Localized Mucosa-Associated Lymphoid Tissue Lymphoma Treated With Radiation Therapy Has Excellent Clinical Outcome

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Purpose: **Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) is a distinct lymphoma with unique clinicopathologic features. We report the clinical outcome of stage I and II MALT lymphoma treated with involved field radiation therapy (RT).**

Patients and Methods: **From 1989 to 2000, 103 patients with stage IE and IIE disease were referred. Their median age was 60 years, with a 2:1 female predominance. Presenting sites were stomach (17 patients), orbital adnexa (31 patients), salivary glands (24 patients), thyroid gland (13 patients), and other sites (18 patients). Ninety-three patients received RT— 85 received RT alone, and eight received chemotherapy and RT—with a median dose of 30 Gy. The median follow-up time was 5.1 years.**

Results: **A complete response (CR) to RT alone was achieved in 84 of 85 patients. Among CR patients, 14 experienced relapse. Relapse sites were mostly contralateral paired-organ or distant MALT locations and, infrequently, lymph nodes. The crude local control rate with RT was 95.3% (81 of 85 patients). No relapses were observed in patients with stomach or thyroid lymphoma, whereas 14 of 63 patients (22%) experienced relapse in the other sites. The overall 5-year survival rate was 98%, and the disease-free survival rate was 77%. Transformed lymphoma was observed in 14% of patients (two of 14) experiencing relapse.**

Conclusion: **Moderate-dose RT achieved excellent local control in localized MALT lymphomas and had curative potential for three fourths of the patients. Gastric and thyroid MALT lymphomas had better outcome, whereas distant failures were common for other sites. Despite relapse, the disease often maintained an indolent course.**

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MUCOSA-ASSOCIATED LYMPHOID tissue (MALT) lymphoma was first described by Isaacson and Wright in 1983[1] and is now recognized as a distinct lymphoma with unique clinicopathologic features.[2-4] However, the etiology, sites of presentation, and biologic behavior remain variable and heterogeneous.

MALT lymphoma accounts for 4% to 13% of patients seen in individual cancer centers,[5,6] and approximately 70% of patients with MALT lymphoma present with stage I or stage II disease.[6-8] In gastric MALT lymphoma associated with *Helicobacter pylori*, therapy to eradicate this microorganism results in a 55% to 80% complete regression of MALT lymphoma.[9-14] Patients who are resistant to *H pylori* eradication therapy require more traditional cytotoxic treatments, such as chemotherapy and radiation therapy (RT). Tumors with the chromosomal translocation t(11; 18)(q21;q21) in gastric MALT lymphoma are usually resistant to antibiotic therapy.[15,16] For MALT lymphomas arising in non-gastric locations, etiologic agents have not been identified,[17,18] except anecdotally; for example, *Borrelia burgdorferi* in cutaneous lymphoma[19] and *Chlamydia psittaci* in ocular adnexal lymphoma.[20] However, predisposing conditions to MALT lymphoma of some specific sites are well recognized: for example, Hashimoto's thyroiditis for thyroid MALT lymphoma[21] and Sjögren's syndrome for salivary gland MALT lymphoma.[22,23]

Treatment approaches for MALT lymphomas are still evolving. Because MALT lymphomas tend to remain localized for a long time, local treatments, such as RT, are an attractive treatment strategy. To date, there are few well-documented reports of the efficacy of RT in this disease. We report our experience of involved-field RT for stage I and II MALT lymphomas, documenting the excellent local control with RT and the indolent nature of the disease despite relapse.

PATIENTS AND METHODS

Patients

We reviewed the records of 103 consecutive patients with biopsy-proven diagnosis of stage I or II MALT lymphoma presenting in extralymphatic organs between 1989 and 2000 and treated at Princess Margaret Hospital (PMH; Toronto, Ontario, Canada). All histologic material was reviewed by the PMH hematopathologists, with appropriate immunophenotypic techniques establishing the diagnosis. Patients with transformed lymphoma (MALT lymphoma with areas of diffuse large-cell lymphoma) were not included in this study. Staging included CBC in 99 patients (96%), lactate dehydrogenase (LDH) level in 71 patients (69%), appropriate site-specific imaging, and chest x-ray or computed tomography (CT) of the thorax in 68 patients (66%). CT of the abdomen and pelvis was performed in 95 patients (92%), gallium scan in 44 patients (43%), and bone marrow biopsy in 82

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Table 1. Treatment Details

Treatment	No. of Patients	%
Surgery only	5	4.9
Antibiotics only*	2	1.9
Radiation therapy	93	90.3
RT only	82	
CT† and RT	6	
Antibiotics* then CT† and RT	2	
Antibiotics* then RT	3	
Refused treatment	3	2.9

Abbreviations: RT, radiation therapy; CT, chemotherapy.

