Acta Med. Nagasaki 56: 49－52

Radiotherapy for mucosa-associated lymphoid tissue lymphoma of the ocular adnexa

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Objectives: We investigated the results of radiotherapy for mucosa-associated lymphoid tissue (MALT) lymphoma of the ocular adnexa.

Methods: Twenty-one patients with MALT lymphoma of the ocular adnexa were treated with radiotherapy alone at a dose ranging from 30 to 54Gy. The disease arose from the conjunctiva in 15 patients (9 with bilateral involvement), and from the retrobulbar space in 6 patients (1 with bilateral involvement).

Results: All patients with MALT lymphoma achieved a CR or unconfirmed CR (CRu). The 5-and 10-year overall survival rates of all patients with MALT lymphoma were 100% and 90%, respectively. The 5-and 10-year cause-specific survival rates were 100% and 100%, respectively. In all patients with delayed toxicity, the radiation dose was more than 40Gy.

Conclusions: Excellent local control and survival can be achieved for patients with MALT lymphoma of the ocular adnexa using radiotherapy alone.

ACTA MEDICA NAGASAKIENSIA 56: 49－52, 2011

Keywords: Radiotherapy, Mucosa-associated lymphoid tissue lymphoma, Ocular adnexa

Introduction

We previously reported that radiotherapy was useful for the treatment of mucosa-associated lymphoid tissue (MALT) lymphoma of the ocular adnexa[1)]. MALT lymphoma was first described by Isaacson and Wright in 1983 as an extranodal B-cell lymphoma arising in the marginal zone of mucosa-associated lymphoid tissue and was established in the new WHO classification[2-3)]. Radiotherapy is useful for the treatment of MALT lymphoma of the ocular adnexa and is the first choice for this disease. We investigated the long-term follow-up results of radiotherapy for MALT lymphoma of the ocular adnexa.

Methods and Materials

Twenty-one patients with MALT lymphoma of the ocular adnexa treated with radiotherapy alone at Hiroshima Prefectural Hospital between 1998 and 2010 were retrospectively analyzed (Table 1). In 15 patients the disease arose from the conjunctiva, and in 6 patients, it originated from the retrobulbar space. Bilateral conjunctival involvement was found in 9 patients, and involvement of the bilateral retrobulbar space was found in 1 patient.

The median follow-up of the surviving patients was 86 months (range, 11-157).

The histological diagnoses obtained via an incisional biopsy in all cases were categorized according to the criteria

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Received May 12, 2011; Accepted July 12, 2011

Table 1. Characteristics of 21 patients with ocular-adnexal MALT lymphoma

Characteristic	No. of patients
Stage	
I_{AE}	11
I_{AE2}	10
Age (years)	
Range	29-83
Median	55
Gender	
Male	9
Female	12
Location	
Conjunctiva	15
Retrobulbar space	6
Involved site	
Unilateral	12
Bilateral	9

established by the WHO classification. During the staging work-up, gallium scans, computed tomography of the chest and abdomen, and FDG-PET were performed for all patients. Patients with I_{AE} or I_{AE2} disease according to the American Joint Committee on Cancer TNM Classification were treated with radiotherapy alone (Table 2)[4]. Lesions confined to the conjunctiva were treated with a single anterior direct field using a 6-12 MeV electron beam. The entire bulbar and palpebral conjunctiva were treated. Retrobulbar tumors were irradiated with 18 MeV electron or 6-MV X-rays. The clinical target volume was the entire orbital cavity. The field arrangement was the anterior field, wedged anterior and oblique fields, or opposing lateral fields. A median dose per fraction of 2.0Gy (range 1.8-2.5) was administered, with the total dose ranging between 30 and 54Gy (median, 38Gy). Lead eye shields were used for radiotherapy of conjunctival lymphoma. Lens protection was not used for radiotherapy of retrobulbar lymphoma except for one patient (case 16). Complete regression of the tumor mass after treatment was considered a complete remission (CR). The absence of regrowth after a follow-up period of more than 3 months indicated an unconfirmed CR (CRu)[5].

