Morphologic and Immunologic Characterization of 50 Peripheral T-Cell Lymphomas

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Fifty T-cell lymphomas, excluding mycosis fungoides and lymphoblastic lymphoma, were studied morphologically and immunohistochemically with a panel of monoclonal antibodies reactive with T-cell differentiation antigens in fresh frozen tissue. Histologically, 36% of the lymphomas were large-cell immunoblastic, 26% were diffuse large-cell, 22% were diffuse mixed small and large-cell, and 16% were monomorphic medium-sized-cell lymphomas. By immunologic studies, 64% of the lymphomas were of helper phenotype, 12% were of cytotoxic/suppressor phenotype, 8% expressed both helper and cytotoxic/suppressor antigenic markers, and 16% lacked detectable markers for either helper or cytotoxic/suppressor cells. There was no correlation between histologic category and immunophenotype. A common finding, and one which may prove to be helpful in the diagnosis of T-cell lymphomas, was the loss of one or more of the pan-T antigens Leu 1, 4, and 5 or the T-cell antigen Leu 9 in 32 cases. The expression of Leu 1 and Leu 9 was lost in 46% of cases, expression of Leu 4 was lost in 26%, and expression of Leu 5 was lost in 24%. About three-quarters of the lymphomas expressed Ia antigens. (Am J Pathol 1985, 118:316–324)

ADVANCES in immunology have enabled the characterization of malignant lymphomas on the basis of their relationship to normal lymphoid populations.[1,2] Most malignant lymphomas have been found to show B-cell differentiation and have been separated into histologic subclasses which have been found to have biologic as well as clinical significance. Similarly, subsets of T-cell lymphomas such as mycosis fungoides and lymphoblastic lymphoma have been well studied and shown to have distinct clinicopathologic features.[3–6] T-cell lymphomas other than mycosis fungoides and lymphoblastic lymphoma have been less well studied, and meaningful correlations between morphology, immunology, and clinical aspects have been less well defined.[7–19] The reasons for this are twofold. First, T-cell lymphoma outside of Japan is an uncommon entity, and few large series of Western cases have been studied.[20] Second, the ability to characterize subsets of T-cell lymphocytes with the use of monoclonal antibodies has only been recently achieved and may offer novel ways to separate T-cell lymphomas into meaningful categories.[21]

The purpose of this paper is to report a large series of immunologically characterized peripheral T-cell lymphomas, excluding mycosis fungoides and lymphoblastic lymphoma, and to determine whether morphologic and immunologic features can enable one to better define these lymphomas.

Materials and Methods

During the years 1981 through 1984, of the cases studied in the Laboratory of Immunopathology at Stanford University Medical Center, 63 were found to have phenotypes consistent with or suggestive of T-cell lymphoma, excluding cases of mycosis fungoides and lymphoblastic lymphoma. During this time period, peripheral T-cell lymphomas comprised approximately 20% of the diffuse malignant lymphomas typed in this laboratory. Thirteen cases were excluded from analysis because of either inadequate histologic or immunologic

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examination, morphologic features on review that were not convincing for malignant lymphoma, or immunologic features on review that were more suggestive of Hodgkin's disease or B-cell lymphoma; therefore, 50 cases were studied for this report. Twelve of these cases have been previously reported.[22] Fifty-five tissue samples were studied from the following sites: lymph nodes (27), skin (19), nasal region (2), lung (2), spleen (1), gastrointestinal tract (1), mediastinum (1), and chest wall (1). The paraffin sections of all cases stained with hematoxylin and eosin (H&E) were reviewed by at least one author (L.M.W.) and classified using a modification of the International Working Formulation.[23] The category of monomorphic medium-sized-cell lymphoma was added as defined by Japanese investigators.[17,24] The category angioimmunoblastic lymphadenopathy-like (AILD-like) T-cell lymphoma as defined by Shimayama et al[25] was recognized as a subcategory of diffuse, mixed small- and large-cell lymphoma. Each lymphoma was evaluated for the presence or absence of a variety of histologic features. Prominence of eosinophils, plasma cells, and epithelioid histiocytes was noted when easily observed in most fields of the lymphoma. The presence of clear cells, pleomorphic cells and signet cells was also noted when easily observed. The presence of Reed-Sternberg-like cells was noted even when rare or confined to a small area of the lymphoma. An estimation was made of whether each lymphoma was suggestive of T-cell derivation or B-cell derivation or indeterminate by criteria discussed by Nathwani and Winberg.[26] Briefly, clear-cell, polymorphous or epithelioid immunoblastic lymphomas were considered suggestive of T-cell type, while other large cell lymphomas were considered suggestive of B-cell type. Diffuse mixed-cell lymphomas were considered suggestive of T-cell type when exhibiting a spectrum of cell sizes with transitional forms and were considered suggestive of B-cell type when composed of a population of small and large cells with characteristics of follicular center cells.

All specimens were frozen, processed, and stained as previously described.[27,28] Briefly, the staining consists of a first stage incubation with one of the monoclonal antibodies listed in Table 1. After washing, biotin-conjugated goat anti-mouse $F(ab')_2$ antibody (Tago, Burlingame, California) or horse anti-mouse antibody (Vector Laboratories, Inc., Burlingame, California) is applied prior to a third stage of avidin-conjugated horseradish peroxidase (Vector). The sections are then incubated in diaminobenzidine (DAB) followed by copper sulfate and counterstained with methylene blue. The recorded phenotypes represent the staining pattern for the majority of the lymphoma cells; we cannot exclude a different antigenic profile in a minor population of cells.