*Patients with stomach lymphoma, for which *Helicobacter pylori*–eradication therapy was unsuccessful.

†Chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone (three courses, two patients; four, five, and six courses, one patient each); cyclophosphamide, vincristine, and prednisone (one course, one patient); and chlorambucil (two courses, two patients).

patients (80%). Upper endoscopy and gastric biopsies were performed in all patients with gastric lymphoma, but not in the patients with nongastric disease. *H pylori* was documented in biopsy specimens in eight of 15 patients with gastric lymphoma.

Treatment

Treatment details are shown in Table 1. Ninety-three patients (90%) received RT. Five patients were treated with complete surgical excision only (stomach, one patient; salivary gland, two patients; lung, two patients), two patients with gastric lymphoma were treated with antibiotics only, and three patients refused all treatment and were lost to follow-up. The RT prescription was 25 Gy in 10 to 15 fractions (during the course of 2 to 3 weeks) for orbital lymphoma and 30 to 35 Gy in 15 to 20 fractions (3 to 4 weeks) for other sites. Actual RT doses are listed in Table 2. Dose per fraction varied from 1 to 3 Gy. Only involved-field RT was used, encompassing the involved organ, with or without the adjacent first-echelon lymph node region. At our institution, combined-modality therapy (CMT) was recommended for transformed MALT lymphoma. For the eight patients who received CMT, there were no reasons for the use of chemotherapy apart from the patients' treatment with chemotherapy before referral to PMH. The outcome analysis focuses on the 85 patients who received treatment with RT alone.

Response assessment was performed at 2 to 6 months after RT with clinical examination and imaging of the affected area (computed tomography or MRI as appropriate). Routine endoscopy was performed for gastric lymphoma patients every 4 to 6 months for 2 to 3 years. Patients were seen in clinic with physical examination and routine CBC and LDH level (every 3 to 4 months for 2 years, then every 6 months up to the fifth year, then yearly), with no additional routine imaging test. The median follow-up time for all patients was 5.3 years (range, 1 to 13.4 years), and 4.9 years (range, 1 to 10.7 years) for the RT-alone group.

Statistical Analysis

The end points considered were the overall survival (OS), cause-specific survival (CSS), failure-free rate (FFR), and the disease-free survival (DFS) for the RT-alone group (n = 85). Time was calculated from the date of diagnosis to the event of interest, which was death (resulting from any cause) for calculating survival, death as a result of lymphoma or its treatment complication for calculating CSS, first treatment failure for calculating FFR, and first failure or death for calculating DFS. The graphs and the 5-year rates for survival and DFS are based on the Kaplan-Meier estimates.[24] CSS and FFR rates were estimated on the basis of cumulative incidence.[25] The difference between the FFR curves was tested using the log-rank test. In the RT-alone group, there were three deaths (two cause-specific deaths), 15 treatment failures, and 17 events for DFS. Several variables were tested as potential prognostic factors: age, sex, nodal involvement, stage, bulk at treatment, LDH level, anatomic site, and treatment modality.

RESULTS

Patients

Patient characteristics, including the presenting sites, are listed in Table 3. Among the 24 salivary gland lymphomas, 20 were located in the parotid gland. Among the 31 orbital lymphomas, there were 12 conjunctival lesions, nine lacrimal gland lesions, eight periorbital soft tissue lesions, and two eyelid lesions. For the 12 patients with stage IIE disease (regional lymph node involved), the sites were thyroid (one patient, cervical node), salivary gland (five patients, upper cervical nodes), lung (one patient, hilar; one patient, mediastinal nodes), and stomach (two patients, paragastric nodes; two patients, celiac nodes).

