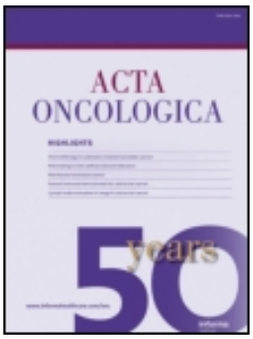

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RADIATION THERAPY OF ADULT T-CELL LEUKEMIA

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Between January, 1983 and December, 1991, 30 adult patients with T-cell leukemia (ATL) and lymph node or skin lesions resistant to chemotherapy were treated by irradiation. Thirty Gy of high energy x-rays, ^{60}Co gamma rays or electrons was delivered to 22 lymph node lesions in 17 patients, for focal cutaneous lesions in 6 patients, and as total skin irradiation in 7 patients. Irradiation therapy was effective in all patients with skin lesions and in 12 of 17 patients with lymph node lesions. Symptoms such as pain or itching diminished in all cases and no severe side effects were observed. Radiation therapy thus achieved good control of ATL associated focal lesions resistant to chemotherapy. Even if the prognosis of ATL is poor, radiation therapy should be considered as a palliative therapy.

Adult T-cell leukemia/lymphoma (ATL) is a human T-cell leukemia virus type 1 (HTLV-1) associated malignancy, mostly seen in the southwestern part of Japan, the Caribbean basin, and the southeastern part of the United States (1–6). The physical findings in ATL include lymph node swelling (86%), hepatomegaly (77%), splenomegaly (51%), and skin lesions (49%) (3). Although there is no established definitive treatment for ATL, multiple-drug chemotherapy is as a rule used as the first treatment. However, ATL may show strong drug resistance and focal lesions such as lymph node swelling or skin lesions are very often difficult to control with chemotherapy alone (7, 8).

In the present report, the radiation response of focal ATL lesions is studied and the role of radiotherapy in the management of ATL patients discussed.

Material and Methods

Between January 1983 and January 1991, 30 ATL patients were treated by irradiation at Kumamoto University Hospital. All these patients were diagnosed clinically and confirmed by antibody reacting with human T-cell lymphoma virus type 1 (HTLV-1). There were 13 patients of cutaneous type with focal or diffuse skin lesions and 17 patients of acute type with lymph node swelling. All cases except one patient with skin lesions were initially treated by chemotherapy. Focal lesions of these patients showed resistance to chemotherapy and the patients were referred to our department for radiation therapy of the focal lesions.

To local lesions, a total dose of 30 Gy was given by 6 to 12 MeV electron from a linear accelerator, with three fractions per week and a fraction dose of 3 Gy. In 8 patients a total dose of 30 Gy was delivered to the entire skin using 6 MeV electron beam with acryl bolus and a fraction dose of 1.5 Gy. The source–surface distance (SSD) was 350 cm and 2 pairs of angled beam (4 fields) were used. The left anterior oblique and right posterior oblique fields were treated one day and the right anterior oblique and left posterior oblique the following day so that a total dose of 3 Gy was delivered in 2 days. The patient was treated 4 days a week up to a total dose of 30 Gy in 5 weeks. In six patients, total skin irradiation was used as the initial radiotherapy. To lymph node lesions, a total dose of 12 to 40 Gy was given by 3 MV to 10 MV x-rays or ^{60}Co gamma rays with 5 fractions per week and a fraction dose of 1.5 to 2 Gy. The clinical features, irradiation source/dose, and previous treatment of our patients are summarized in Tables 1 and 2. The initial effect was evaluated at two weeks after the end of irradiation, and