The monoclonal antibodies employed in this study are listed in Table 1. All cases were stained for Leu 1 through Leu 5, Leu 9, Ia, μ heavy chains, κ and λ light chains, and B lineage markers B1 or T015. Thirty-two cases were stained for Leu 6.

Table 1—Monoclonal Antibodies Reactive With Hematopoietic Cells

Antigen/clone/similar antigens	Expression	Other expression
Leu-1/L17F12*/T1, T65	T cells, thymocytes	B-CLL, B lymphoma
Leu-2a/SK1*/T5, T8	Cytotoxic/suppressor T cells, thymocytes	Splenic sinusoids
Leu-3a/SK3*/T4	Helper T cells, thymocytes	Monocytes, macrophages, Langerhans cells
Leu-4/SK7*/T3	T cells, thymocytes	Purkinje cells
Leu-5/ATM1.1*/T11, Lyt-3	T cells, thymocytes	
Leu-6*/SK9/T6	Cortical thymocytes	Langerhans cells
Leu-9/4H9*/3A1	Cytotoxic/suppressor T cells, most helper T cells and thymocytes	Monocytes, macrophages
Cytoplasmic μ, no light chains	Pre-B cells	
Surface and/or cytoplasmic Ig of κ or λ type*†	B cells and plasma cells	
Ia/L203†	B cells and precursors	Activated T cells, myeloids, monocytes macrophages, Langerhans cells, epithelium
Ia/L227†		
B1/H299‡	B cells and precursors	Monocytes, macrophages
T015§	B cells and precursors	

* Becton-Dickinson, Mountain View, California.
† Dr. R. Levy, Stanford, California.
‡ Coulter-Clone, Hialeah, Florida.
§ Dr. D. Y. Mason, Oxford, England.

Table 2—Summary of Morphologic Features

Histologic type*	No.	%	Suggestive of T-cell	Suggestive of B-cell	Indeterminate for B or T-cell	Eosinophils	Plasma cells	Epithelioid histiocytes	Prominent vessels	Clear cells	Pleomorphic cells	Signet cells	Reed–Sternberg-like cells
Immunoblastic	18	36	15	2	1	5	6	4	3	8	7	1	3
Polymorphous	6	12	5	0	1	3	3	0	2	1	6	0	1
Clear	7	14	7	0	0	1	3	1	0	7	0	0	1
Epithelioid	3	6	3	0	0	1	0	3	1	0	0	0	1
Plasmacytoid	2	4	0	2	0	0	0	0	0	0	1	1	0
Diffuse large-cell	13	26	0	13	0	3	1	1	1	0	0	1	0
Diffuse mixed small and large	11	22	10	0	1	4	1	3	8	2	2	0	2
Angioimmunoblastic-like	4	8	4	0	0	3	1	1	4	2	0	0	0
Other	7	14	6	0	1	1	0	2	4	0	2	0	2
Monomorphic medium-sized	8	16	8	0	0	0	0	1	0	0	0	0	0
Total	50	100	33	15	2	12	8	9	12	10	9	2	5

* The histologic classification is that of the International Working Formulation modified to include the angioimmunoblastic-like and monomorphic medium-sized cell lymphomas (17, 23, 24, 25)

Results

Morphologic Observations

A modification of the Working Formulation to include observations of Japanese investigators was found to provide an adequate system of classification for the peripheral T-cell lymphomas (see Table 2). Over 60% of the cases were large-cell lymphomas, either immunoblastic or diffuse large-cell. Representative examples of the monomorphic medium-sized-cell lymphoma, the AILD-like T-cell lymphoma, polymorphous immunoblastic lymphoma, and clear-cell immunoblastic lymphoma are illustrated in Figures 1 through 6. A follicular pattern was not observed, nor were any cases of well-differentiated lymphocytic lymphoma/chronic lymphocytic leukemia encountered. Two-thirds of the cases were histologically suggestive of T-cell derivation, while in 30%, the histologic features were more suggestive of B-cell origin. Although eosinophils, plasma cells, epithelioid histiocytes, and prominent vessels were common findings, none of these features was present in the majority of cases. Reed–Sternberg-like cells were present in 5 cases; and in 3 of these, the diagnosis of Hodgkin's disease was seriously considered (lymphocyte predominant in 2, nodular sclerosis in 1). Entities considered in the histologic differential diagnosis included numerous reactive conditions, especially AILD and other malignant conditions, including B-cell lymphomas and lymphomas of true histiocytic origin.