Treatment Outcome—Surgery Only and H pylori *Eradication Only*

Among the five patients treated with surgical excision only, two experienced relapse locally (lung and minor salivary gland

Table 2. Radiation Therapy Dose and Anatomic Location of MALT Lymphoma for the 93 Patients

Disease Site	No. of Patients	Radiation Therapy Dose					
		17.5 Gy	20 Gy	25 Gy	30 Gy	31-34 Gy	35 Gy
Stomach	13		2	6	1 (3)		1
Orbital adnexa	30			29	1*		
Salivary gland	21	1†		2	17		1
Thyroid	13				10		2 (1)
Lung	3				(2)	(1)	
Other head and neck	5			1	3 (1)		
Bladder	3					1	2
Skin	2				2		
Breast	2				1		1
Rectum	1						1
Total	93	1	2	38	41	2	9

NOTE. Numbers in parentheses represent patients also treated with chemotherapy.

Abbreviation: MALT, mucosa-associated lymphoid tissue.

*Partial response.

†Local relapse. Patient refused additional radiation at 17.5 Gy (planned dose, 30 Gy). See Results.

Table 3. Patient and Tumor Characteristics (N = 103)

Characteristic	No. of Patients	%
Age, years		
Median	60	
Range	23-83	
Sex		
Male	35	34
Female	68	66
Ann Arbor stage		
IA	91	88.3
IIA	10	9.7
IIB	2	1.9
Maximum tumor bulk after biopsy, cm		
0	45	43.7
≤ 2.5	23	22.3
2.6-5	19	18.4
> 5	5	4.9
Not stated	11	10.7
Anatomic location		
Stomach	17	16.5
Orbital adnexa	31	30.1
Salivary gland	24	23.3
Thyroid	13	12.6
Lung	5	4.9
Other head and neck*	5	4.9
Bladder	3	2.9
Other sites†	5	4.9

*Nasopharynx (three patients), larynx (one patient), sinus (one patient).
†Breast (two patients), skin (two patients), rectum (one patient).

in oral cavity). Both patients were subsequently treated with chemotherapy (oral chlorambucil), had partial responses, and are alive with disease at last follow-up (12 and 9 years from initial diagnosis, respectively). Three patients had complete surgical excision for stage IE MALT lymphoma in the lung, submandibular salivary gland, and stomach, and were free of recurrent disease after 5.5, 8.5, and 7.1 years of follow-up, respectively.

Two patients with gastric MALT lymphoma treated with *H pylori* eradication therapy only were free of recurrent disease after 4.5 and 6 years of follow-up, respectively.

Treatment Outcome—Chemotherapy With RT

Eight patients were treated with CMT (Table 1). After chemotherapy, five had complete responses (CRs; stomach, three patients; thyroid, one patient; larynx, one patient), and three patients had partial responses (lung lymphoma, three patients). Seven patients were free of recurrent disease at a median follow-up time of 5.3 years (range, 3.2 to 10.4 years). One patient (12%) with larynx MALT lymphoma experienced disease relapse. This patient was initially treated with cyclophosphamide, vincristine, and prednisone (one cycle) followed by RT 30 Gy, and 1 year later was diagnosed with recurrent disease limited to the oral cavity mucosa. She was treated with oral chlorambucil and prednisone (eight cycles), had a CR, and was alive and free of disease 5.6 years from the time of relapse. Because of the small number of patients, the heterogeneous chemotherapy regimens, and the number of cycles administered, a meaningful comparison between the CMT and the RT-alone groups cannot be made.

