Int. J. Cancer: **37**, 335–341 (1986)

CLINICAL ANALYSIS OF 33 PATIENTS WITH ADULT T-CELL LEUKEMIA (ATL)-DIAGNOSTIC CRITERIA AND SIGNIFICANCE OF HIGH- AND LOW-RISK ATL

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The clinical characteristics of 33 patients with adult T-cell leukemia (ATL) are described. All patients were born and have lived in Miyazaki Prefecture (southwest of Japan). Because of a wide range of clinical presentations and courses, they were subdivided into 2 groups. In the high-risk group, patients presented with high white-cell counts (WBC $\geqq$ 20,000/μl) and over 30% of abnormal lymphoid cells (18 patients) and hypercalcemia with a low percentage of leukemic cells (5 patients). In this group the median survival time was only 3 months despite various modes of treatment. In contrast, patients of the second group exhibited a low percentage of abnormal lymphoid cells (WBC < 20,000/μl and/or leukemic cells < 30%) and had no hypercalcemia (8 patients). Their clinical course was chronic with a median survival of 8 months, regardless of modalities of treatment. Two patients went through a period when the number of circulating leukemic cells was low ($\leq$ 5%) before overt leukemia appeared. Other clinical features, signs, symptoms, routine laboratory data, serum anti-ATL-associated antibody, cell membrane markers and cytogenetic studies were similar to those observed in other districts of Kyushu island.

Since adult T-cell leukemia (ATL) was initially described by Uchiyama *et al.* in 1977, many case reports have been collected and analyzed for clinical characteristics. However, the higher the number of patients, the more complicated are the clinical features. The type of ATL varies from smoldering and chronic to acute, and smoldering or chronic ATL may end up in acute phase of the disease (crisis) (Yamaguchi *et al.*, 1983*a*). Typical ATL usually shows helper/inducer antigen OKT4 but a lack of antigen OKT8 (Yamada, 1983). However, $OKT4^+/OKT8^+$ ATL has been also reported, suggesting the presence of phenotypic heterogeneity (Schnitzer *et al.*, 1982; Tamura *et al.*, 1985). In addition, the cell membrane markers of ATL cells may change in the course of disease (Ichimaru *et al.*, 1984).

In contrast to investigation of clinical aspects of the disease, much progress has been made with respect to etiological aspects, such as discovery of human T-cell leukemia virus (HTLV-I). Virtually all patients with ATL carry the antibody to HTLV-I as well as proviral DNA in their leukemic cells (Yoshida *et al.*, 1984). Yamaguchi *et al.* (1984) recently proposed that T-cell malignant diseases should be classified further by studying HTLV-I proviral DNA in the neoplastic cells. They also suggested that detection of proviral DNA might be a useful means of diagnosing atypical ATL. It is our opinion, however, that ATL must be diagnosed clinically and that complicated analysis of proviral DNA may not always be necessary to make a diagnosis. Clinical features of 33 patients with clinically-diagnosed ATL are summarized in this report to define the simplified diagnostic criteria and to subgroup ATL patients.

PATIENTS AND METHODS

We have just reported the analysis of 237 patients who were histologically diagnosed as having malignant lymphoid malignancies during the period from 1979 to 1982 (Suzumiya *et al.*, 1985). Twenty-five of these patients met the diagnosis of ATL according to the diagnostic criteria of Uchiyama *et al.* (1977). Since June 1980, studies have been performed on serum anti-ATL-associated (anti-HTLV) antibody and more definite cell surface marker analysis including a battery of monoclonal antibodies (MAbs). Because of the strong association between HTLV-I and ATL, this report summarizes data from patients with ATL occurring after June 1980. During the period from June 1980 to December 1983, we saw over 300 patients with leukemia and lymphoma in Miyazaki Prefectural Hospital and Miyazaki Medical College Hospital. These patients were reviewed by two groups, *i.e.* the Lymphoma Study Group and the FAB Study Group of Miyazaki. For 33 patients a diagnosis of ATL was established. Despite the wide range of clinical features seen in ATL, relatively few problems were encountered in making the diagnosis, since ATL is endemic in our district. However, it was far more difficult to differentiate ATL from T-cell lymphoma with leukemic transformation. The differential points will be discussed later. There were 16 male and 17 female patients whose ages ranged from 31 to 75 years (aver-

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Received: March 30, 1985 and in revised form July 15, 1985.

age 54). All were born and had lived in Miyazaki Prefecture. Information concerning blood transfusion was available on 14 patients, and 2 of them had received blood products prior to development of ATL.

