Orbital Lymphoma: Results of Radiation Therapy

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Abstract

Orbital lymphoma is a rare presentation of non-Hodgkin's lymphoma. Treatment with radiotherapy is well-established. Twenty cases of orbital lymphoma treated at the Singapore General Hospital with radiation therapy were reviewed. All patients had improvement of their initial presenting symptoms and complete remission after radiation. Long-term local control was achieved in 17 of 20 (85%) of the treated orbits.

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Introduction

Orbital lymphoma is a rare presentation of extranodal non-Hodgkin's lymphoma, accounting for less than 1% of the total.[1] The role of radiotherapy in its management is well-established.[2-7] This is a report of 20 cases of orbital lymphoma at the Singapore General Hospital (SGH) treated primarily with radiotherapy.

Materials and Methods

The cancer registry of the Therapeutic Radiology Department, SGH, was searched for cases of non-Hodgkin's lymphoma with orbital involvement diagnosed between 1980 and 1994 inclusive. All cases treated with radiotherapy at SGH were reviewed. A total of 24 cases were traced. Four patients were not included in the analysis for the following reasons: three patients were lost to follow-up and one patient did not complete the treatment as planned. Thus, a total of 20 cases were analysed.

Patients' Characteristics

The clinical and pathologic characteristics of the 20 patients are shown in Table I.

There were 14 males and 6 females, with ages ranging from 33 to 81 years (median 52 years). Their racial origins were 15 Chinese, 3 Malays, 1 Indian, and 1 Bangladeshi. The patients had a variety of presenting symptoms: 11 had proptosis, 5 had a visible mass, 5 had periorbital swelling, 2 had ptosis, 1 had conjunctivitis, 1 had excessive tearing, 1 had diplopia, and 1 had eye pain. Some patients had more than one symptom at presentation. The right orbit was affected in 10 patients and the left orbit in 10 patients.

The diagnosis was obtained by biopsy in all patients. The pathology was small lymphocytic lymphoma in 18 patients, diffuse large cell (B cell) in 1 patient; and mucosa-associated lymphoid tissue (MALT) lymphoma in 1 patient.

All patients underwent clinical staging with complete physical examination, full blood count, chest X-ray, computed tomography of the abdomen and pelvis, and bone marrow aspirate and biopsy. Seventeen patients had Stage IAE disease. One patient with small lymphocytic lymphoma had bone marrow involvement and was thus Stage IV. Another patient had Stage III disease with involvement of the neck and paraaortic nodes. The patient with MALT lymphoma also had involvement of the submandibular gland (Stage II).

Radiotherapy

Nineteen patients were treated with photons and 1 patient was treated with electrons. The median prescribed dose was 36 Gy (range 30 to 40 Gy). Radiation field arrangements were: wedge pair in 15 patients, direct field in 4 patients, and mixed wedge pair and direct field in 1 patient. In the wedge pair arrangement, the radiation beams were arranged to minimise exposure to the unaffected orbit (Fig. 1). The anterior field was treated with the eye open. The penetration of the megavoltage X-rays allows for some sparing of the

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TABLE I: CHARACTERISTICS OF THE 20 PATIENTS WITH ORBITAL LYMPHOMA AND TREATMENT OUTCOME

