Conjunctival Lymphoma: Retrospective Analysis of the Treatment Result and Complications with Radiation Therapy

Kyoung Ju Kim, M.D., Seung Do Ahn, M.D., Eun Kyung Choi, M.D., Hyesook Chang, M.D. and Jong Hoon Kim, M.D.

Department of Radiation Oncology, College of Medicine, University of Ulsan, Seoul, Korea

**Purpose:** In order to evaluate the response to radiation therapy and to analyze the patterns of failure, survival and complications, we performed a retrospective analysis of patients with conjunctival lymphoma.

**Materials and Methods:** From November 1991 to March 1999, 11 patients were diagnosed as conjunctival lymphoma at Asan Medical Center. Five patients had bilateral involvements, and a total of 16 eyes received radiation therapy. Using 6 to 9 MeV electrons or 4 MV photon beams, all patients were treated with a single anterior field to total doses ranging from 30 Gy to 45 Gy delivered in 10 to 25 fractions. The median follow up period was 57 Months.

**Results:** All patients achieved a complete response with radiation therapy. Two of 16 eyes that were treated (12.5%) developed local recurrence after radiation therapy, however they were salvaged with 30 Gy of reirradiation. The five-year local control was 88.9%. One out of 11 patients (9.9%) developed lung metastasis and received chest irradiation. At the last follow up, one had died of pneumonia and 10 patients were alive without disease evidence. The five-year overall survival rate was 77.8% and 5-year disease free survival was 77.8%. Cataract and dry eye occurred in one patient (9.9%) respectively.

**Conclusion:** Radiation therapy is a very effective and safe treatment modality for conjunctival lymphoma. The local control rate of radiotherapy was excellent and complications were acceptable. Radiation therapy is also an effective treatment modality for recurrent conjunctival lymphoma. It generally requires more than three months to achieve complete response following radiation therapy, thus we recommend evaluating the response to radiation therapy at three months after completion of treatment. *(Cancer Research and Treatment 2002;34:58-61)*

**Key Words:** Conjunctival lymphoma, Radiation therapy

---

INTRODUCTION

Less than one percent of patients with non-Hodgkin’s lymphoma present with a primary orbital lymphoma (1). In Korea, extranodal lymphoma occurs in about 63.3% of patients with non-Hodgkin’s lymphoma and primary orbital presentation has been estimated to account for 3.9% of all non-Hodgkin’s lymphoma (10). The lymphoid tissue is found in the subconjunctiva and the lacrimal gland. Malignant lymphomas are thought to arise from malignant transformation of these tissues. Radiotherapy is usually considered to be the treatment of choice for conjunctival lymphoma and the local control and survival rate are excellent (1–8). Radiation therapy of the eye is technically difficult. Moderate doses (approximately 30 Gy) are required for local control, which may lead to cataract formation. Lens shielding is an important aspect of this treatment method. In order to assess the response of radiation therapy and to analyze the pattern of failure, survival and complications, a retrospective analysis was performed of patients diagnosed with conjunctival lymphoma at Asan Medical Center.

**MATERIALS AND METHODS**

1) **Patients**

Between November 1991 and March 1999, eleven patients were diagnosed with conjunctival lymphoma and received radiation therapy at Asan Medical Center. The age of the patients ranged from 29 to 66, with a mean age of 36 years. There were 5 males and 6 females. Five of eleven patients had bilateral involvements. A diagnosis was established by either biopsy or excision. The histologic subtype was small lymphocytic lymphoma in 6 patients, small cleaved cell lymphoma in 2 patients, and mucosa associated lymphoid tissues (MALT) lymphoma in 2 patients. In one patient, a histologic subtype was not specified (Table 1). The staging workup consisted of complete history taking, physical examination, complete blood count, chest radiograph, abdominal CT scans, and bone marrow biopsy in all patients. To define the disease extent, orbital CT or MRI was obtained in all patients. Based on the staging
workup, ten patients demonstrated stage I disease and one patient had stage IV disease with bone marrow involvement. The median follow-up period was 57 months.