Routine physical examination and laboratory studies, including complete blood counts, blood chemistry and chest X-ray, were performed on all patients. Most patients were studied with computerized tomography or abdominal sonography for intra-abdominal lesions. Purified-protein-derivative (PPD) skin tests and serum immunoglobulin determinations were also performed. Peripheral blood smears of all patients were examined after staining with May-Grünwald-Giemsa solution. Bone-marrow specimens were also reviewed when they were available. Histological diagnosis of malignant lymphoma was made according to the classification proposed by the Lymphoma-Leukemia Study Group of Japan (Suchi *et al.*, 1979), when lymph-node or skin biopsy was performed. Cytogenetic studies were carried out on aspirated bone-marrow specimens or peripheral blood by the trypsin-G-banding method. Cell surface marker studies were carried out on mononuclear cell suspensions from peripheral blood by the indirect immunofluorescence method using a series of MAbs (OKT series, Ortho Diagnostic Systems, Raritan, NJ) and FITC-conjugated goat anti-mouse IgG antibody (TAGO, Burlingame, CA) as a secondary reagent.The fluorescein-positive cells were assessed by means of an Olympus BHF microscope (Olympus, Tokyo) with epi-illumination. Investigation for Tac antigen was kindly performed by Dr. K. Sagawa at Kurume University. The cells were also studied for their ability to form rosettes with sheep erythrocytes (E), antibody-complement-sensitized ox erythrocytes (EAC) and autologous erythrocytes (AE); surface immunoglobulin (sIg) determinations were done as described previously (Tamura *et al.*, 1984*b*). The patients' sera were examined for the antibody against anti-ATL-associated antigen by the indirect immunofluorescent antibody technique described by Hinuma *et al.* (1981).

RESULTS

Miyazaki Prefecture, with a population of 1,166,257, comprised in 1982 9 cities, 28 towns and 7 villages. Thirty-three patients with ATL were found in 7 cities and 7 towns (Fig. 1), although the northern part of Miyazaki could not be fully covered by our institutions. The majority of these areas are located along or near the sea coast. ATL was found in 14 patients (42.4 %) between March and June, suggesting that the disease often manifests itself between spring and early summer.

Signs and symptoms (Table I)

One-third of the patients presented general fatigue, fever and/or respiratory symptoms. Physical examination showed a slight enlargement of lymph nodes which were usually less than 2 cm in diameter in 3/4 patients. Hepatosplenomegaly was also frequently seen in these patients. There was a wide variety of skin lesions, including erythrodermia, maculopapular rash and nodular lesions. Fungal infection of the skin was also commonly observed. Only a few patients had anemia, jaundice or anasarca on physical examination.

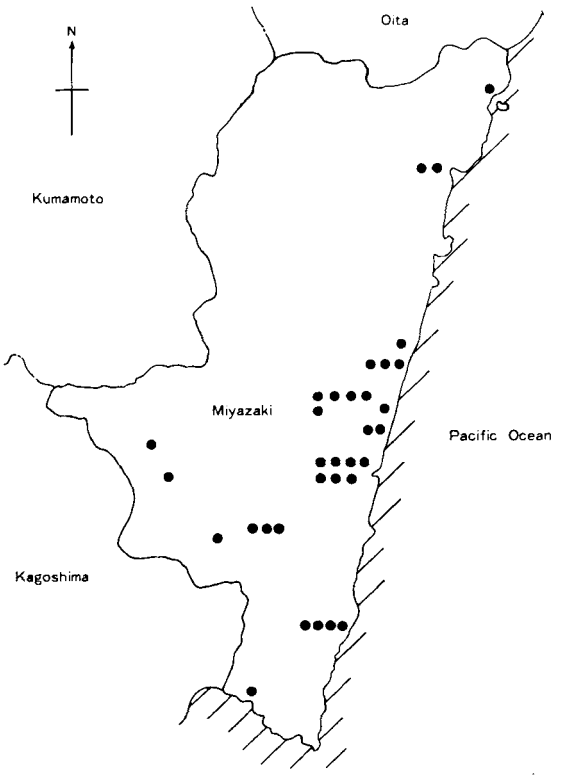


FIGURE 1 – Distribution of patients in Miyazaki Prefecture. The majority of the patients had lived in the areas near the coast before ATL was diagnosed.

