

## Palliative Thyroidectomy for Malignant Lymphoma of the Thyroid

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**Background:** Current treatment of malignant lymphoma of the thyroid consists of chemotherapy and external beam radiation. The diagnosis can routinely be made by fine-needle aspiration, obviating the need for surgery. However, a significant number of patients present with symptoms of obstruction, necessitating thyroidectomy for palliation.

**Methods:** To determine the outcomes of patients with malignant thyroid lymphoma after palliative thyroidectomy, we reviewed our experience. Between 1980 and 2001, 27 patients with thyroid lymphoma and symptoms or signs of airway and/or esophageal obstruction were evaluated at 1 of 3 academic institutions.

**Results:** The mean age of the patients was  $66 \pm 3$  years, and the majority was female. Patients presented with symptoms of dyspnea/stridor (30%), dysphagia/pain (30%), or impending airway obstruction (40%). All underwent palliative surgery. In addition to surgery, 10 patients had combined chemo- and radiotherapy, 10 had radiotherapy alone, and 4 had only chemotherapy. Symptom-free survival after palliative surgery was determined by Kaplan-Meier analysis. The mean actuarial symptom-free survival of patients with symptomatic, malignant thyroid lymphoma was 10 years (95% confidence interval, 7.67 to 12.33 years).

**Conclusions:** Patients with malignant lymphoma of the thyroid can present with obstructive symptoms requiring palliative intervention. In this group of patients, thyroidectomy can be associated with good long-term palliation and low morbidity.

**Key Words:** Thyroid—Lymphoma—Thyroidectomy—Palliation.

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Primary thyroid lymphomas are rare tumors that comprise less than 5% of thyroid malignancies.<sup>1-3</sup> The majority of thyroid lymphomas are non-Hodgkin's lymphomas of B-cell origin.<sup>2,4,5</sup> A significant portion of these tumors arise within a background of Hashimoto's thyroiditis.<sup>6</sup>

The diagnosis of primary lymphoma of the thyroid is typically made between the ages of 50 and 80, with a peak incidence in the sixth decade.<sup>7</sup> It occurs more frequently in

women than men.<sup>2,5</sup> The most common symptom is a rapidly enlarging thyroid mass. The mass may cause symptoms due to compression or infiltration of the surrounding neck organs. Symptoms resulting in airway or esophageal obstruction occur in approximately 30% of all cases.<sup>4</sup> The most commonly reported symptoms are dyspnea, dysphagia, choking, and pain. Symptoms are most common in those tumors that are rapidly enlarging.<sup>4</sup> During a physical exam, the thyroid can be palpated as a hard, smooth, rubbery mass. It can be either bilateral or unilateral.<sup>5</sup>

Thyroid lymphoma should be suspected in any patient with a history of Hashimoto's thyroiditis and a rapidly enlarging neck mass. An important distinction to make is between anaplastic thyroid carcinoma and non-Hodgkin's lymphoma. Anaplastic thyroid carcinoma is rapidly progressive and has a much poorer prognosis, with few patients living beyond 2 years.<sup>8</sup>

Open surgical biopsy has traditionally been required to diagnose thyroid lymphoma. However, fine-needle aspira-

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tion combined with modern immunophenotypic analysis has greatly increased our ability to diagnose lymphoma.<sup>9</sup> Fine-needle aspiration can now eliminate the need for surgical intervention for diagnosis in most patients.

The standard of care for the treatment of patients with diffuse large B-cell lymphoma is chemotherapy consisting of cyclophosphamide, doxorubicin, vincristine, and prednisone and external beam radiation.<sup>5,10</sup> Retrospective data support the use of combined modality therapy. Doria et al.<sup>1</sup> found that distant and overall relapse rates were significantly lower in those patients who received combined modality therapy in comparison with either chemotherapy or radiotherapy individually.

The 5-year disease-specific survival ranges from 35% to 79%.<sup>4,11</sup> Most deaths caused by disease occur within the first 3 years of diagnosis.<sup>4</sup> Symptoms due to locally aggressive tumors have been associated with a poorer prognosis, but no comprehensive data exist to confirm this commonly held belief.