Immunologic Observations

The immunologic phenotypes of the lymphomas are summarized in Tables 3–7. None of the lymphomas showed staining for kappa or lambda light chains, mu heavy chain, the B-cell markers B1 or T015, or Leu 6. As can be seen from the tables, 32 lymphomas were of helper phenotype (Leu $2^- 3^+$), 6 lymphomas were of cytotoxic/suppressor phenotype (Leu-$2^+ 3^-$), 8 lymphomas were of undefined phenotype (Leu $2^- 3^-$), 3 lymphomas showed both helper and cytotoxic/suppressor phenotype markers (Leu $2^+ 3^+$), and 1 case showed cytotoxic/suppressor phenotype at one time and helper phenotype 3 years later. The pan-T antigens Leu 1 and Leu 9* were absent in about half of the cases (46% for both); while loss of expression of the pan-T antigens Leu 4 and Leu 5 was less often seen (26% and 24%, respectively). A representative case showing loss of Leu 1 is illustrated in Figures 1 and 2. Ia antigen was pres-

* Although Leu 9 is not expressed on all nonneoplastic T-cells and is thus not technically a pan-T antigen, it is expressed on a majority of T-cells and would be expected to be present in a population of nonneoplastic T-cells. Thus, for the purposes of this study, it may be regarded as a pan-T antigen.

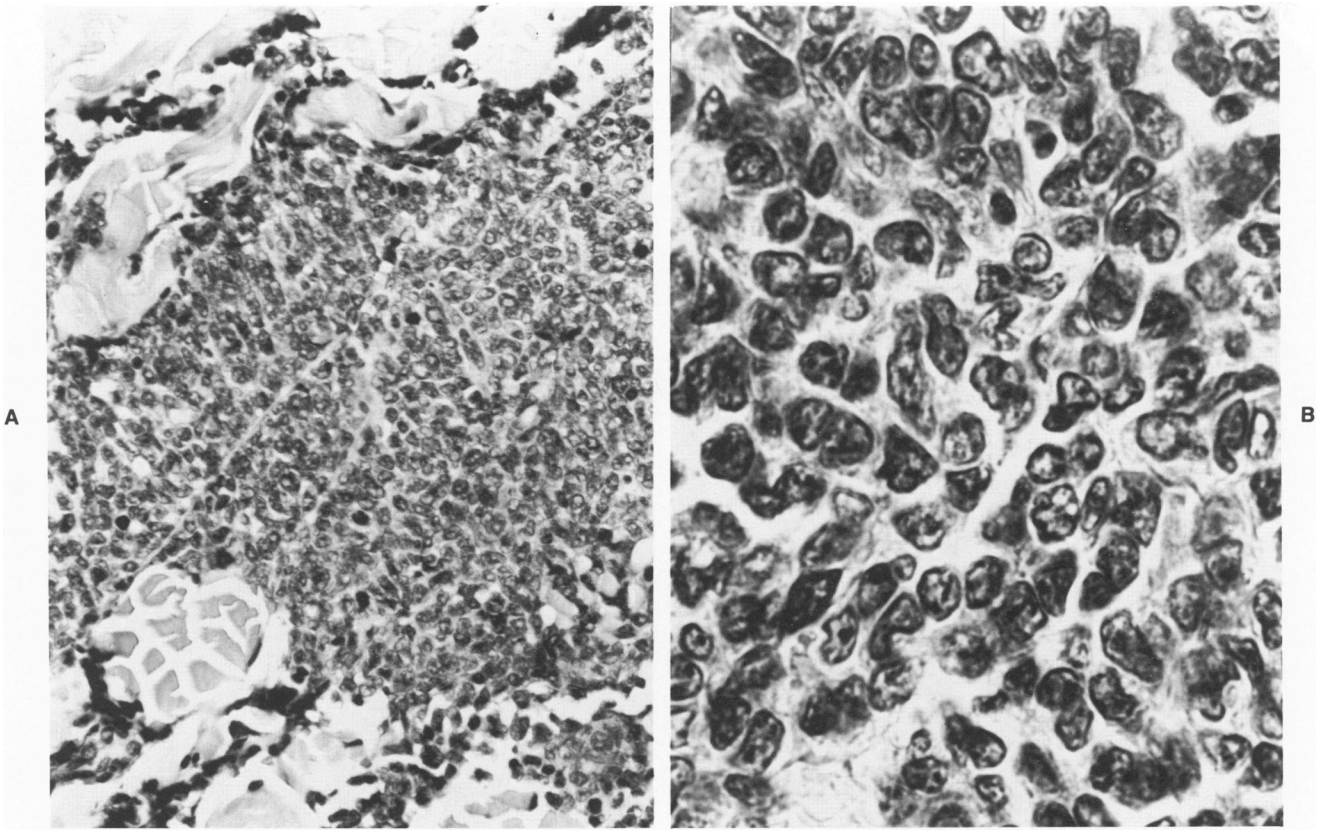


Figure 1—Monomorphic medium-sized cell lymphoma (**A**) shows lymphoma in reticular dermis. **B**—The lymphoma is composed of a uniform population of lymphocytes with highly irregular nuclei slightly larger than small cleaved lymphocytes. An occasional nucleolus can be seen. (H&E, **A**, ×300; **B**, ×1200)