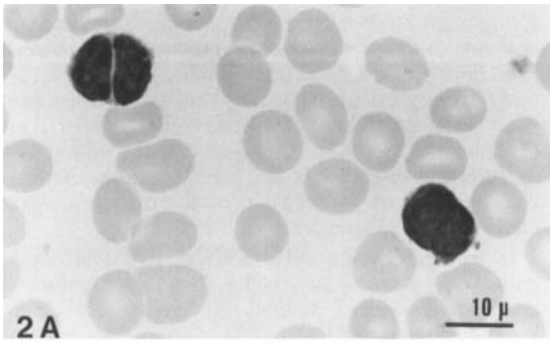
TABLE I - CLINICAL FEATURES

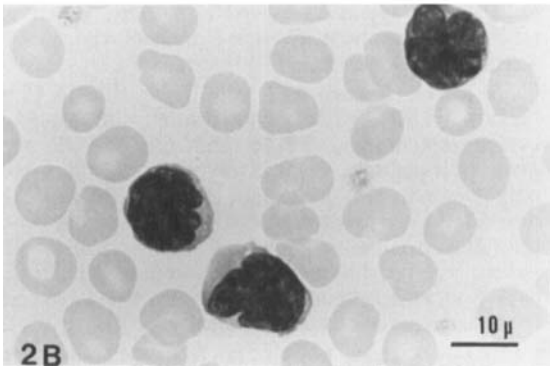
Number of patients	33
Age: mean ± SD (range)	54 ± 12 years (31–75)
Sex: male/female	16/17
Symptoms (%)	
Cough, sputum, shortness of breath	39.4
General malaise	39.4
Fever	33.3
Abdominal pain and distension	15.2
Itching	6.1
Signs (%)	
Lymphadenopathy	75.8
Hepatomegaly	45.5
Splenomegaly	36.4
Skin lesion	75.8
Anemia	9.1
Jaundice	6.1
Anasarca	6.1

Laboratory findings (Table II)

The majority of the patients had normal erythrocyte and thrombocyte counts but a few exhibited mild anemia and/or thrombocytopenia. White cell count (WBC) was significantly elevated to an average of 49,500/μl with 5 to 99% abnormal lymphocytes. Two patients had normal WBC with 2 to 5% abnormal lymphocytes.

Abnormal lymphocytes can be divided into 3 types (Fig. 2*a-c*). Many cells in the patients having a high





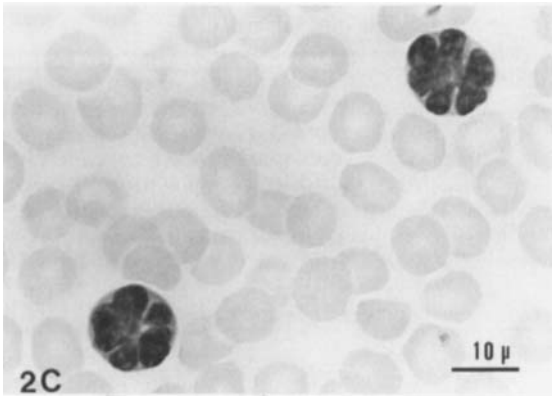


FIGURE 2 – (*a*) Type 1: Mature-looking lymphocytes with cleaved and separated nuclei. (*b*) Type 2: A monocytoid cell and abnormal lymphoid cells with cerebriform nuclei. There are one or two distinct nucleoli in the nuclei. (*c*) Type 3: Polymorphic lymphoid cells with typical lobulated or cauliflower nuclei.