Despite the fact that surgical intervention is rarely required in the treatment of malignant lymphoma of the thyroid, a subset of patients continue to receive surgical therapy to palliate their symptoms. These patients present with symptoms that compromise their airway or cause severe pain. Because surgical intervention can be done with minimal delay and has an immediate effect, some advocate its use in this subset of patients. The main reasons given against surgical therapy is the efficacy of combined modality therapy and the risks of surgical intervention. Given this background, we evaluated the complication rate and long-term survival of patients with malignant thyroid lymphoma who were treated initially with surgery because of their symptomatology.

## METHODS

To determine the outcome of patients with malignant thyroid lymphoma after palliative thyroidectomy, we reviewed our experience. A retrospective chart review was performed of data taken between the years of 1980 and 2001. Three different academic institutions were involved in collecting the data: the University of Wisconsin (Madison, WI), the University of Michigan (Ann Arbor, MI), and Northwestern University (Chicago, IL). A total of 27 patients were identified who met all of the inclusion criteria: (1) a diagnosis of primary malignant lymphoma of the thyroid; (2) symptoms due to either esophageal or tracheal obstruction/invasion; and (3) surgical treatment to minimize symptoms before other treatment.

The statistical analysis was performed using the Kaplan-Meier method of survival analysis. The SPSS software package (SPSS, Inc., Chicago, IL) was used to

complete data analysis and generate survival curves. The complication of hypoparathyroidism was excluded if the patient had a normal postoperative calcium level and no symptoms of hypocalcemia. Nerve injuries were ruled out if the patients had no vocal complaints or changes postoperatively or if direct laryngoscopy was normal.

## RESULTS

### Patient Demographics

A total of 27 patients met the study admission criteria. The mean age of the patients was  $66 \pm 3$  years, and 93% ( $n = 25$ ) were female. A previous diagnosis of Hashimoto's thyroiditis was present in 30% ( $n = 8$ ) of the patients. All patients presented with signs or symptoms of esophageal or airway obstruction or invasion. The most common presenting symptom was impending airway obstruction, accounting for 40% ( $n = 11$ ) of the patients. The remaining patients were divided evenly, each representing 30%, between dyspnea/stridor ( $n = 8$ ) and dysphagia/pain ( $n = 8$ ) as the chief complaint (Table 1).

### Treatment

All 27 patients underwent surgical intervention before the initiation of either chemotherapy or radiation. The surgery performed was determined by the individual surgeon based on the intraoperative findings. The extent of surgery was based on the size of the tumor, the level of symptoms, and the ability to perform a safe resection. A lobectomy/isthmusectomy was performed in 56% ( $n = 15$ ) of the patients. The remaining 44% ( $n = 12$ ) either underwent a subtotal ( $n = 11$ ) or total thyroidectomy ( $n = 1$ ). There were no operative mortalities. In all cases, care was taken to preserve the parathyroid glands as well as the recurrent laryngeal nerves. There were no complications of hypoparathyroidism or nerve injuries identified in this series. A tracheostomy was required in five patients. Four of the tracheostomies were placed at the time of surgery because

TABLE 1. Patient data

Patient/tumor characteristics	n = 27	%
Age (mean $66 \pm 3$ )		
Less than 65 y of age	8	30
Over 65 y of age	19	70
Gender		
Male	2	7
Female	25	93
Main symptom at presentation		
Impending airway obstruction	11	40
Dysphagia/pain	8	30
Dyspnea/stridor	8	30
Hashimoto's thyroiditis		
Present	8	30
Absent	19	70

of tracheal invasion, edema, and concern of airway patency. The fifth tracheostomy was performed on postoperative day 5 because of the inability to maintain an airway. In addition to surgery, 37% (n = 10) of patients were treated with combined modality therapy of chemo- and radiotherapy. An additional 37% (n = 10) of patients were treated with radiotherapy alone. Chemotherapy was the only adjuvant in 15% (n = 4), and 11% (n = 3) had no additional therapy (Table 2).