Treatment Outcome—RT Alone

A CR (including unconfirmed CR) was achieved in 84 of 85 patients. Partial response was seen in one patient with extensive bilateral orbital lymphoma invading into ethmoid sinus, with residual disease subsequently treated with fludarabine plus cyclophosphamide, doxorubicin, vincristine, and prednisone. This patient died as a result of sepsis related to the chemotherapy for his lymphoma, 5 years from initial diagnosis. Among the 84 complete responders, 14 experienced relapse. Five patients experienced relapse in the nonirradiated contralateral paired organ (orbit, three patients; parotid, two patients), six in distant sites, two in both local (both salivary gland) and distant sites, and one locally only (orbit; Table 4). Overall, the local control rate was 95.3% (81 of 85 patients). The six patients with distant relapse experienced treatment failure in soft tissue of the arm, leptomeninges and duodenum, peritoneum, lung, trachea and lung, and parotid and cervical lymph node, respectively. Three patients had died (one as a result of lymphoma treatment, one from second malignancy, and one from an unrelated brain aneurysm). To date, two of 14 (14%) transformed MALT lymphomas (diffuse large cell) were diagnosed at relapse (in trachea and cervical lymph node, respectively). The 5-year OS was 98%, CSS was 98%, and DFS was 77% (Fig 1). To date, no relapses have been observed in patients with MALT lymphoma in stomach and thyroid (Fig 2). The 5-year FFR for stomach or

Table 4. Patients With Persistent or Relapsed Disease After Initial Treatment, RT With or Without CT Group (n = 93)

Initial Site	No. of Patients	No. of Treatment Failures	Site of First Failure		
			Local	Contralateral	Distant
Stomach	13	0	—	—	—
Orbital adnexa	30	8	2	3	3
Salivary gland	21	4	2*	2	2*
Thyroid	13	0	—	—	—
Other head and neck	5	3	—	—	3
Lung	3	0	—	—	—
Bladder	3	0	—	—	—
Other sites	5	1	—	—	1
Total	93	16	4	5	9

Abbreviations: RT, radiation therapy; CT, chemotherapy.
*Patient had both local and distant sites of relapse.

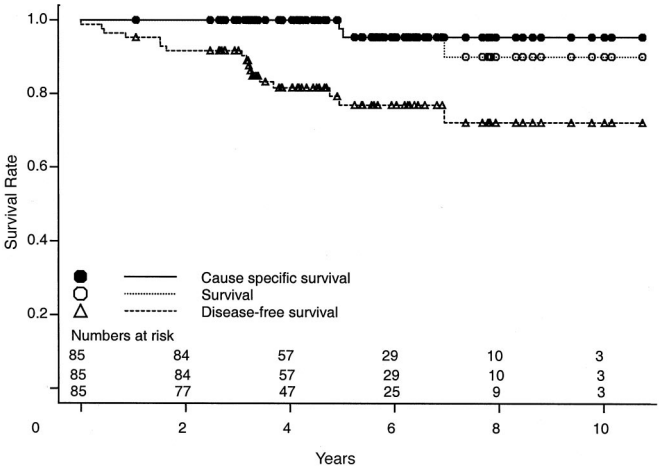

Fig 1. Overall survival, cause-specific survival, and disease-free survival data for the radiotherapy-alone group of 85 patients with stage I and II mucosa-associated lymphoid tissue lymphoma.

thyroid patients was 100%, in contrast to 71% for other sites ($P = .01$).

Side Effects of RT

RT was well tolerated, with no serious acute toxicity observed. Patients with orbital lymphoma often developed a cataract, 2 to 5 years after treatment, which was successfully treated with surgical extraction. When appropriate lens shielding was possible, the risk of cataracts was reduced to 10%. Patients with gastric lymphoma developed transient anorexia and malaise and occasional nausea or dyspepsia, and were treated conservatively. Late ulceration or hemorrhage was not observed. Patients with Sjögren's syndrome and MALT lymphoma of salivary glands had significant residual xerostomia after RT, which was often symptomatic and required permanent modifications in their dietary habits (eg, sipping fluid frequently during meals). Patients with lung lymphoma manifested imaging evidence of radiation pneumonitis after treatment, evolving in the irradiated lung tissue into permanent but nonprogressive fibrosis, and were clinically asymptomatic. Nine patients had second cancers (Table 5). One of these patients died from metastatic adenocarcinoma of the pancreas, with the second cancer located within the previous radiation field given for MALT lymphoma of the stomach, whereas seven second cancers occurred outside the RT field.