TABLE II – LABORATORY FINDINGS

	Mean (Range)
Peripheral blood (33 pts[1])	
Hb (g/dl)	13.0 (4.9–17.5)
Platelets × $10^4/\mu l$	20.7 (1.2–55.0)
WBC/μl	49,500 (6,400–274,300)
Abnormal lymphocytes (%)	(5–99)
Bone marrow (25 pts)	
Nucleated cell count/μl	99,300 (16,000–580,000)
Abnormal lymphocytes (%)	(0.4–95.5)
Dry tap (%)	4.0
Blood chemistry (33 pts)	
LDH (w.u/ml)	1,475 (238–7,020)
Ca (mg/dl)	9.3 (7.8–18.0)
Total Bilirubin (mg/dl)	0.81 (0.13–4.70)
TP (g/dl)	6.16 (4.60–7.78)
Immunoglobulin (mg/dl)	
IgG	1,074 (548–1,819)
IgA	203 (22–572)
IgM	123 (26–518)
Negative PPD test (27 pts) (%)	96.3
Anti HTLV-I antibody (33 pts) (%)	93.9

[1]Pts: patients.

white-cell count were of type 3, *i.e.* polymorphic abnormal lymphoid cells, while the patients with a low percentage of leukemic cells and lower white cell count showed predominantly type-1 abnormal lymphoid cells. It is suggested that the higher the leukocyte and leukemic cell counts, the more polymorphic are the abnormal lymphoid cells. In contrast to peripheral blood, the bone marrow was involved by abnormal cells to a lesser extent. Pathological specimens were obtained from 24 patients. All showed diffuse histology, with medium-sized cell type in 12, large cell type in 2 and pleomorphic type in 10 patients.

Blood chemistry profiles revealed elevated lactate dehydrogenase (LDH) (84% of the patients), hypoproteinemia (63%), hypercalcemia (24%) and hyperbilirubinemia (22%). When LDH level was higher than 1,000 IU/ml (14 patients), median survival time was only 2 months, while 10/19 with LDH level < 1,000 IU/ml survived for 6 1/2 months. All the former patients but 3 presented over 20,000/μl of WBC, *i.e.* high LDH level was a reflection of high WBC with a high percentage of leukemic cells ($r=0.5173$, $p < 0.01$). Serum immunoglobulin level was within normal limits in the majority of the patients. PPD skin test was performed on 27 patients, and was negative in all but one patient.

Antibody to ATL-associated antigen was positive in 31 of 33 patients. Short-term culture of leukemic cells was performed on the 2 negative patients. One patient became positive for ATL-associated antigen, but in the other patient the number of leukemic cells was too low for culturing, since he had been intensively treated with antineoplastic agents prior to referral. Cytogenetic study revealed abnormal karyotypes in 7 of 12 patients as shown in Table III. There was seemingly no common aberration in our patients. Membrane surface marker study showed E-rosette(+), EAC-rosette(−), sIg(−), AE-rosette(−), OKT3(+) or (−), OKT4(+), OKT8(−), OKT11(+), Bl(−), OKIal(+) or (−), and anti-Tac(+) or (−). There was one patient with OKT4(+)/OKT8(+) phenotype.

TABLE III – CYTOGENETIC FINDINGS

Abnormality rate	58.3% (7/12)
i)	46XY, $2p^-$, $3q^-$, −13, $18p^-$, $15p^+$, $19q^+$, +mar
ii)	46XY, −3, −13, −18, +mar 1, 2, 3.
iii)	46XX, −13, −13, −22, +mar 1, 2, 3, $1p^+$, $18p^+$
iv)	47XY, $+7q^+$, $14q^+$
v)	47XX, +4
vi)	47–50XY, $1q^+$, $12p^+$
vii)	49XX, −7, −15, $+1p^-$, +8, +9, +mar 1, 2, $13q^+$
	49XX, −7, −8, −15, −18, $+1p^-$, +3, +9, +mar 1, 2, 3, 4, $3q^+$

Treatment response and survival

Before response and survival are discussed, ATL must be subdivided into at least 3 groups, since it has a wide range of clinical courses as suggested by Yamaguchi *et al.* (1983*a*) who divided it into acute, chronic and smoldering ATL. Their classification appears to be vague and, therefore, difficult to apply to our patients. We have felt that a more descriptive classification might easily be applied to our patients, and the following classification is proposed as presented in Table IV.

TABLE IV - CLASSIFICATION OF ATL

High-risk group
1. High percentage ATL
   WBC count $\geqslant 20{,}000/\mu l$
   and
   leukemic cells $\geqslant 30\%$
2. Low percentage ATL with hypercalcemia
   WBC count $< 20{,}000/\mu l$
   and/or
   leukemic cells $< 30\%$
   and
   hypercalcemia (> 10.5 mg/dl) at the time of diagnosis

Low-risk group
1. Low percentage ATL without hypercalcemia
   WBC count $< 20{,}000/\mu l$
   and/or
   leukemia cells $< 30\%$
   and
   no hypercalcemia at presentation
2. Pre-ATL
   WBC count normal
   and
   leukemic cells $\leqslant 5\%$
   This condition must last at least 2 months

Crisis
The patients' clinical course may change from that of low-risk group to that of high-risk group. Some patients may develop hypercalcemia crisis with no increase in number of leukemic cells.