**Pathology**

All 27 patients had non-Hodgkin's lymphoma. All of the tumors were of B-cell origin. The tumors were classified using the Working Formulation.<sup>12</sup> Using this classification, 66% of the tumors were defined as intermediate grade (n = 18). The majority of these intermediate grade tumors were diffuse large cell tumors. High-grade tumors accounted for 4% (n = 1) of the cases. The remaining 30% (n = 8) were classified as low grade, with the majority of these being a mixed follicular pattern or small lymphocytic tumors

With the development of the Revised European-American Lymphoma classification system in recent years,<sup>13</sup> a subgroup of small lymphocytic tumors are now being identified as a separate entity, called low-grade B-cell lymphomas of mucosa-associated lymphoid tissue type. If we were to apply this newer classification system to our pathology specimens, all of the small lymphocytic cell tumors would be more appropriately labeled with the mucosa-associated lymphoid tissue designation (Table 3).

**Survival Analysis**

The mean follow-up time was 3.5 ± 0.7 years. Six patients (22%) died during the follow-up period. Three of the patients died as a result of their disease, two within the first year (mean of 5.5 months) and the third after 38

**TABLE 2. Therapy**

Treatment variables	n = 27	%
Surgical treatment		
Lobectomy/isthmusectomy	15	56
Subtotal/total thyroidectomy	12	44
Surgical morbidity and mortality		
Required tracheostomy	5	19
In-hospital mortality	0 <sup>a</sup>	NA
Treatment in addition to surgery		
Chemotherapy only	4	15
Radiotherapy only	10	37
Both Chemotherapy and radiotherapy	10	37
No additional treatment	3	11

NA, not applicable.

<sup>a</sup> One patient died at home on postoperative day 10 due to a myocardial infarction.

**TABLE 3. Pathology results**

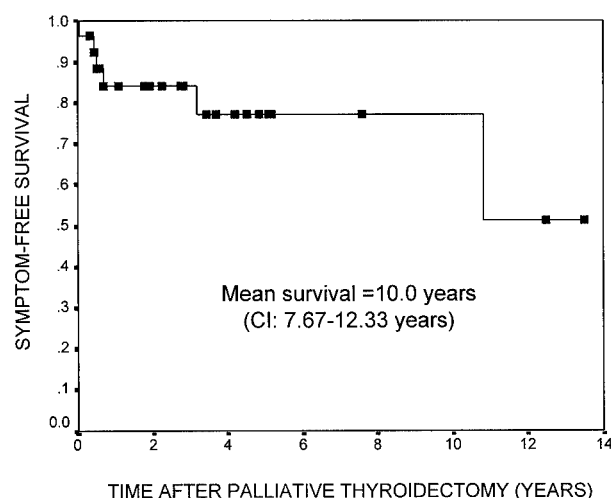
Tumor pathology	n = 27	%
High grade	1	4
Lymphoblastic lymphoma	1	
Intermediate grade	18	66
Diffuse large cell	16	
Diffuse small cleaved cell	2	
Low grade	8	30
Follicular mixed	4	
Small lymphocytic <sup>a</sup>	4	

<sup>a</sup> Applying the most recent lymphoma classification system, the Revised European-American Lymphoma system, these tumors would now be termed low-grade B-cell lymphomas of mucosa-associated lymphoid tissue type.

months. One patient died at home as the result of a myocardial infarction on postoperative day 10. The remaining two patients died from other causes, with no evidence of disease at their last follow-ups. The projected overall 5-year survival rate for our patients was 77%. The mean actuarial symptom-free survival of patients was 10 years (95% confidence interval, 7.67 to 12.33 years) (Fig. 1).

**DISCUSSION**

Malignant tumors of the thyroid are rare, with an incidence of one to two cases per 100,000 people.<sup>14</sup> Thyroid lymphomas comprise less than 5% of those thyroid malignancies and 2% of all malignant lymphomas.<sup>1-3</sup> They typically present as a rapidly enlarging neck mass, frequently causing obstructive symptoms. The role of surgery in the treatment of malignant lym-



**FIG. 1.** Kaplan-Meier symptom-free survival curve for patients with malignant thyroid lymphoma undergoing palliative thyroidectomy. CI, confidence interval.