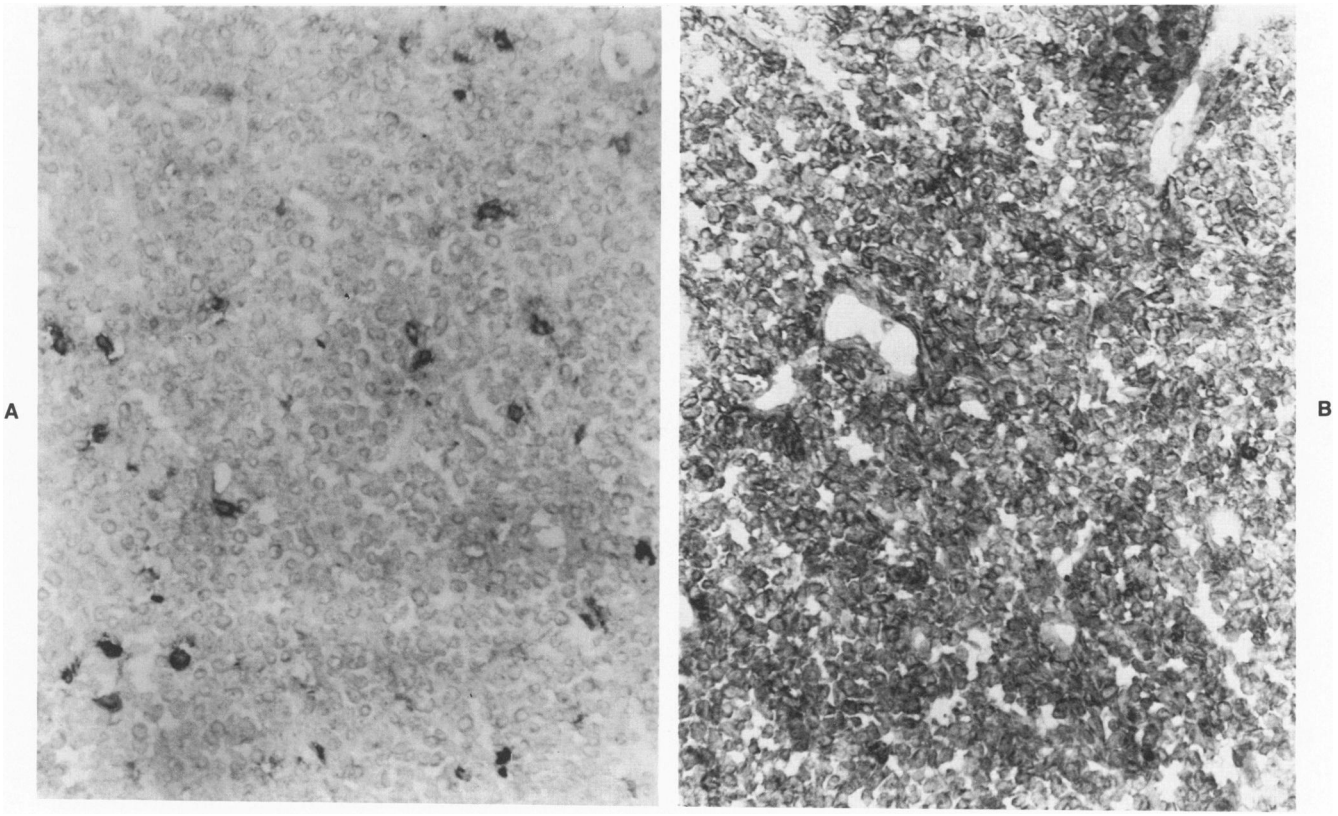


Figure 2—Cryostat sections of a monomorphic medium-sized-cell lymphoma (same case as Figure 1) stained for Leu 1 (**A**) and Leu 3 (**B**) by an immunoperoxidase method and methylene blue counterstain. The lymphoma cells do not express Leu 1 (**A**) but do express Leu 3 (**B**). The occasional dark granular staining in **A** represents endogenous peroxidase activity in eosinophils or mast cells. (×300)