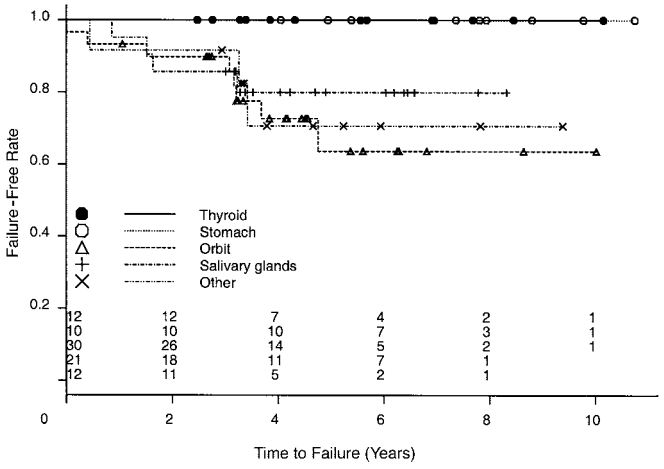

Fig 2. Failure-free rate for patients with stage I and II mucosa-associated lymphoid tissue lymphoma treated with radiotherapy alone for the following sites: thyroid (n = 12), stomach (n = 10), orbit (n = 30), salivary gland (n = 21), and other sites (n = 12).

Treatment Outcome After Relapse—RT With or Without Chemotherapy

Among 16 patients experiencing treatment failure for whom the initial treatment was RT with or without chemotherapy, there were two patients for whom treatment failed in the local site only (both orbital MALT lymphoma; one such patient died as a result of salvage treatment and lymphoma 5 years after initial diagnosis). The other patient was diagnosed with in-field relapse in the conjunctiva 3.5 years after RT (25 Gy) and was not assessable because of short follow-up. Among the five patients with contralateral organ relapse (orbital, three patients; parotid, two patients), all received RT, achieved CR, and remain disease-free 0.7 to 5.4 years from relapse (average follow-up, 3.0 years from relapse).

Two patients with parotid lymphoma experienced treatment failure both locally and at distant sites. One patient's disease relapsed 3 years after an incomplete course of local RT—the patient refused treatment after receiving 17.5 Gy—with parotid, neck node, and bone marrow involvement. She was treated with chemotherapy and remains alive with disease 2.6 years after relapse. The other patient (with parotid MALT lymphoma) experienced relapse 1 year after RT (30 Gy), locally and at distant sites, including the kidneys, and received chemotherapy with partial response. He is alive with disease 1.9 years after relapse.

Among the seven patients who experienced relapse exclusively at distant sites, six were re-treated with RT and/or chemotherapy, and five achieved CR and remain alive and free of disease 1.9 to 6.2 years from relapse (average follow-up, 4.0 years from relapse). This included the two patients with transformed lymphoma. One patient with orbital lymphoma experienced disease recurrence with a solitary lung nodule, biopsy-proven to be MALT lymphoma, and has been observed without treatment for 2 years with no progression of disease.

Therefore, among the 16 patients with residual or recurrent MALT lymphoma, 10 (63%) were rendered disease free again with additional courses of RT (seven patients), chemotherapy (one patient), and CMT (two patients), with a median follow-up of 3.8 years from first relapse.

Prognostic Factors for Treatment Failure

Of the prognostic factors analyzed, the only significant factor was anatomic site. Patients with stomach and thyroid lymphomas had a 100% disease control rate, with significantly inferior results for the other sites (Fig 2). Other factors examined were age, sex, stage (I *v* II), LDH level, type of surgery (excision versus biopsy), tumor bulk, and treatment

Table 5. Characteristics of Patients With Documented Second Cancer Diagnosed After Diagnosis of MALT Lymphoma