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Table 1

ATL patients with skin lesions

Case	Age	Sex	Skin lesions	Previous medical treatment	RT source/dose	Initial response	In-field recurrence	Out-field	Follow-up	
1	57	F	Entire skin	VEPA	6E/30 Gy	CR*	4M	(-)	disease free	63M
2	56	M	Axilla, groin, neck	Interferon	6E/30 Gy	CR**	26M	4M	disease free	63M
3	70	M	Entire skin	PUVA, COPP	6E/30 Gy	PR*	regrowth	(-)	dead	7M
4	68	F	Extremities	CPM + Pred	6E/30 Gy	CR	(-)	(-)	dead[1]	32M
5	59	M	Entire skin	VEPA	6E/30 Gy	CR	(-)	(-)	dead	9M
6	53	M	Entire skin	VEPA	6E/30 Gy	CR*	4M	(-)	alive with disease	36M
7	48	F	Extremities	VEPA	6E/30 Gy	CR	(-)	(-)	dead[2]	11M
8	39	M	Extremities	BLM/VEPA + VP16	3X/30 Gy	CR	3M	1M	alive with disease	18M
9	50	F	Extremities	MY-1, Interferon	6E/30 Gy	CR	1M	1M	dead	147M
10	34	F	Entire skin	MY-1, COPP, VEPA	6E/30 Gy	CR**	9M	4M	dead	8M
11	78	F	Entire skin	PUVA	6E/30 Gy	CR*	(-)	(-)	dead	12M
12	69	F	Trunk	(-)	6E/30 Gy	CR*	(-)	(-)	disease free	54M
13	78	M	Entire skin	VEPA	6E/30 Gy	CR*	(-)	(-)	dead[3]	46M

MY-1: immunotherapy
VEPA: Vincristine/VCR, cyclophosphamide/CPM, prednisone/pred, doxorubicin
COPP: CPM, VCR, natulan, pred
PUVA: Psolaren ultraviolet A assay
BLM: Bleomycin
* total skin irradiation as initial treatment
** total skin irradiation as second treatment
1: died of rhabdomyosarcoma of heart
2: no recurrent tumor at death, died of other disease
3: died of lingual carcinoma
Radiation quality: 6E = 6 MeV electrons; 3X = 3 MV x-rays
M = months

evaluated for PD (progression of disease), NC (no change), PR (more than 50% reduction of lymph node size or pronounced regression of skin lesions), and CR (complete remission).

Results

The initial response, clinical course, and findings during the follow up period are summarized in Table 1. Skin lesions of ATL were well controlled (PR + CR = 100%) by radiotherapy without major complications and the mean survival in these patients was 37.7 months. Although good initial response (CR + PR = 69%) was obtained in lymph node lesions, the prognosis was poor (mean survival = 5.4 months). All patients with lymph node lesions died of progressive ATL. Only four patients with skin lesions were alive at the time of reporting with observation times of 63 months (disease-free), 54 months (disease-free), 36 months (with disease) and 18 months (with disease). Four patients with skin lesions died of other diseases, in two of them other malignancies (lingual carcinoma and rhabdomyosarcoma of the heart respectively).

In the patients treated by local skin irradiation, recurrence outside the treatment fields was frequently seen (in 4 out of 7 cases) and numerous additional irradiation ports (54 ports in 4 patients; mean = 13.5) were needed to control these recurrent lesions. Two of these six patients were finally treated by total skin irradiation. In the patients treated by total skin irradiation as the initial treatment, local recurrence was observed in two patients (hand, thigh and head).

Discussion

Adult T-cell leukemia (ATL) is a distinct clinical entity associated with human T-cell leukemia/lymphoma virus-1 (HTLV-1) which sometimes produces focal lesions such as skin eruptions and/or nodules, lymph node swellings, and intracranial lesions (3). ATL is divided into four types; the acute type, the chronic type, the smoldering type, and the crisis type. The acute type is the most common form and the survival period is only a few months (3). The chronic type is considered to be a form of T-cell chronic leukemia in which the leukemia cells contain the proviral DNA of HTLV-1. The smoldering type is characterized by a long survival and the presence of a few ATL cells (0–3%) in the peripheral blood. The crisis type of ATL is the result of acute progression from the chronic or smoldering types. Recently, another subtype of ATL with predominant skin lesions (cutaneous type) has been proposed (9). The pa-