Table 2. Treatment methods and results

Patient	Site	Beam energy	Dose, Gy	Results	I.D.C.L	Survival months
1	bilateral conjunctiva	6MeV electron	48 R, 40 L	CR	28d R, 28d L	NED 157
2	bilateral conjunctiva	6MeV electron	41.5 R, 50 L	CR	10d R, 8m L	NED R 151, L 132
3	R conjunctiva	6-9 MeV electron	40	CR	26d	NED 129
4	bilateral conjunctiva	6MeV electron	40 R, 40 L	CR	0d R, 0d L	NED 103
5	R conjunctiva	6MeV electron	38	CR	1m	NED 104
6	bilateral conjunctiva	6MeV electron	38 R, 38 L	CR	9m R, 39d L	NED 73
7	bilateral conjunctiva	6MeV electron	38 R, 38 L	CR	0d R, 8m L	NED 73
8	bilateral conjunctiva	6MeV electron	38 R, 38 L	CR	3m R, 3m L	NED 49
9	bilateral conjunctiva	6MeV electron	38 R, 38 L	CR	14m R, 14m L	NED 56
10	L conjunctiva	6MeV electron	36	CR	47d	NED 53
11	L conjunctiva	6MeV electron	38	CR	11d	NED 48
12	bilateral conjunctiva	6MeV electron	30.6 R, 30.6 L	CR	NA	NED 33
13	L conjunctiva	6MeV electron	30.6	CR	NA	NED 17
14	L conjunctiva	12MeV electron	30.6	CR	NA	NED 17
15	bilateral conjunctiva	6MeV electron	30.6 R, 30.6 L	CR	NA	NED 11
16	L conjunctiva, L retrobulbar mass	18MeV electron	40	CRu	—	DOOD 125
17	R retrobulbar mass	6MV X-ray	54	CR	—	NED 139
18	bilateral retrobulbar mass	6MV X-ray	30 R, 30 L	CRu	—	NED 109
19	L retrobulbar mass	6MV X-ray	40	CR	—	DOOD 98
20	R retrobulbar mass	6MV X-ray	40	CR	—	NED 103
21	L retrobulbar mass	6MV X-ray	38	CR	—	NED* 67

R=right eye, L=left eye, I.D.C.L=interval of disappearance of conjunctival lymphoma, m=month, d=day
*=Although local retrobulbar lymphoma disappeared, a right submandibular mass 21 months after radiotherapy. Histological examination of the resected mass showed follicular, mixed, B cell type lymphoma.
NED=no evidence of disease DOOD=die of other disease
NA=data not available

Results

Fifteen patients with conjunctival lymphoma achieved a CR. There have been no signs of recurrence or metastasis in any of these patients, with a follow-up ranging from 11 to 157 months after treatment (Table 2). Conjunctival lymphoma disappeared within 14 months after therapy.

Six patients with lesions of the retrobulbar space achieved a CR or CRu. There have been no signs of recurrence or metastasis in any of these patients, with follow-up ranging from 67 to 139 months after treatment. Two patients died of other diseases. One patient died of lung cancer (case 16), and another patient died of progressive supranuclear palsy (case 19). Although local retrobulbar lymphoma disappeared, a right submandibular mass was observed 21 months after radiotherapy in case 21. The patient underwent a tumorectomy. A histological examination of the resected mass showed a follicular mixed B cell type lymphoma. The 5-and 10-year overall survival rates of all patients with MALT lymphoma were 100% and 90%, respectively (Fig. 1). The 5-and 10-year cause-specific survival rates were 100% and 100%, respectively (Fig. 2).

Seven eye-balls developed delayed toxicity (Table 3). Four eye-balls with conjunctival lymphoma experienced dry eye syndrome, and four eye-balls developed cataracts. One patient with retrobulbar lymphoma experienced both dry eye syndrome and cataracts (case 16). The vision of patients with cataracts was restored by surgery. In seven eye-balls, the radiation dose had been 40Gy or more.