Age	Sex	Lymphoma Site	Diagnosis Date	Treatment	Second Malignancy	Date of Diagnosis of Second Carcinoma	Status at Last Follow-Up, Date
68	F	Left lung	6/1989	Surgery	Squamous carcinoma (skin) with parotid node involved	5/2000	Resected, with postoperative RT (NED). Alive with recurrent MALT, 9/2001
79	F	Stomach	3/1994	RT	Pancreatic carcinoma* (metastatic)	2/1999	Died as a result of metastatic carcinoma, 3/1999
52	M	Stomach	6/1995	RT	Right lung carcinoma (large cell)	9/2002	Resected, alive, NED, 5/2003
74	F	Breast	7/1995	RT	Carcinoma in ampulla of Vater	9/1998	Resected, alive with recurrent MALT lymphoma, 11/2001
69	F	Right lung	2/1996	CHOP + RT	Left lung carcinoma (adenocarcinoma and squamous carcinoma)	9/1999	Unresectable, alive with metastatic carcinoma 6/2001
67	M	Thyroid	10/1997	RT	Prostate carcinoma	7/2001	Prostatectomy, alive, NED, 5/2003
82	M	Right orbit	10/1998	RT	Cutaneous melanoma (arm)	2/1999	Alive, NED, 3/2003
53	F	Right parotid	11/1999	RT	Left renal cell carcinoma	5/2000	Alive, NED, 5/2003
77	M	Bilateral orbit	3/2000	RT	Prostate carcinoma	9/2001	Leuprolide treatment, alive, NED, 10/2002

Abbreviations: MALT, mucosa-associated lymphoid tissue; F, female; M, male; RT, radiotherapy; NED, no evidence of disease; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone.

*Located within the previous RT fields.

modality (RT *v* CMT), and these did not predict relapse. However, given the small number of events, these results should be interpreted with caution.

DISCUSSION

MALT lymphoma, a term used synonymously with extranodal marginal zone B-cell lymphoma (MZL), is a distinct type of B-cell lymphoma.[2-4] Characteristic genetic abnormalities can include trisomy 3[26] and chromosomal translocations t(11;18)(q21;q21),[27-32] t(1;14)(p22;q32),[33] and t(14;18)(q32;q21).[34] The t(11;18) translocation resulting in an API2-MLT fusion transcript, although implicated in the molecular pathogenesis of gastric MALT lymphomas,[29,35] has also been reported to associate with resistance to *H pylori* eradication therapy.[16] That t(11;18) translocation is also found in MALT lymphoma arising from nongastric sites such as lung and orbit[27] suggests a common genetic mechanism in the development of disease in these sites for some patients, but not in those with other sites (salivary gland, thyroid gland) where abnormal autoimmune response may be implicated.

The median age (60 years) and female predominance in our series are similar to other reports in the literature.[7,8,36-38] The distribution of anatomic sites in our patients differs from that in other series, with the four most common sites in our patients being orbit, stomach, salivary gland, and thyroid. This distribution of anatomic sites probably reflects local referral patterns because of the specialized surgical and radiation oncology programs and expertise (eg, orbital tumor program) of our institution, as well as the local prevalence of the predisposing conditions (eg, *H pylori* infection in stomach lymphomas). Other series have a higher proportion of stomach,[7] lung,[38] salivary,[8] or skin lymphomas.[7,8,38]

Our data showed that MALT lymphomas respond extremely well to moderate-dose RT, with a high CR rate and durable local control. This study updated and expanded on our previous report of 70 patients,[39] with longer follow-up and an emphasis on the outcome of patients with relapsed disease after initial management. Similar to our experience, Schechter et al[40] reported a local control rate of 100% in 17 patients with stage I and II gastric MALT lymphomas. Liao et al[36] also reported durable local disease control in all 14 stage I and II patients with nongastric MALT lymphoma who were managed with RT with or without chemotherapy. However, local failure is still infrequently observed, particularly if the RT dose is less than 30 Gy; this could be a contributory factor in two of our patients who experienced local relapse after 17.5 and 25 Gy, respectively. More importantly, we observed a pattern of preferential recurrence in paired organs and in distant mucosal sites. This has also been documented by other investigators, who reported spleen[41] and diverse mucosal site involvement that may include the bone marrow either at diagnosis or at relapse.[7,8,37,38,42] The majority of our patients experienced relapse in a localized fashion, either in the contralateral paired organ or other mucosa-associated sites, and were treated with a second course of RT (with or without chemotherapy) and achieved control of disease once again. The median duration of follow-up from first relapse is less than 4 years, and additional observation will determine if these second remissions are durable.