Pt	Age/ Sex	Race	Sites of initial involvement	Histology	Surgery	RT dose (Gy) / fractions (isodose)	RT field arrangement	RT modality	Status
1	77/M	C	L orbit Bone Marrow	SLL	Bx	39.8 / 22 (80%)	Wedge	6 MV	NED in L orbit (49 months)
2	53/F	C	L orbit	SLL	Bx	39.5 / 21 (90%)	Wedge	Cobalt	NED (142 months)
3	52/F	C	R orbit	SLL	Bx	39.5 / 21 (depth of 5 cm)	Direct	Cobalt	AWD (114 months) LR @ 43 months
4	49/M	C	L lower eyelid	SLL	Bx	40 / 19 (90%)	Direct	Electrons 7MeV	NED (118 months)
5	60/M	C	L orbit	SLL	Bx	40 / 23 (depth of 5 cm)	Direct	Cobalt	AWD (32 months) LR @ 26 months and recur in R orbit
6	51/M	C	R orbit	SLL	Bx	36 / 23 (90%)	Wedge	6 MV	NED (107 months)
7	49/F	C	R orbit	SLL	Bx	32 / 20 (85%)	Wedge	6 MV	NED (99 months)
8	33/M	M	L conjunctiva L orbit	SLL	Bx	36 / 20 (85%)	Wedge	6 MV with bolus	NED (19 months)
9	49/M	C	L orbit	SLL	Bx	30 / 15 (90%)	Wedge	6 MV	NED (26 months)
10	41/M	M	R orbit	SLL	Bx	40 / 20 (100%)	Wedge	6 MV	NED (15 months)
11	54/M	C	R orbit	SLL	Bx	30 / 17 (85%)	Wedge	6 MV	NED (59 months)
12	69/M	C	R orbit and R lacrimal gland	SLL	Bx	30 / 18 (85%)	Wedge	6 MV	NED (42 months)
13	45/M	M	R orbit	SLL	Bx	35 / 20 (85%)	Wedge - 20 Gy Direct - 15 Gy	6 MV	NED (42 months)
14	49/F	C	L orbit	SLL	Bx	36 / 18 (90%)	Wedge	6 MV	NED (44 months)
15	64/M	C	R orbit	SLL	Bx	32 / 20 (90%)	Wedge	6 MV	NED (36 months)
16	81/M	C	R lower eyelid	MLL	Bx	40 / 20 (95%)	Wedge	6 MV with bolus	NED (12 months)
17	47/F	I	L orbit	SLL	Bx	36 / 18 (90%)	Wedge	6 MV	AWD (14 months) LR @ 8 months
18	77/M	B	L orbit R Neck Paraaortic nodes	SLL	Bx	30 / 15 (90%)	Wedge	6 MV	NED in L orbit (14 months) Progression in neck @ 6 months
19	47/F	C	L conjunctiva L lacrimal gland L submandibular gland	MALT Lymphoma	Bx	34.2 / 19 (90%)	Wedge	6 MV with bolus	NED (14 months)
20	52/M	C	R lower eyelid R orbit	SLL	Bx	36 / 20 (95%)	Direct	10 MV with bolus	NED (19 months)

Pt: patient; M: male; F: female; I: Indian; E: Eurasian; C: Chinese; M: Malay; B: Bangladeshi; R: right; L: left; MLL: malignant lymphoma, large cell; SLL: small lymphocytic lymphoma; MALT: mucosa-associated lymphoid tissue; Bx: biopsy; RT: radiotherapy; Gy: gray; NED: no evidence of disease; AWD: alive with disease; LR: local recurrence

anterior structures in the eye. With the eye open, the maximal dosage is reached by 1.5 cm depth. The lens is located from 0.3 to 0.9 cm depth, so it usually receives 80% to 90% of the prescribed dose when the eye is treated open and the lens is not shielded. In addition, 2 patients had shielding of the lens on the anterior beam. When the lens is shielded, the dose to the lens is cut to about 50% of the prescribed dose. In the remainder of the

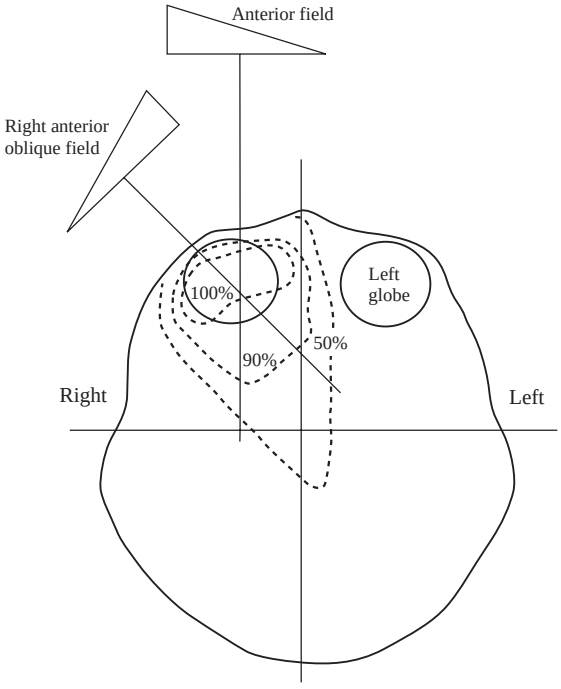

Fig. 1. Dosimetric isodose lines of a wedge pair arrangement for radiation treatment of the right orbit.