phoma of the thyroid has evolved significantly over the last 20 years. Whereas surgery was previously the primary treatment, the current standard of care consists of chemotherapy and external beam radiation.<sup>1,5,8</sup> Since thyroid lymphoma now can often be diagnosed by fine-needle aspiration, the need for surgical intervention is less common.<sup>9</sup>

Although surgical intervention is rarely required in the treatment of malignant lymphoma of the thyroid, a subset of patients continue to undergo palliative surgical therapy. These patients present with symptoms of severe compression, or invasion of surrounding neck structures. Because surgical intervention can be done with minimal delay and has an immediate effect on symptoms, some surgeons advocate surgical decompression in this subset of patients.<sup>11,15,16</sup> The arguments given against surgical therapy are the perceived complication rate and lack of survival benefit over combined modality therapy.

One of the advantages of surgery is the early control of symptoms, especially in patients with severe airway compromise. Although both chemotherapy and radiotherapy are beneficial in treating symptoms, the time course to improvement is longer than surgery. Any delay in treatment in a patient with an unstable airway puts that patient at risk of death. Given this background, we decided to evaluate the complication rate and long-term survival of patients with malignant thyroid lymphoma who were treated initially with surgery because of their symptomatology.

The majority of our patients were elderly women. They all presented with an enlarging neck mass but also had significant symptoms secondary to the mass. The majority of the patients had impending airway obstruction as their main symptom (40%), and the remainder had stridor/dyspnea or severe pain/dysphagia (30% each). We selected this subset of patients for our analysis, but it is estimated that 31% to 66% of patients with thyroid lymphoma present with signs or symptoms of obstruction.<sup>4,16,17</sup>

The presence of Hashimoto's thyroiditis was only documented in 30% of our patients. Because of the retrospective nature of our study, this number may be misleadingly low. The diagnosis of Hashimoto's thyroiditis in our pathology reports has increased dramatically in recent years. This change is probably due to an increased awareness of the relation between the two diseases.

All of our patients were initially evaluated by surgeons who felt that they would benefit from palliative surgical intervention. There were no operative mortalities, nerve injuries, or cases of hypoparathyroidism. Five patients did require placement of a tracheostomy. Four were done prophylactically as there was significant concern regard-

ing airway patency because of tracheal involvement of the tumor. The third was done postoperatively after the patient developed progressive airway concerns. Our lack of complications is in contrast to the complication rate of up to 44%, which is cited in the literature.<sup>16</sup>

The projected overall 5-year survival rate for our patients was 77%. The mean actuarial symptom-free survival of patients was 10 years (95% confidence interval, 7.67 to 12.33 years). These numbers are similar to the reported series in the literature over the same time period.<sup>4,16,18</sup> Skarsgard et al.<sup>16</sup> reviewed 27 cases of thyroid lymphoma that occurred from 1981 to 1990 and found a 5-year survival of 70%. In a series of 17 patients treated with combined modality therapy, Viglotti et al.<sup>18</sup> reported a 5-year survival of 77%. Our study is also consistent with the finding of other reports that the presence of obstructive symptoms in patients with thyroid lymphoma does not lower their 5-year survival rates.<sup>16,19</sup>

We do not propose that surgical intervention should replace combined modality therapy; nor do we suggest that surgery should be performed on every patient with a rapidly enlarging neck mass. However, we do feel that, based on our experience, it is reasonable to perform an initial surgical resection in patients with malignant thyroid lymphoma and severe compressive symptoms. Good surgical judgment is essential, and extreme care must be taken to preserve the recurrent laryngeal nerves as well as the parathyroid glands. Postoperatively, the patients should be treated with combined modality therapy based on the grade and stage of the primary tumor.

Malignant lymphoma of the thyroid is a rare condition, which is now routinely diagnosed by fine-needle aspiration and can be treated nonsurgically with external beam radiation and chemotherapy. However, patients with malignant lymphoma of the thyroid can present with severe obstructive symptoms, which lead to palliative surgical intervention. Although palliative thyroidectomies are not infrequently performed, no one has ever examined the outcomes of this subset of patients. In this group of patients, thyroidectomy was associated with good long-term palliation and low operative morbidity. Therefore, in select patients with thyroid lymphoma that is causing significant symptoms or physical compromise, palliative thyroidectomy should be considered as a treatment option.

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