Our overall 5-year DFS of 77% is comparable with those reported in the literature.[7,8,36,38] Despite recurrence of MALT lymphoma, the disease behaves in an indolent fashion, and we have observed continued survival of all patients who experienced relapse. Regardless of whether the initial treatment cures the disease, prolonged survival is highly likely given that it has also been reported by other investigators. The 5-year survival was 95% in 75 patients with nongastric MALT lymphomas from Italy,[38] and a 10-year survival estimate of 80% was documented among 158 patients with stage I to IV disease from France.[7] Patients with stage III and IV disease also have an indolent course.[7,8,36] However, the experience reported by the Southwest

Oncology Group[43] showed a 10-year survival of only 39% in a retrospective analysis of 43 patients who received cyclophosphamide, doxorubicin, vincristine, and prednisone chemotherapy in their clinical trials. These patients were reclassified as having MZL by subsequent pathologic review; 44% of them (19 of 43 patients) had disease involving a MALT site, with or without nodal disease.[43]

The nodal and splenic subtypes of MZL usually present in advanced stages (III and IV). They tend to behave in an indolent fashion as well, with one recent series of 124 patients having a median survival time of 9.1 years.[44] However, the nodal subtype of MZL has also been reported to have a poorer prognosis in comparison with MALT lymphomas, even when corrected for the International Prognostic Index score.[45] The fact that these are separate disease entities from MALT lymphoma is also supported by the lack of the t(11;18)(q21;q21) translocation in nodal MZL.[29,32]

Our data showed no relapses in gastric and thyroid MALT lymphomas treated with RT with or without chemotherapy (Fig 2). The Memorial Hospital experience also confirms the good prognosis of gastric MALT lymphomas treated with RT.[40,46] Although *H pylori* eradication therapy is highly effective, recent data have reported that MALT lymphomas that possess the t(11;18)(q21;q21) translocation have a high failure rate with eradication therapy.[16] An association between this same translocation was also discovered in the 5% to 10% of gastric MALT lymphomas in which *H pylori* infection was absent.[15] RT remains a good treatment option for these patients for whom antibiotic therapy fails or patients who are negative for *H pylori* (by serology or carbon-14 urea breath tests). When additional data become available, the routine testing of the t(11;18)(q21;q21) translocation at initial diagnosis will be useful in the initial selection of therapy.

Patients who present with thyroid involvement also have an excellent outcome. The series of nongastric MALT lymphomas reported by Zinzani et al[38] showed no relapses in the seven patients with thyroid MALT lymphomas, in contrast to other sites (lung, orbit, and skin), for which the relapse rate was 20% to 30%. Similarly, Zucca et al[8] reported no relapses in the 10 patients with thyroid lymphoma but much higher relapse rates for the other sites. Patients treated with thyroidectomy in one small series had excellent outcome.[47] Therefore, the role of RT is unclear if a patient undergoes complete tumor excision with total thyroidectomy.

There is extensive documentation of excellent local control with RT in orbital lymphomas[48,49] and small series of patients for the other sites.[50-53] Patients generally tolerate treatment well, and long-term toxicity is infrequent. However, the risk of relapse in distant extranodal sites remains a significant problem.[8,54] Therefore, it is tantalizing to consider an initial role for chemotherapy in this disease,[54] although this has not been extensively studied. One multi-institutional study of 180 patients with stage I to IV disease did not find a difference in clinical outcome between initial localized treatment approaches with systemic chemotherapy.[8] Consequently, chemotherapy does not seem necessary for patients with MALT lymphomas, at least in the early stages, when the disease remains localized. Oral alkylating drugs, such as chlorambucil, cyclophosphamide, and 2-chlorodeoxyadenosine, appear to be active agents[14,55,56] and can be considered for more advanced stages of the disease. Given that the majority of MALT lymphoma cells express CD20, rituximab has been reported to have significant clinical activity, with a response rate of 73% in 34 patients so treated, and a median response duration of 10.5 months.[57]

We observed nine subsequent cancers in this series, but only one arose within the radiation field (adenocarcinoma of pancreas, with liver metastasis) 5 years after RT to the stomach. Some series reported a higher incidence of other malignancies in patients with MALT lymphomas,[58,59] but not in another series.[60]

In light of the high local control rate and low incidence of toxicity, together with the indolent biology of the disease, we conclude that moderate-dose RT (25 to 30 Gy) is a safe and effective choice for stage I and II MALT lymphomas.

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The authors indicated no potential conflicts of interest.

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