High-percentage ATL and low-percentage ATL with hypercalcemia fell into a high-risk group with a median survival of 2 to 3 months, while low-percentage ATL without hypercalcemia had a more chronic course with a median survival of 8 months. Pre-ATL was seen in 2 patients. One of them had had 2-3% abnormal lymphoid cells in the peripheral blood associated with erythrodermia for 5 years. The disease terminated in an aggressive phase and the patient died of general deterioration 4 months after the acute transformation despite aggressive treatment. Another patient showed abnormal lymphoid cells in 5% of 6,800 leukocytes/μl associated with papular skin lesions. She had a fairly chronic course, but died of systemic herpes infection associated with crisis 8 months after diagnosis. The treatment plan for our ATL patients varied from one institution to another.

Combination chemotherapy in general consisted of vincristine, cyclophosphamide, 6-mercaptopurine and prednisolone (VEMP) (Shimoyama and Kimura, 1972), cyclophosphamide, adriamycin, vincristine and prednisolone (CHOP or VEPA) (McKelvery *et al.*, 1976; Lymphoma Study Group, 1982), vincristine and prednisolone (VP), pepleomycin, vincristine and prednisolone (POP) (Tamura *et al.*, 1984*a*), and VP-16. Total body irradiation (TBI) was given as reported previously at a total dose of 100 to 150 rads per course (Tamura *et al.*, 1983). Response criteria were denoted as complete response (CR), partial response (PR), no change (NC) or progression of the disease as previously defined (Tamura *et al.*, 1983).

In low-percentage ATL without hypercalcemia (8 patients), 3 patients survived 7, 7 and 9+ months with no therapy, while 2 patients survived 3 (early death) and 21 months (PR) with TBI. One patient had local radiation therapy and survived 17 months. VEMP and VEPA regimens were given to 2 patients who survived 4 (PD) and 7+ months (PR) respectively.

For low-percentage ATL with hypercalcemia (5 patients), VAMP (VEMP with adriamycin instead of cyclophosphamide), VP-16 and CHOP-POP were given to 3 patients, respectively. Survival times were only 3 months (PR), 1 month (early death) and 2 1/2 months (NC), respectively. One patient died one month after diagnosis before treatment could be started. One patient received 130 rads of TBI and has been alive for over 5 months, although she requires intensive treatment for hypercalcemia periodically.

Eighteen patients fell into the high-percentage ATL category. Four patients received the VEMP regimen and survived 2 weeks (early death), 2 months (PR), 3 months (PD) and 7 months (PR). VP-16 was given to 2 patients with a survival of 21 days (early death) and 4 months (PR). Four patients received POP (PR), VP (PD and PR) or VEPA (early death), but all died within 2 months of diagnosis. TBI was given to 8 patients, all of whom achieved PR except for one patient with complete remission who has survived over 28 months. Seven patients with PR showed a survival time of 2, 3, 4, 4, 6, 7+ and 9+ months. The survival curve is shown in Figure 3. Survival has been evaluated by the Kaplan-Meier method and compared by means of the log-rank test. There was a significant difference in survival between high- and low-risk groups ($p < 0.05$).

Causes of death were basically the same among the 3 groups. Thirteen patients died of respiratory infection. This was the leading cause of death, followed by

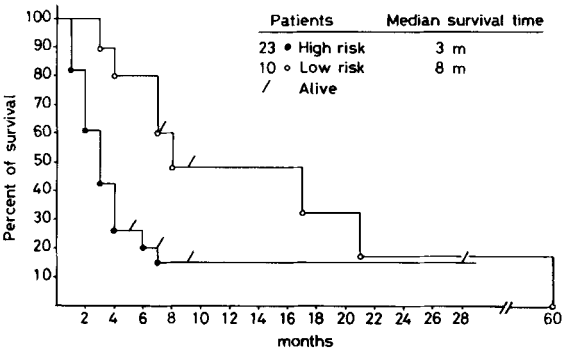


FIGURE 3 - Survival curve for patients with low- and high-risk ATL. There was a significant difference between the two groups ($p < 0.05$). "Alive" denotes patients alive at the time of this report.

general deterioration due to massive leukemic infiltration to the vital organs (5), renal failure (3), central nervous system involvement (2),gastrointestinal bleeding (2), systemic herpes infection (1) and disseminated intravascular coagulopathy (1). Only 6 patients were alive at the end of December, 1983.