Table 2

ATL patients with lymph node lesions

Case	Age	Sex	Site of lymph node swelling	Previous medical treatment	RT source/dose	Initial response	In-field relapse	Out-field recurrence	Follow-up
14	39	M	Axilla	VEPA	6E/30 Gy	CR	(-)	(-)	dead 1M
15	46	F	Para-aortal	VEPA + COP	10X/50 Gy	CR	6M	4M	dead 8M
16	53	M	Neck, groin	VEPA	10X/30 Gy	CR	(-)	1M	dead 1M
17	48	M	Neck, para-aortal	VEPA	10X/19.8 Gy	PR	12M	13M	dead 16M
18	77	F	Neck	VEPA + COP	10X/12.6 Gy	NC		leukemia	dead 1M
19	66	M	Para-aortal	VEPA + COP	10X/20 Gy	CR	(-)	leukemia	dead 3M
20	63	M	Neck	VEPA + COP	6E/12 Gy	CR	(-)	6M	dead 7M
21	66	F	Neck	VEPA	Co/40 Gy	CR	(-)	leukemia	dead 16M
22	77	M	Neck	VEPA	3X/30.6 Gy	PR	3M	leukemia	dead 3M
23	46	M	Para-aortal, neck	VEPA	10X/27.2 Gy	CR	10M	10M	dead 13M
24	66	M	Neck	VEPA	3X/10.8 Gy	PD		leukemia	dead 5M
25	52	M	Groin	VEPA	18E/30 Gy	NC		1M	dead 3M
26	76	M	Para-aortal	VEPA	10X/27.6 Gy	NC		leukemia	dead 1M
27	28	F	Neck	VEPA + COP	10X/22 Gy	NC		leukemia	dead 4M
28	62	F	Neck	VEPA	10X/30 Gy	CR	(-)	leukemia	dead 3M
29	58	M	Axilla	VEPA	6E/30 Gy	CR	(-)	1M	dead 2M
30	77	F	Para-aortal	VEPA	10X/16 Gy	PR	(-)	leukemia	dead 4M

For abbreviations: see Table 1.

tients with cutaneous type show only skin lesions at the time of diagnosis and the survival is usually short compared to the smoldering type (10). When focal lesions of ATL are resistant to chemotherapy, radiotherapy should be considered for control of such lesions. Koga et al. (11) and Tamura et al. (12) reported that 12 patients treated by total body irradiation with 1 to 1.5 Gy showed similar prognosis as patients treated by multiple drug chemotherapy, and in a previous paper we reported good initial response of focal lesions in five ATL patients (13). However, the role of radiation therapy in the management of ATL is still not defined.

In the present study, 29 of the 30 patients were referred to our department because initial treatment had failed to control focal lesions. More than 80% of these lesions (25/30) showed good initial response to radiotherapy with relatively low dose (mostly at 30 Gy or less). These results reconfirmed the usefulness of radiation therapy suggested in our first report (13). The prognosis of ATL is strongly dependent on its subtype. The prognosis of acute type of ATL is quite poor while that of the smoldering type is relatively good. In our study, the patients with lymph node and skin lesions belonged to the acute type and the cutaneous type respectively. Therefore, the usefulness of radiation therapy for lymph node lesions and skin lesions should by discussed separately.

Patients with lymph node lesions, in spite of relatively good initial response, usually died of progressive disease within a few months. In these patients critical symptoms secondary to the leukemia, as hypercalcemia and carinii pneumonia developed in addition to lymph node lesions. However, even in such cases radiation therapy could have a palliative value and relieve symptoms such as pain, cosmetic disturbances and the feeling of abdominal fullness.

There are only 4 other case reports besides our previous reports on radiation therapy of skin lesions in ATL (13–17). In all four cases good initial response was reported with doses between 15 to 45 Gy. In our cases, all 13 patients showed good initial response without major complications such as leukocytopenia. Due to the rather long survival (mean 38 months) the radiotherapy was in these cases of considerable palliative value. The skin lesions of ATL are similar to those of mycosis fungoides and the differential diagnosis is sometimes difficult without serological information. Miyagi et al. (14) reported one case with ATL and skin lesion clinically diagnosed as mycosis fungoides. Skin lesions of both ATL and mycosis fungoides seem to show quite similar response to radiotherapy. Frequent out of field recurrences after local skin irradiation suggest that total skin irradiation may be preferable. However, after total skin irradiation recurrences are often observed in axillae, thighs, soles, palms and heads; i.e. places with complicated anatomy where for technical reasons, underdosage is often obtained.

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