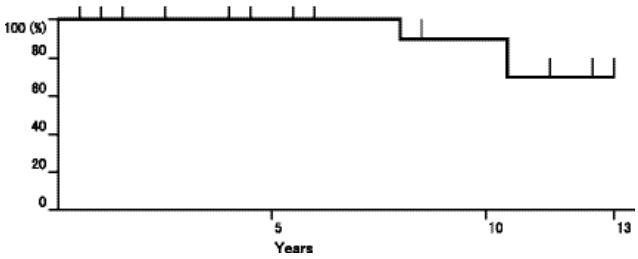

Fig. 1. Overall survival rate

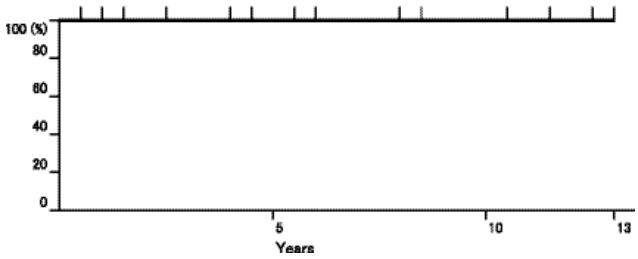

Fig. 2. Cause-specific survival rate

Table 3. Summary of delayed toxicity

Patient	Site	Dose, Gy	Dry eye syndrome	Outcome of DES (duration)	Operation for cataract
1	bilateral conjunctiva	48 R	(+) 33 months	non-improvement (89m)	(-)
		40 L	(-)		(-)
2	bilateral conjunctiva	41.5 R	(-)		[+] 34 months
		50 L	(-)		[+] 25 months
3	R conjunctiva	40	(-)		[+] 28 months
4	bilateral conjunctiva	40 R	(+) 33 months	non-improvement (70m)	(-)
		40L	(+) 33 months	non-improvement (70m)	(-)
16	L conjunctiva, L retrobulbar mass	40L	(+) 19 months	non-improvement (106m)	[+] 50 months
17	R retrobulbar mass	54	(-)		(-)
19	L retrobulbar mass	40	(-)		(-)
20	R retrobulbar mass	40	(-)		(-)

(+) : the interval between radiotherapy and diagnosis of dry eye syndrome.
[+] : the interval between radiotherapy and operation for cataract.
DES=dry eye syndrome m=month
R=right eye, L=left eye

Discussion

Most MALT lymphomas originate from the stomach and lung, which represents 5-16% of malignant lymphomas. Orbital MALT lymphoma accounts for 11-27% of MALT lymphomas[6-8].

In all of the present cases, MALT lymphoma of the ocular adnexa was well-controlled after radiotherapy. Suh et al. reported 52 eye lesions with orbital MALT lymphoma that were treated with radiotherapy. The radiation doses ranged from 5.4 to 30.6Gy (median, 30.6Gy). Forty-six of their lesions showed a complete response, while the remaining six lesions demonstrated a partial response. Three patients experienced local recurrences. The 10-year actuarial relapse-free survival, cause-specific survival, and overall survival rates were 93%, 98%, and 87% respectively, in that study[9]. Nevertheless, when 30-54 Gy was delivered as in our study, the local control of MALT lymphoma of the ocular adnexa was excellent. This indicates that the tumor dose in MALT lymphoma of the ocular adnexa does not always participate in local control. Letschert et al. advocated a tumor dose of 30Gy with a local control rate of more than 90% achieved for MALT lymphoma of the ocular adnexa[10]. Bayraktar et al. reported that radiation doses of 30.6Gy should be given in Ann-Arbor stage I disease, since lower doses may be more frequently associated with relapse, including CNS relapses[11]. Suh et al. suggested that 30Gy may be sufficient for the treatment of MALT lymphoma in the ocular adnexa[9]. A dose of less than 30Gy does not develop dry eye syndrome which represents the delayed adverse event of the lacrimal gland. Dry eye syndrome develops 5-25% by a dose of 30-40Gy, rapidly increases by a dose of more than 40 Gy, and develops 100% by a dose of more than 57Gy[12]. As a dose of more than 30Gy develops dry eye syndrome or cataract, the dose must not exceed 30Gy for safe treatment of MALT lymphoma of the ocular adnexa.

At present, based on our study and these previous studies, we administer a radiation dose of 30.6Gy with a fraction size of 1.8Gy for MALT lymphoma of ocular adnexa treatment.

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