DISCUSSION

Approximately 3 years after a new disease entity, adult T-cell leukemia, was proposed in 1977 (Uchiyama *et al.*), hematologists, dermatologists, pathologists and technicians working in our district were grouped into the Lymphoma Study Group of Miyazaki.

Miyazaki is a fairly big prefecture with population of a little over one million. Two hospitals involved in this study are located in the middle of the prefecture along the sea coast and, therefore, we have probably covered around 50% of population in Miyazaki. From this approximation, the estimated incidence of ATL would be about 2 new patients/100,000/yr in addition to over 5 patients/100,000/yr of malignant lymphoid malignancies in our district (Suzumiya *et al.*, 1985), which appears to be higher than the incidence of malignant lymphoma in Japan (Watanabe, 1980). Because both peripheral T-cell lymphoma and ATL are malignant diseases of peripheral T cells, they have been categorized as adult T-cell leukemia/lymphoma (ATLL). However, T-cell lymphoma appears to be clinically different from ATL. The former presents large lymph nodes, usually over 2 cm in diameter, and responds better to treatment with longer survival, which may be partly due to a much lower incidence of complications such as infections and hypercalcemia. When T-cell lymphoma becomes leukemic, the leukemic cells are rather larger and more monocytoid than those of ATL. The degree of immunodeficiency, as shown by negative skin tests or incidence of infectious complications, seems to be far lower in peripheral T-cell lymphoma than in ATL. In this respect our experience agrees with that of Nomura and Matsumoto (1981), although these workers found no difference in survival between ATL and T-cell lymphoma patients. If the heterogeneity of ATL had been considered by these authors, treatment response and prognosis would have differed greatly between ATL and T-cell lymphoma. Abnormal lymphoid cells in peripheral T-cell lymphoma also carry a different membrane surface phenotype from that of ATL (Tamura *et al.*, 1984).

Clinical features of ATL in Miyazaki reported here are similar to those in some other prefectures located in Kyushu island, such as Kumamoto (Yamaguchi *et al.*, 1983*b*), Nagasaki (Kinoshita *et al.*, 1982) and Kagoshima (Nomura and Matsumoto, 1981). The diagnosis of ATL has been made according to clinical features first presented by Uchiyama *et al.* (1977) and later by Yamaguchi *et al.* (1983*a*) who have pointed out a variety of clinical pictures and courses. Because of this clinical heterogeneity, diagnostic criteria have become more vague and difficult to apply to the patients. Therefore, we decided to propose the following simplified diagnostic criteria (Table V) for suspected cases of ATL. (1) Adult onset. (2) More than 5 % of abnormal lymphoid cells (Fig. 2) in the peripheral blood, not accompanied by recent viral or rickettsial infection. (3) Lymphadenopathy frequently seen, but with a low degree of lymph-node enlargement (nodes usually less than 2 cm in diameter. No palpable or visible lymph-node enlargement at all in some patients). (4) Abnormal lymphoid cells in the circulation and lymph nodes with a T-cell marker and positive E-rosetting, usually exhibiting OKT4 or Leu3a-positive phenotype. (5) Histology of the involved tissues showing diffuse medium-sized cell, large-cell or pleomorphic type of non-Hodgkin's lymphoma: cases with lymphoblastic histology excluded. These 5 features must be sought before ATL is considered. Patients who have less than 5% of abnormal lymphoid cells in the peripheral blood not associated with viral or rickettsial infection, should be followed up regularly for possible progression of the disease. They can be considered as having smoldering ATL or pre-ATL only when symptoms of full-blown ATL develop.