2) Treatment

The treatment characteristics are summarized in Table 2. Four patients received systemic chemotherapy prior to radiation therapy (three with stage I and one with stage IV). Three patients received more than 6 cycles of chemotherapy and one patient only one cycle. The remaining seven patients received radiation therapy only. The total radiation dose ranged from 30 Gy to 45 Gy. The dose fractionation was as follows: Nine patients received 30 Gy in 10 fractions, one patient received 44 Gy in 22 fractions, and the remaining patient received 45 Gy in 25 fractions. The radiation dose was determined regardless of histologic subtype. We used a 6 MV photon beam in 3 patients and 6 to 9 MeV electron beams in 8 patients. All patients were treated through a single anterior field. In all cases, the lens was protected by a specially designed eye block that was placed on the top of the cornea after two drops of local anesthetic (Fig. 1). To determine the dose distribution to the lens, small TLD dosimeters were used in a specially designed polystyrene phantom. The patients who developed local recurrence following radiotherapy received an additional 30 Gy in 10 fractions of radiotherapy.

RESULTS

1) Local control

Among the four patients who received chemotherapy, only one patient achieved a complete response (CR). However, this patient developed a local recurrence 2.5 years after chemotherapy and was later treated using radiation therapy. The other 3 patients achieved a partial response (PR) to chemotherapy and also received radiation therapy. All 4 patients achieved CR after the local radiotherapy. CR was observed in all patients who

Table 1. Patient characteristics (1991. 11 ~ 1999. 3)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>11</td>
</tr>
<tr>
<td>Median F/U</td>
<td>57 M</td>
</tr>
<tr>
<td>Age</td>
<td>Median</td>
</tr>
<tr>
<td>Range</td>
<td>29 ~ 66</td>
</tr>
<tr>
<td>Sex</td>
<td>M 5 (45%)</td>
</tr>
<tr>
<td>F</td>
<td>6 (55%)</td>
</tr>
<tr>
<td>Stage</td>
<td>IE 10 (90.1%)</td>
</tr>
<tr>
<td>IV</td>
<td>1 (9.9%)</td>
</tr>
<tr>
<td>Histologic type</td>
<td>MALT+ lymphoma 2 (18.2%)</td>
</tr>
<tr>
<td>Small lymphocytic</td>
<td>6 (54.5%)</td>
</tr>
<tr>
<td>Diffuse small cleaved</td>
<td>2 (18.2%)</td>
</tr>
<tr>
<td>Not specified</td>
<td>1 (9.9%)</td>
</tr>
<tr>
<td>Bilateral involvement</td>
<td>+ 5 (45%)</td>
</tr>
<tr>
<td></td>
<td>- 6 (55%)</td>
</tr>
</tbody>
</table>

*mucosa associated lymphoid tissue

Table 2. Clinical data on 11 patients with conjunctival lymphoma

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/Sex</th>
<th>Histology</th>
<th>Site</th>
<th>Radiotherapy</th>
<th>CTx</th>
<th>Cx</th>
<th>Recurrence</th>
<th>F/U status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29/M</td>
<td>MALT+ lymphoma</td>
<td>Rt.</td>
<td>30 Gy/10 fx</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>34/M</td>
<td>MALT+ lymphoma</td>
<td>both</td>
<td>30 Gy/10 fx</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>65/F</td>
<td>Small lymphocytic</td>
<td>both</td>
<td>30 Gy/10 fx</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>36/F</td>
<td>Small lymphocytic</td>
<td>Rt.</td>
<td>30 Gy/10 fx</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>48/F</td>
<td>Small lymphocytic</td>
<td>Rt.</td>
<td>30 Gy/10 fx</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>59/M</td>
<td>Small lymphocytic</td>
<td>Lt.</td>
<td>30 Gy/10 fx</td>
<td>None</td>
<td>Cataract</td>
<td>Chest recur</td>
<td>DWD</td>
</tr>
<tr>
<td>7</td>
<td>66/M</td>
<td>Small lymphocytic</td>
<td>Lt.</td>
<td>44 Gy/22 fx</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>8</td>
<td>36/F</td>
<td>Small lymphocytic</td>
<td>both</td>
<td>30 Gy/10 fx</td>
<td>CHOP*1</td>
<td>None</td>
<td>Local recur</td>
<td>NED</td>
</tr>
<tr>
<td>9</td>
<td>34/F</td>
<td>Diffuse small cleaved</td>
<td>both</td>
<td>30 Gy/10 fx</td>
<td>CHOP*7</td>
<td>None</td>
<td>None</td>
<td>NED</td>
</tr>
<tr>
<td>10</td>
<td>34/F</td>
<td>Diffuse small cleaved</td>
<td>both</td>
<td>30 Gy/10 fx</td>
<td>CVP*6</td>
<td>None</td>
<td>Local recur</td>
<td>NED</td>
</tr>
<tr>
<td>11</td>
<td>53/M</td>
<td>Not specified</td>
<td>Lt.</td>
<td>45 Gy/25 fx</td>
<td>COP*6</td>
<td>Dry eye</td>
<td>None</td>
<td>NED</td>
</tr>
</tbody>
</table>

