype. In 15 cases it was impossible to decide immunophenotype by the results of immunostaining alone. In interpretating the results of immunostaining, it has been found that MT1 and UCHL1 also stained granulocytes and histiocytes in addition to T-cells and MB2 also stained epithelial cells of the upper aerodigestive tract, so it was possible to confirm that these antibodies are not lineage specific. Because these antibodies are not lineage specific and in consideration of the reports that a small number of T-cell and B-cell lymphomas showed positivity to MB2 and MT1 respectively the results of immunostaining should be interpreted with caution (Poppema *et al.* 1987; Hall *et al.* 1987; Dobson *et al.* 1987) According to our

results, 4 cases showed positivity to both UCHL1 and MB2 and 1 case showed positivity to MT1, UCHL1 and MB2. The histologic subtypes showing these staining ambiguities included 2 cases of 'diffuse, mixed' type, 2 cases of 'Burkitt' type, 1 case of 'lymphoblastic' type and 1 case of 'diffuse, large cell' type. In 10 cases they were negative to all MT1, UCHL1 and MB2 antibodies. This was probably due to the fact that in many cases of peripheral T-cell lymphoma, there was some loss of T-cell markers in association with technical problems of immunostaining such as fixation time, type of fixatives, titer of primary antibody and type of immunostaining (Grogan *et al.* 1985; Borowitz *et al.* 1986; Doi *et al.* 1989). Combining the results of immunophenotypic and morphologic classification, we found that 1 out of the 4 cases of 'small lymphocytic' type and 5 out of the 7 cases of 'lymphoblastic' type showed T-cell phenotype, which approximates the frequency of T-cell phenotype in western countries, but the majority of 'diffuse, mixed' type (36/45) and 'large cell, immunoblastic' type (8/11) showed T-cell phenotype (Norton *et al.* 1986; Hall *et al.* 1987).

Because the Working Formulation was based on non- Hodgkin's lymphoma from western countries which is predominantly of the B- cell phenotype, it is not suitable for use in Asian countries where the incidence of peripheral T-cell lymphomas, the majority of which belong to 'diffuse, mixed' type is high (Maski *et al.* 1982; Gu 1982; Liang *et al.* 1985; Su *et al.* 1988). Classifying malignant lymphomas of T-cell origin according to Suchi's classification allows subdivision of peripheral T-cell lymphomas morphologically (Suchi *et al.* 1987). There were 5 cases of 'lymphoblastic' lymphoma of thymic origin and 45 cases of peripheral T-cell lymphoma. Within peripheral T-cell lymphoma, there were 18 cases of low grade lymphoma (13 cases of pleomorphic small, 3 cases of AILD-like T- cell lymphoma,1 case of lymphoepithelial and 1 case of CLL) and 27 cases of high grade lymphoma (22 cases of pleomorphic medium and large and 5 cases of immunoblastic).

The incidence of extranodal lymphoma (52 cases) was higher than nodal lymphoma (27 cases). This is due to the fact that peripheral T-cell lymphomas have a tendency to occur at extranodal sites; in this study we regarded 'polymorphic reticulosis' occurring in the upper aerodigestive tract as a form of peripheral T-cell lymphoma. Lymphomas occurring in the upper aerodigestive tract often present as mass lesions or as ulcerodestructive lesions. The latter have been variously named as 'polymorphic reticulosis' or 'midline malignant reticulosis' and there have been many disputes as to their nature and classification (Eichel and Maybery 1968; Kassel *et al.* 1969). Several studies have recently suggested that 'polymorphic reticulosis' represent in reality peripheral T-cell lymphoma occurring at the upper aerodigestive tract (Weis *et al.* 1986; Chan *et al.* 1987; Lippman *et al.* 1987; Chott *et al.* 1988). According to our results, 14 of 23 cases of malignant lymphoma presenting at the upper aerodigestive tract showed T-cell phenotype and there were no cases showing B-cell phenotype.

All cases of peripheral T-cell lymphoma showed characteristic morphologic features, such as polymorphism of tumor cells, clear cytoplasm, proliferation of high endothelial-lined venules, fine intercellular fibrosis and infiltration of inflammatory cells. But it was impossible to predict immunophenotypes morphologically in cases of 'small lymphocytic' type, 'lymphoblastic' type and one of the 'plasmacytoid, large cell immunoblastic' type with T-cell phenotype. These cases illustrate the need for immunologic studies for accurate immunophenotyping of malignant lymphoma.

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