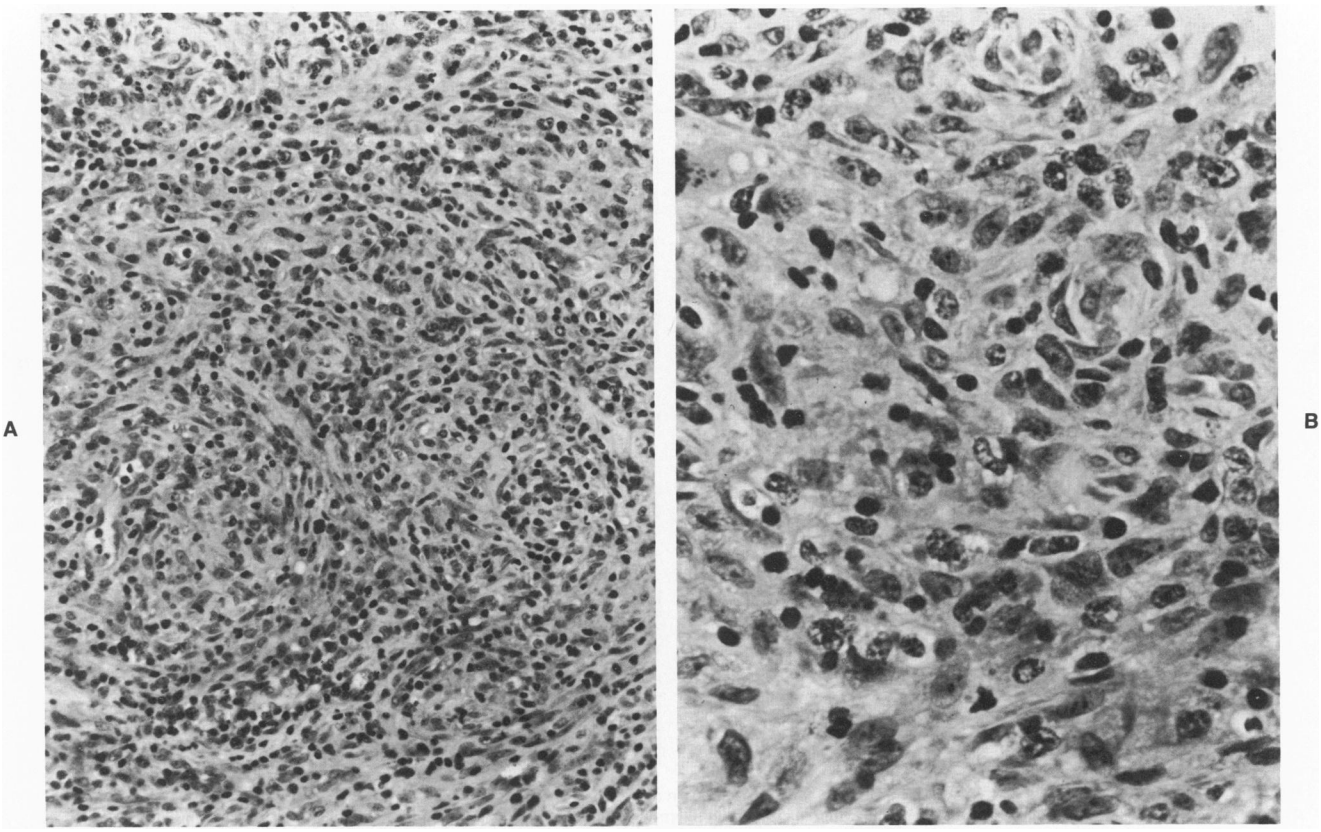


Figure 3—Angioimmunoblastic-like lymphoma **A**—A generally cell-poor lymphoma with a prominent vascular pattern. **B**—The lymphoma is composed of a mixture of cell types with amorphous debris present in the background. (H&E, **A**, ×192; **B**, ×480)

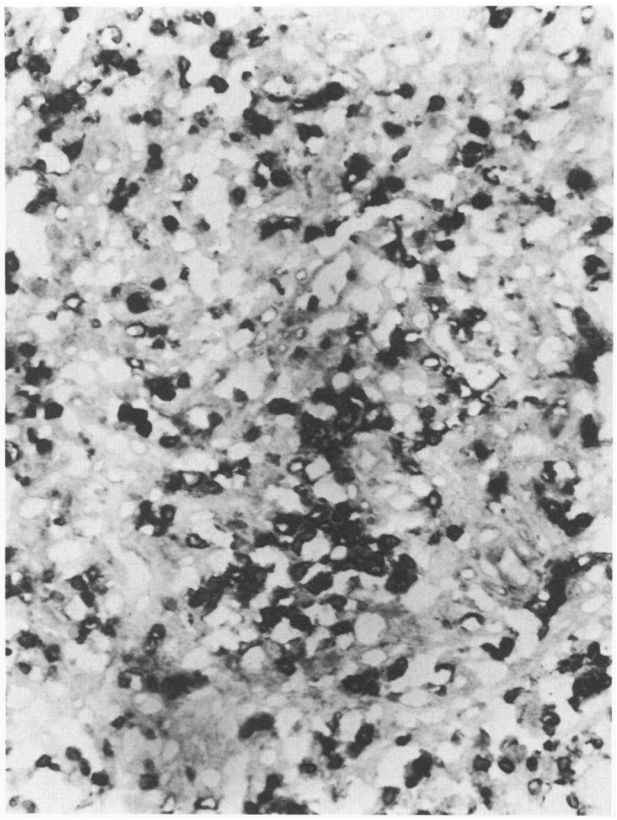
ent in 72% of the cases. Overall, in 36 of the 50 lymphomas, a diagnosis of malignant lymphoma was supported immunologically on the basis of an abnormal phenotype (loss of one or more of the pan-T antigens or non-helper/suppressor phenotype). In 13 cases, the diagnosis was supported by the presence of abnormal proportions of cells of normal phenotype, ie, a marked predominance of tumor cells of either helper or cytotoxic/suppressor phenotype along with morphologic evidence strongly suggestive of malignancy. In 1 case, a predominant helper or cytotoxic/suppressor phenotype was not observed. The 8 cases lacking either helper or cytotoxic/suppressor phenotype were distinguished from B-cell lymphomas or other tumors (including tumors of true histiocytic origin) by the expression of one or more of the T-cell antigens (most often Leu 4 or Leu 5), along with the lack of expression of B-lineage markers.

As can be seen in Tables 3–7, there was no correlation of morphologic subtypes and immunophenotypes.

Tissue from two sites was available for immunologic studies in 5 patients. In the four instances in which the two biopsies were obtained within a month of each other, the phenotypes were similar. In the 1 case where the material for immunophenotyping was obtained from two biopsies more than 1 month apart, a cytotoxic/suppressor phenotype was observed initially (in a skin biopsy), and a helper phenotype was observed (in a lymph node and skin biopsy) 3 years later. In addition, there was loss of an additional pan-T marker (Leu 1).