*mucosa associated lymphoid tissue, * chemotherapy, $^\dagger$ complication, $^\#$ no evidence of disease, $^{*}$ death without disease, $^\dagger$ follow up
received 30 to 45 Gy of radiation therapy. Nine patients received 30 Gy in 10 fractionation. One of them had bilateral disease and there was residual disease in one eye after 30 Gy of radiotherapy. He received additional 15 Gy in 5 fractions to the eye with residual disease. Two patients received 44 to 45 Gy in 22 to 25 fractions. The time to CR varied: Only 2 patients achieved CR by the end of radiation therapy and 8 patients achieved CR at 3 month post-treatment. All patients achieved CR at 6 months after radiation therapy (Table 3). One patient had no residual disease after excision. A total of 16 eyes (5 bilateral disease) were treated with radiation therapy. Two of 16 eyes (12.5%) developed local recurrence after a radiation dose of 30 Gy in 10 fractions. (Table 4). However, they were salvaged successfully with 30 Gy of reirradiation. The five-year local relapse free survival rate was 88.9%. Two patients who developed local recurrence remained free of disease after reirradiation. The overall local control rate after radiation therapy was 100%.

2) Survival

One patient died of methicillin resistant staphylococcus aureus (MRSA) pneumonia 4 years after the initial diagnosis. He had small lymphocytic lymphoma and was treated with radiation therapy alone, however he then relapsed in the lung 3.5 years after the initial radiotherapy to the conjunctiva. He underwent 39.6 Gy in 22 fractions of chest radiation therapy with complete response. At 6 months after chest radiation therapy, he developed pneumonia and died. The remaining 10 patients are alive without evidence of disease. The overall 5-year survival rate is 88.9% and the 5-year cause specific survival rate is 100%. The 5 year disease free survival rate is 77.8% (Table 5).

3) Complications

The complications due to radiation therapy have been minimal. Most patients experienced mild conjunctival injection or skin erythema during treatment. One patient who received 30 Gy in 10 fraction developed a cataract at 3.5 years after treat-
remission at 3 months after reirradiation without complications.

The time interval between radiotherapy to CR varied. Bolek et al reported that there was clinically complete remission at a median 20 days after treatment (range 1 – 60 days) (11). In this study, only 2 patients achieved CR by the end of radiation therapy and most patients (8/10) achieved CR at 3 months after radiation therapy. Therefore, we recommend evaluation of the response to radiation therapy more than three months after completion of treatment.

The role of systemic chemotherapy is unclear. There is no data to compare the results of systemic chemotherapy with primary radiotherapy. Bessel reported that 62.5% of patients with high grade orbital lymphoma developed disseminate disease (3). Bolek et al recommended adjuvant chemotherapy and radiotherapy in patients with intermediate or high grade disease because distant relapse occurred in those patients which was unlikely to be salvaged (11). However, Chao et al. (8) suggested that radiation therapy alone appeared sufficient for the local control of intermediate grade lymphoma and Esik et al. (7) reported that chemotherapy showed a very slow response and sometimes no effect on localized orbital lymphoma. In our study, only one of four patients who received systemic chemotherapy achieved complete remission after chemotherapy. We would not recommend chemotherapy for stage I conjunctival lymphoma with low or intermediate grade because the response to chemotherapy was not satisfactory and these diseases were successfully managed by radiotherapy alone.

CONCLUSIONS

Radiation therapy is a very effective and safe treatment for conjunctival lymphoma. The response rate to radiotherapy was excellent and complications were acceptable. Radiation therapy is also an effective treatment modality for recurrent conjunctival lymphoma. We hold that local recurrence without systemic dissemination can be treated successfully with 30 Gy in 10 fractions of reirradiation. It generally requires more than three months to achieve complete response following radiation therapy, therefore we evaluation of the response to radiation therapy at three months after completion of treatment.

REFERENCES