TABLE V – DIAGNOSTIC CRITERIA FOR ATL

Major criteria
1. Adult onset
2. Over 5% of peripheral white blood cells abnormal (Fig. 2*a-c*)
3. Abnormal cells E-rosette-positive (usually OKT4 or Leu3a-positive)
4. Serum anti-ATLA (anti-HTLV-I) antibody positive (proviral DNA found in leukemic cells)

Other findings
1. Lymphadenopathy (small, less than 2 cm in diameter). Histologically, medium, large or pleomorphic type excluding lymphoblastic histology
2. Immunodeficient conditions
3. Hypercalcemia
4. Skin involvement

Other important findings are: The disease is endemic in the south-western district of Japan and the Caribbean islands, *i.e.* rural areas with a warm and humid climate near the sea coast. Virtually all patients carry the antibody to HTLV-I. Monoclonal integration of proviral DNA in the leukemic cells has recently been reported (Yoshida *et al.*, 1984). Immunodeficient conditions are seen with frequent opportunistic infections including viral, fungal and Gram-negative bacterial infections as well as infection with *Pneumocystis carinii*, most patients dying of pulmonary infection. Skin involvement is common (about 60%). Mild hepatomegaly and/or splenomegaly are often seen (about 40%). Hypercalcemia with or without renal failure occurs in about 30% of cases.

The clinical courses of our patients varied widely, as suggested by Yamaguchi *et al.* (1983*a*) who used the terms of acute, chronic and smoldering ATL. We have analyzed our findings with a more descriptive classification (Table IV) which appeared to better represent their features, *i.e.* the higher the leukocyte count, the poorer the prognosis associated with short survival; presence of hypercalcemia is an ominous sign independent of the degree of leukemic infiltration. Kinoshita *et al.* (1983) reported a significant difference in survival between patients having WBC $\geqq$ 35,000/μl and those with $<$ 35,000/μl, but these workers did not analyze the percentage of leukemic cells. Our data showed that WBC $\geqq$ 20,000/μl and more than 30% of leukemic cells were apparently the most important prognostic factors. Serum LDH level seemed to move in parallel with the activity of the disease, *i.e.* the

number of leukemic cells and tumor masses, and therefore, it was also well correlated with prognosis. Kinoshita *et al.* (1983) also observed a short survival with more than 500 IU/ml of LDH, and they placed more weight on LDH than on WBC as a prognostic factor and for the treatment plan. Our data, however, indicated that both the number of leukemic cells and the calcium level were the predictive prognostic factors.

Variable chromosome abnormalities were observed in our patients, but no common abnormal features have been noted. Significance of $14q^+$ or trisomy 7 was reported (Ueshima *et al.*, 1981; Miyamoto *et al.*, 1982), but their implication remains to be studied. Membrane surface marker study showed OKT4+/OKT8− (helper/inducer) phenotype, except for one patient whose leukemic cells expressed both OKT4 and OKT8 antigens. Despite helper/inducer phenotype, leukemic cells of typical ATL were reported to have potent suppressor activity against B-cell differentiation by pokeweed mitogen and immunoglobulin synthesis by normal B cells (Uchiyama *et al.*, 1978; Yamada, 1983).

In terms of treatment, administration of antineoplastic agents did not seem to alter the clinical course in high-risk ATL. New modalities of treatment including new agents should be investigated for ATL as suggested by our data and other reports (Lymphoma Study Group, 1982). A low-percentage ATL appeared to have a better prognosis with a long clinical course, regardless of the modality of treatment. Even no therapy might be justified when little progression is noted.

In contrast to a variety of clinical features, there has been some progress in etiological study of the disease. Almost 100% of the patients show positive anti-ATL-associated antibody (Hinuma *et al.*, 1981), and clonal integration of HTLV-I proviral DNA is found in the leukemic cells (Yoshida *et al.*, 1984). Yamaguchi *et al.* (1984) proposed that T-cell malignant disease, including atypical ATL, should be classified further by studying HTLV-I proviral DNA in the neoplastic cells. However, from the clinical point of view, we feel that this complicated, time-consuming and expensive analysis of proviral DNA may not always be necessary in making a specific diagnosis and classifying the disease. The diagnostic criteria described above would suffice in most of the patients, and practical and descriptive classification is more important than etiological classification. Adult T-cell leukemia is a distinct disease entity. Because of variable clinical presentations and courses, practical and simplified diagnostic criteria and classification are proposed here in this report. However, the management of ATL is extremely difficult. Intensive investigation is needed for the elaboration of proper treatment plans, established according to the activity of the disease.

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