Discussion

This study confirms the generally held opinion that peripheral T-cell lymphomas represent a diverse group of tumors. Morphologically, they can present a wide variety of histologic patterns. Some are suggestive of or are distinct T-cell lymphomas; and many are histologically indistinguishable from other tumors, most notably B-cell lymphomas, tumors of true histiocytic origin, and Hodgkin's disease. Common histologic features present in many of the lymphomas in this series were the presence of a polymorphous infiltrate with tumor cells showing a spectrum of cell size, a frequent admixture of eosinophils, plasma cells, and histiocytes, often with prominent vessels. Frequently large bizarre cells, often multinucleated, or cells with cleared cyto-



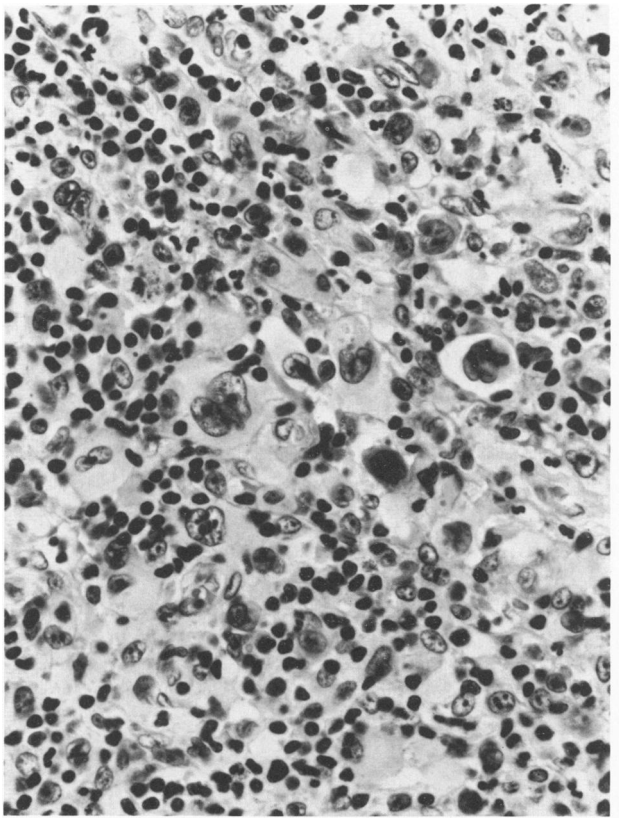


Figure 4—Cryostat sections of an angioimmunoblastic-like lymphoma (same case as Figure 3) stained for Leu 2 with an immunoperoxidase method and methylene blue counterstain. The neoplastic cells show strong staining for Leu 2 and did not show expression of Leu 3 (not shown); this lymphoma therefore expresses a cytotoxic/suppressor phenotype. (×300) **Figure 5**—Polymorphic immunoblastic lymphoma. This lymphoma was initially diagnosed as an inflammatory malignant fibrous histiocytoma. Reed–Sternberg-like cells were also present; raising the possibility of Hodgkin's disease. The lymphoma expressed a helper phenotype with loss of the pan-T antigen Leu 1. (H&E, ×400)

plasm were observed. However, these features were not seen in many of the lesions (ie, diffuse large-cell and monomorphic medium-sized-cell lymphomas), and several lymphomas were histologically suggestive of other neoplasms (eg, the two plasmacytoid immunoblastic lymphomas and 1 additional case with signet ring cells). In addition, B-cell lymphomas occasionally have numerous eosinophils, histiocytes, and prominent vessels, mimicking peripheral T-cell lymphoma. The monomorphic medium-sized-cell lymphoma had distinctive morphologic features (see Figures 1 and 2). These cases were composed of a uniform population of cells intermediate in size between small cleaved cells and large transformed lymphocytes. The nuclear contours were often irregular and convoluted. The chromatin pattern showed a denser heterochromatin pattern, and there was a lower mitotic rate than in lymphoblastic lymphoma. An admixture of eosinophils and plasma cells was not seen in this subtype.

The incidence of the different subtypes of peripheral T-cell lymphoma differed from that of Jaffe et al, who did not find any cases of nonimmunoblastic large-cell lymphoma in 32 cases of human T-cell leukemia/lymphoma virus-negative peripheral T-cell lymphomas.[9,10] Our results more closely parallel the findings of Suchi et al in a study of T-cell lymphomas in a nonendemic area of Japan, although they had no cases of mixed cell type and a large number of "miscellaneous" T lymphomas.[20,29]

The immunologic studies are of relevance to both the diagnosis and the characterization of the lymphomas. The results suggest that a useful phenotypic finding supporting the diagnosis of T-cell lymphoma is the loss of one or more pan-T markers, present in 64% of the cases, particularly because we have not observed this phenomenon in any nonneoplastic disorders to date (unpublished observation). In most instances, there was loss of more than one marker, but in 10 cases there was loss of only one antigen, stressing the utility of as wide a battery of T-cell markers as is possible. A frequent loss of pan-T markers, including Leu 5, the sheep erythrocyte receptor, highlights the problems of attempting to identify T-cell lymphomas on the basis of only one or even several of the markers. When more markers are employed, a greater number of T-cell lymphomas may be identified. In a previous study of large-cell lym-

