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Brief Note

Percentage of the Lymphocyte with IL-2 Receptor in Reactive and Neoplastic Lymphoproliferative Conditions

— Could its High Content be Significant in the Diagnosis of Adult T Cell Leukemia/Lymphoma? —

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Key words : IL-2R — ATL — lymph node — lymphoproliferative disease

Interleukin 2 (IL-2), originally named as T cell growth factor ; TCGF, stimulates immunocompetent cells, especially T lymphocytes, to differentiate and proliferate. On the other hand, those T cells provide receptors for IL-2 (IL-2 receptor ; IL-2R) on their cell surface. IL-2R is an acidic glycoprotein of 60,000-65,000 molecular weight.[1] Recently, monoclonal antibodies against IL-2R have been produced and have enabled the identification of activated T cells, in cell suspension by immunofluorescent technique using spectrophotometry, and *in situ* in the tissue with immunohistochemistry.

Adult T cell leukemia/lymphoma (ATLL) is a newly identified lymphoproliferative disorder[2] characterized by relatively pathognomonic multilobated lymphoid cells in the peripheral blood which express T helper/inducer cell markers (CD4) but exhibit suppressor activity. Antibodies against ATLL-associated antigen (ATLA) or human T-lymphotropic virus I (HTLV-1) associated antigen are present in these patients.[3] It is also now characteristically demonstrated that IL-2 receptor (equivalent to Tac antigen) is expressed by ATLL cells,[4] although IL-2R expression of ATLL cells in peripheral blood is not always extensive.

During our study of T cell markers in reactive and neoplastic lymphoproliferative conditions, we raised questions that tumor cells in swollen lymph nodes from patients with ATLL may express IL-2R in high proportion, and that high content of the cells with IL-2R in the lymph node, when examined by spectrophotometry, may be an indication of ATLL. In order to test whether our hypotheses are correct or not, we examined lymphocytes in a variety of lymphadenopathic conditions for its surface markers including IL-2R.[5] In addition, we asked clinicians to inquire about the presence of ATLA antibodies in patients' sera when such test could be permitted. Reported herein is our preliminary result on this subject.

Twenty-five lymph nodes ; 18 from 18 cases of malignant lymphomas, 7 from 7 cases of reactive lymphadenopathy, and five tissue samples other than lymph nodes ; 3 of malignant lymphomas, one of plasmacytoma, and one of reactive lymphoid proliferation, were utilized for this study (Table 1). A small piece of the fresh tissue from each case was minced manually with scissors and was put in fetal calf serum (FCS)-added phosphate-buffered saline (PBS)

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TABLE 1. Materials examined and the result of serum ATLA antibodies

Organs and histological diagnosis	ATLA antibodies		
	Not determined	Determined	
		(−)	(+)
1. Lymph nodes			
Malignant lymphoma			
diffuse pleomorphic	1	2	0
diffuse large cell			
B cell type	1	1	0
T cell type	0	2	0
unspecified	3	1	0
focal involvement	0	0	1
diffuse medium sized	1	0	0
diffuse mixed (ATLL)	0	0	2
Benign lymphadenopathy			
Follicular hyperplasia	1	0	0
Mixed hyperplasia	3	1	0
Paracortical hyperplasia	1	0	0
Necrotizing lymphadenitis	1	0	0
2. Other organs			
Malignant lymphoma			
unspecified	1	0	0
diffuse mixed	2	0	0
Plasmacytoma	1	0	0
Pseudolymphoma	1	0	0

until use (4°C). This free cell suspension was then passed through a millipore filter (300 mesh) and a cell pellet was collected. IL-2R on the lymphocytes were detected by Spectrum III at Special Reference Laboratory (SRL), using antibodies against IL-2R purchased from Becton-Dickinson (Mountain View, CA).

As depicted in Fig. 1, our results indicate that the percentage of IL-2R (+) lymphoid cells is not necessarily high in cases of ATLL. This may be due to a polymorphism seen in lesions of this neoplasm; namely, a marked admixture of reactive lymphoid cells as well as other kinds of inflammatory cells. Seemingly, the number of IL-2R (+) lymphoid cells may correlate well with the serum level of ATLA antibodies. However, further studies are definitely needed for this conclusion. In general, non-lymphomatous lymph nodes contain IL-2R (+) cells below 5 percent. Lymphomas other than ATLL may show its percentage as high as ATLL. Therefore, high content of IL-2R (+) lymphocytes in the lymphoid tumor does not always indicate the presence of ATLL. IL-2R (+) lymphocytes are now considered to represent activated T cells,[1,6] and lymphomas of activated T cells other than ATLL may show high inclusion ratio. It is of great interest that a lymphoma case of possible B cell origin possessed 15.4% of IL-2R positivity which is as high as that of ATLL. This case was diagnosed as such because of the immunohistochemical demonstration of MB-1 in tumor cells and their morphology. Unfortunately, the serum titer of ATLA antibodies could not be determined in this case. The presence of IL-2R (+) cells in B cell lymphomas may be explained either by

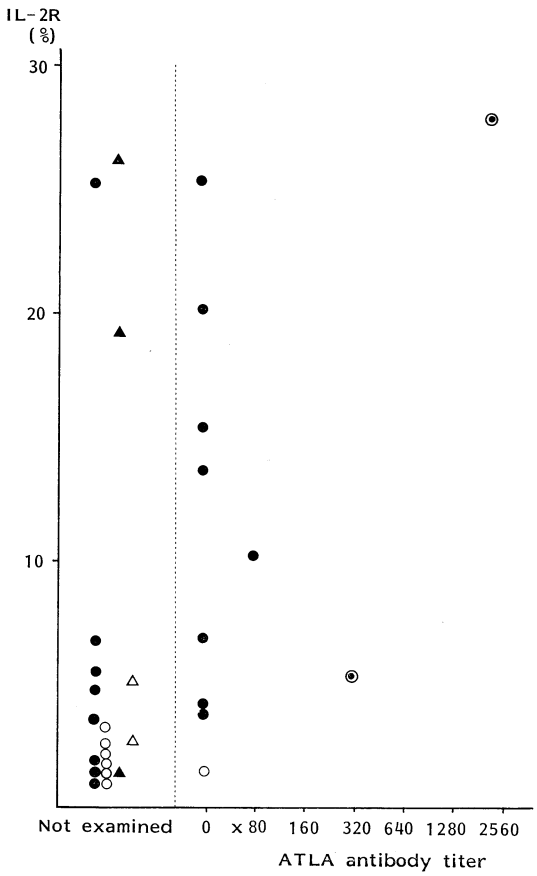

Fig. 1. Relation between the percentage of lymphocytes with IL-2R and serum level of ATLA antibodies
(●: Malignant lymphoma, lymph node; ⊙: ATL; ○: Benign lesion, lymph node; ▲: Malignant lymphoma, other organs; △: Benign lesion, other organs)

the mixture of reactive activated T cells in the tumor or by the co-expression of IL-2 receptor of neoplastic B lymphocytes. We think that comparative immunohistochemical studies are necessary to prove or disprove these possibilities.

In summary, it is concluded from the result we obtained that high content of IL-2R positive cells itself does not substantiate ATLL, and that the percentage of IL-2R (+) cells is not necessarily high in cases of ATLL.

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