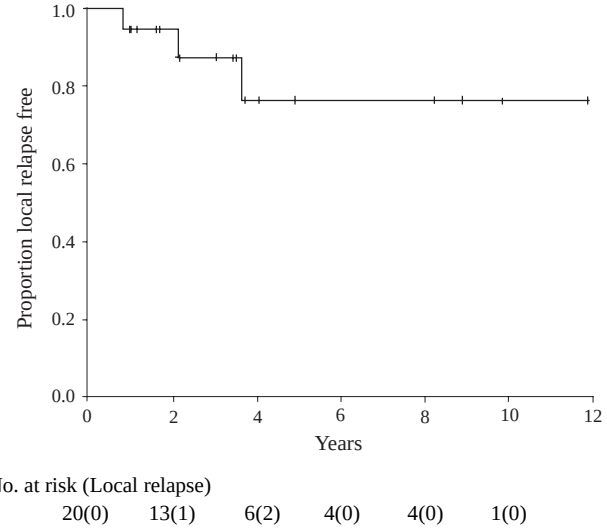

Fig. 2. The Kaplan-Meier plot for local relapse-free survival in 20 patients treated with radiotherapy for orbital lymphoma.

patients, lens shielding was not possible as it would also have shielded a portion of the tumour. The lacrimal gland was shielded in the patients who did not have lacrimal gland involvement. In patients who had involvement of superficial structures such as the eyelid, bolus was used to ensure adequate dosage to the entire tumour volume. A dosimetric treatment plan was generated for each patient and doses were prescribed to an isodose line to encompass the tumour volume. In the cases treated with a direct field, doses were prescribed to a certain depth to ensure adequate coverage of the tumour.

Results

All patients had complete remission after initial radiotherapy. Median follow-up was 39 months (range 12 to 142 months). The current status of the 20 patients is shown in Table I. All patients were alive at last follow-up. Local recurrence in the treated orbit has occurred in 3 / 20 (15%) of the patients. All 3 patients are alive with disease. The Kaplan-Meier 5-year local relapse-free survival was 77% (Fig. 2). Two of the 3 patients refused further treatment. The third patient underwent palliative chemotherapy. Two patients have had recurrences of low grade lymphoma at other sites: 1 in the previously unaffected orbit, and 1 in the neck region.

All patients had improvement of their presenting symptoms after radiation. All patients with proptosis had symptomatic relief by the end of the course of radiation. The patients with visible masses on the eyelids and conjunctiva had complete resolution. The patient with diplopia had some improvement but slight diplopia was still evident after treatment.

Cataracts were observed in 8 of the treated eyes. Although it was not possible to track the initial onset of cataract formation, most of the cataracts were noted by the third or fourth year of follow-up. Symptomatic dry eye was noted in 6 of the treated patients. No cases of radiation retinopathy were observed.

Discussion

Radiotherapy is a well-established treatment modality for orbital lymphoma.[3-8] Primary chemotherapy has minimal efficacy in localised low-grade orbital lymphoma and thus is not advocated as a first-line treatment.[8] Different radiation techniques can be used depending on the extent of involvement. For tumours limited to the eyelids, superficial radiation with electrons or orthovoltage is adequate. However, the majority of orbital lymphomas have involvement of the retrobulbar structures. These lesions require the entire orbit to be included in the radiation portals. This can be accomplished by using a wedge pair arrangement (Fig. 1) or a direct field.

There have been numerous series advocating low dose radiation for treatment of orbital lymphomas.[6-8] In general, 30 Gy is recommended for low grade lymphomas and 40 Gy for intermediate grade lymphomas.[8] In our series, the median prescribed dose was 36 Gy.

Cataracts are a complication of radiation to the orbit. When doses to the lens exceed 15 Gy, there is a 50% chance of cataract formation and hence, visual impairment.[9] The time to cataract formation is 3 to 8 years after radiation. Esik et al[8] reported that unshielded lens doses

>20 Gy will result in cataract formation if follow-up time is adequate, but they did not specify the time interval required. Various techniques of lens shielding have been devised.[4] However, care must be taken that the tumour is not inadvertently shielded as well. Other complications of radiation to the eye for orbital lymphoma include: dry eye syndrome, and rarely glaucoma.[6,8]

Long-term local control of orbital lymphoma can be achieved with radiation therapy. In our series, 17 out of 20 (85%) of the treated orbits were controlled. The risk of distant relapse is related to histology. Those with large cell or diffuse small cleaved (or non-cleaved) lymphomas have higher incidences of systemic relapse as compared to small lymphocytic lymphomas.[10]

Conclusion

Radiation therapy is an effective treatment for orbital lymphoma resulting in local control in the majority of cases. The most common complications of treatment are cataracts and dry eye. It is important to continue long-term follow-up of these patients to assess for local control, complications, and relapse in distant sites.

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