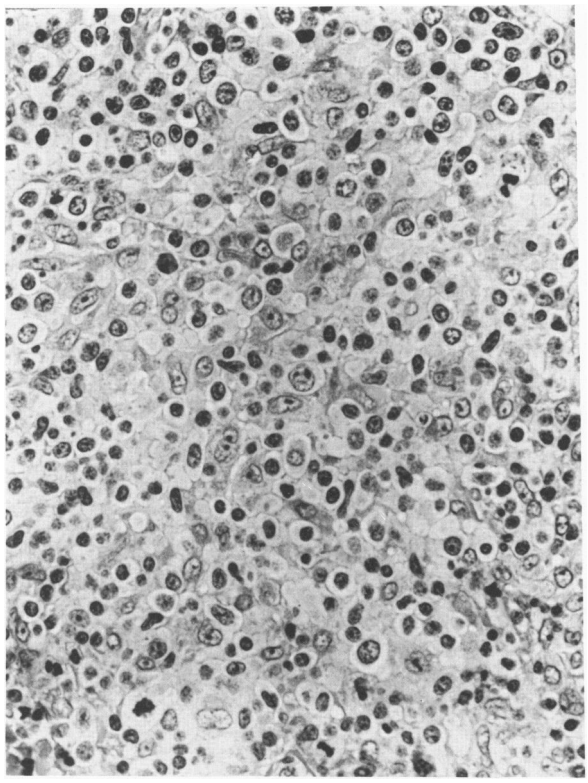


Figure 6—Clear-cell immunoblastic lymphoma. The lymphoma exhibits cells with nuclei with varying degrees of nuclear atypia and abundant clear cytoplasm. This lymphoma expressed a helper phenotype with no loss of pan-T antigen expression. (H&E, ×400)

phomas by one of us (R.A.W.), two T-cell lymphomas were omitted because reliance was placed on Leu 1 expression to identify all T-cell cases.[30]

When there was no loss of expression of normal pan-T antigens, the presence of a dominant population of one phenotype (helper or cytotoxic/suppressor) over another, although less definitive, may also be useful in diagnosis. In these cases, it is especially important to correlate the immunologic findings with the morphology.

The immunologic studies demonstrated that the T-cell lymphomas were immunologically diverse. Loss of pan-T cell markers did not follow any pattern, and the large number of phenotypes confirms earlier findings that there does not appear to be a normal counterpart for each neoplastic phenotype and that, contrary to

Table 3—Lymphomas With Helper Phenotype (Leu 2^-3^+) and Expression of All Pan-T Markers

Histologic pattern	Leu 1	Leu 4	Leu 5	Leu 9	Ia
Polymorphic immunoblastic	+	+	+	+	+
Clear-cell immunoblastic (2)	+	+	+	+	+
Epithelioid immunoblastic (2)	+	+	+	+	–
Diffuse mixed	+	+	+	+	–
Monomorphic medium-sized	+	+	+	+	–
Diffuse mixed, AILD-like	+*	+	+	+	–

* Weakly positive pattern.

Table 4—Lymphomas With Helper Phenotype (Leu 2^-3^+) With Loss of Normal Pan-T Antigen Expression

Histologic pattern	Leu 1	Leu 4	Leu 5	Leu 9	Ia
Polymorphous immunoblastic	–	+	+	+	+
Diffuse large-cell	–	+	+	+	+
Diffuse mixed	–	+	+	+	+
Polymorphous immunoblastic	+	+	+	–	+
Clear-cell immunoblastic	+	+	+	–	+
Diffuse large-cell (2)	+	+	+	–	+
Diffuse mixed	+	+	+	–	–
Polymorphous immunoblastic	–	+	+	–	+
Polymorphous immunoblastic	–	+	+*	–	+
Diffuse large-cell	+	–	–	+	+
Monomorphic medium-sized	–	–	–	+	+
Plasmacytoid immunoblastic (2)†	–	–	+	–	+
Polymorphous immunoblastic	–	–	+	–	+
Diffuse large-cell	–	–	+	–	+
Monomorphic medium-sized (2)	–	–	+	–	+
Clear-cell immunoblastic	–	+	–	–	+
Diffuse large-cell (3)	–	+	–	–	+
Diffuse large-cell	+	–	–	–	+
Monomorphic medium-sized (2)	–	–	–	–	+

* Weakly positive pattern.

† One of these was the 1980 lymph node biopsy from the same patient footnoted in Table 6.

Table 5—Lymphomas With Cytotoxic/Suppressor Phenotype (Leu 2^+3^-) and Expression of All Pan-T Markers

Histologic pattern	Leu 1	Leu 4	Leu 5	Leu 9	Ia
Diffuse large-cell	+	+	+	+	+
Diffuse mixed, AILD-like	+	+	+	+	+
Diffuse mixed	+	+	+	+	+
Clear-cell immunoblastic	+	+	+	+	–
Diffuse mixed	+	+	+	+	–

Table 6—Lymphomas With Cytotoxic/Suppressor Phenotype (Leu 2^+3^-) With Loss of Normal Pan-T Antigen Expression

Histologic pattern	Leu 1	Leu 4	Leu 5	Leu 9	Ia
Diffuse mixed, AILD-like	+	+	+	–	–
Plasmacytoid immunoblastic, 1977*	+	–	+	–	+

* Skin biopsy from the same patient as footnoted in Table 4.

Table 7—Lymphomas of Undefined T-Cell Phenotype

Histologic pattern	Leu 1	Leu 4	Leu 5	Leu 9	Ia
Leu 2^+3^+**					
Diffuse mixed, AILD-like	+	+	+	+	+
Epithelioid immunoblastic	+	+	+	+	–
Diffuse mixed	+	+	+	+	–
Leu 2^-3^-					
Clear cell immunoblastic	+	+	+	+	+
Diffuse mixed	–	+	+	+	+
Diffuse large-cell	–	–	+	+	+
Monomorphic medium-sized	–	–	+	+	+
Monomorphic medium-sized	+	+	–	–	–
Polymorphous immunoblastic	–	+	+	–	–
Plasmacytoid immunoblastic	–	+	–	+	+
Diffuse large-cell	–	+	–	+	–

* In 2 cases the neoplastic cells appeared to co-express Leu 2 and Leu 3, whereas the epithelioid immunoblastic case was of undefined phenotype because of approximately equal numbers of Leu 2^+ and Leu 3^+ cells.

Table 8—Histologic and Immunologic Comparison of Lymphoblastic Lymphoma, Peripheral T-Cell Lymphoma, and Mycosis Fungoides

	T-cell lymphoblastic lymphoma	Peripheral T-cell lymphoma	Mycosis fungoides
Histology			
Uniformity from case to case	Yes	No	Yes
Uniformity of neoplastic cells within a given case	Yes	Monomorphic medium-sized only	Variation in cell size
Cytology	Convoluted or nonconvoluted blast-appearing nuclei	Variable, often with bizarre pleomorphic nuclei	Cerebriform
Admixture of other cell types	Uncommon	Often present	Often present
Immunology			
Leu 6	Often present	Absent	Absent
Leu 2^+3^+ or Leu 2^-3^- phenotypes	Sometimes present	Uncommon	Absent
Leu 2^+3^- or Leu 2^-3^+ phenotypes	Either sometimes present	Either usually present	Usually Leu 2^-3^+ (helper) phenotype
Leu 9	Present in virtually all	Present in one-half	Variably present
Ia expression	Rare	Often present	Uncommon

B-cell lymphomas, peripheral T-cell lymphomas do not show phenotypes that clearly recapitulate stages in lymphoid differentiation. The propensity of either helper or cytotoxic/suppressor T-lymphocytes to become malignant appears random, because the ratio of helper to cytotoxic/suppressor lymphomas (34:7) is quite close to the normal ratio of helper to suppressor lymphocytes in normal tissues.

The peripheral T-cell lymphomas in this study were found to be immunophenotypically distinct from lymphoblastic lymphomas. The differences are summarized in Table 8. The lymphoblastic lymphomas, thought to represent the neoplastic counterpart of developing thymic lymphocytes often express Leu 6, a marker of thymic differentiation.[31] In addition, lymphoblastic lymphomas may often show Leu 2^+ 3^+ or Leu 2^- 3^- phenotypes (markers of thymic differentiation), while these phenotypes were observed in the minority of the peripheral T-cell lymphomas.[31-33] Also, virtually all lymphoblastic lymphomas express Leu 9. Differences between peripheral T-cell lymphomas and mycosis fungoides have been discussed in a previous publication and are summarized in Table 8.[34]

The majority of the peripheral T-cell lymphomas (72%) showed the presence of Ia antigen. This is in agreement with the findings of Borowitz et al and in contrast to the findings of Knowles et al, who found an absence of Ia antigen in all of their T-cell neoplasms.[7,12] It must be noted that almost half of Knowles' cases were either mycosis fungoides or lymphoblastic lymphomas, T-cell lymphomas which usually do not express Ia antigen (see Table 8). Ia antigens are most often detected on B-lymphocytes, monocytes/macrophages, and some hematopoietic stem cells, but are also expressed on activated T-cells. In fact, in Knowles' study, there was evidence of T-cell activation in their tumors, as indicated by reactivity with OKT9, loss of ANAE, and heat-stable E-rosette formation.

An interesting finding in this study was the observation in serial biopsies on one patient performed 3 years apart. In this patient, the lymphoma converted from a cytotoxic/suppressor phenotype in an initial skin biopsy to a helper phenotype with loss of an additional pan-T antigen in a subsequent lymph node and skin biopsy. The loss of the additional marker is not unexpected (and may be explained on the basis of progressive dedifferentiation), but the change from cytotoxic/suppressor to helper phenotype is perplexing. More cases of T-cell lymphoma with serial biopsies over time need to be studied to confirm this observation, the significance of which is unclear.

Contrary to the findings of Shimoyama and Watanabe, there was no correlation of morphology and immunophenotype.[15,35] In their studies, all cases of AILD-like T-cell lymphomas were shown to be of cytotoxic/suppressor phenotype; this was not noted in our study. The interactions among neoplastic cells and between neoplastic and nonneoplastic cells that lead to distinctive morphologic patterns must depend on factors other than the antigens investigated in this study. The prognostic significance of these morphologic and immunologic findings is under study (Horning S, Weiss LM, Crabtree GS, Rouse RV, Warnke RA, in preparation).

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