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# Radical surgery for primary thyroid lymphoma in a Filipino female: Report of a case and review of literature

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## ABSTRACT

**INTRODUCTION:** Primary thyroid lymphomas are rare. They constitute only 2% of all thyroid malignancies. It is important to distinguish it from other tumors of the thyroid due to the marked difference in approach to management. Preoperative diagnostic confirmation is ideal to allow for appropriate therapeutic management, which consists of chemotherapy with or without radiotherapy and to avoid unnecessary surgery. In a select group of patients, surgery may be of benefit to relieve obstructive symptoms and establish diagnosis.

**CASE PRESENTATION:** Presented herein is a 48 year old female with a progressively enlarging neck mass previously being treated for Hashimoto's thyroiditis. Obstructive symptoms and a preoperative diagnosis of anaplastic carcinoma prompted surgical intervention. The patient underwent resection of the tumor with a total thyroidectomy and bilateral neck dissection. Post-operative diagnosis of non-Hodgkins diffuse large B cell type of lymphoma was made.

**DISCUSSION:** Primary thyroid lymphomas are rare tumors that may present similarly with some types of thyroid malignancies. An accurate diagnosis is important because non-surgical treatment options like combination chemotherapy and radiotherapy may be effective while sparing the patient from unnecessary radical surgery.

**CONCLUSION:** Primary thyroid lymphoma must be a differential diagnosis in patients presenting with large thyroid tumors in the background of Hashimoto's thyroiditis. Although chemoradiotherapy is the preferred treatment approach, there is a role for surgery in cases of tumor obstruction and uncertain diagnosis.

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## 1. Introduction

Primary thyroid lymphoma (PTL) is a rare pathological entity and constitutes only 2% of all thyroid malignancies [1]. In local Philippine literature, it has only been reported 8 times [2]. It occurs in less than 2% of all non-Hodgkin's extra-nodal lymphomas. For a lymphoma to be classified as such, it is must only involve the thyroid gland and the loco-regional lymph nodes in more advanced cases. For a diagnosis of primary thyroid lymphoma to be made, disease involvement in other organ systems or location must be ruled out.

Diagnosis of a primary thyroid lymphoma is difficult in majority of cases. Despite the availability of sophisticated imaging modalities and various biopsy techniques, definitive diagnosis may be elusive. Although a non-invasive tissue diagnosis is preferred, surgery may at times be necessary just to arrive at a definitive diagnosis. Preoperative diagnostic confirmation is ideal to

allow for appropriate therapeutic management, which consists of chemotherapy with or without radiotherapy and to avoid unnecessary surgery. Surgery as a primary modality of choice is appropriate in only a select group of patients, particularly when pressure symptoms begin to affect the airway and the digestive tract. Most reported cases of primary thyroid lymphoma are elderly females presenting with a progressively enlarging neck mass with signs and symptoms referable to the mass. Many present with a background of Hashimoto's thyroiditis which may or may not have been diagnosed previously.

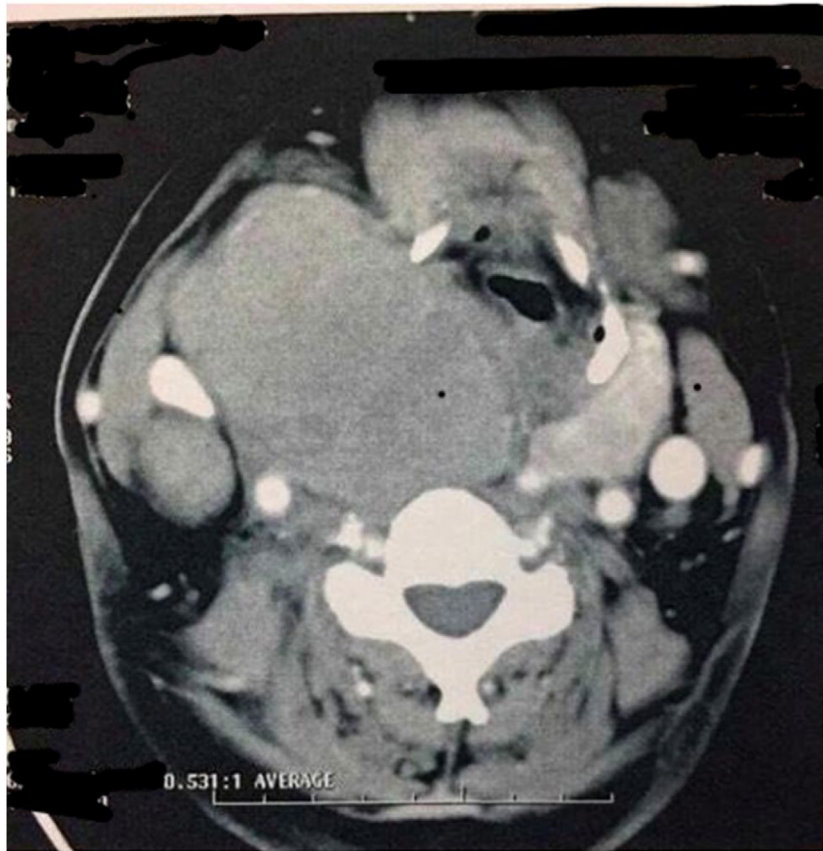
This is the first reported case of a locally advanced primary thyroid lymphoma successfully managed with radical resection in our academic institution. This case is being presented not only for its rarity but for the complexity in diagnosis and management it presented. This report was written in line with the Statement: Updating Consensus Surgical Case Report Guidelines (SCARE) [3].

## 2. Case

A 48 year old Filipino female with a history of Hashimoto's thyroiditis with secondary hypothyroidism on thyroid replacement

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**Fig. 1.** Huge soft tissue mass, more on the right side indistinguishable from the thyroid gland displacing the trachea and esophagus to the left. Multiple matted nodes underneath the sternoleidomastoid bilaterally.

therapy with levothyroxine presented with a 3 year history of gradually enlarging neck mass. Fine needle aspiration biopsy (FNAB) was done showing no evidence of malignancy. Patient noted in the previous 3 months before admission progressive enlargement of her neck mass with development of dyspnea and dysphagia, prompting referral to the surgeon. Physical exam revealed a firm anterior neck mass moving with deglutition more on the right with numerous palpable cervical lymph nodes bilaterally. A core needle biopsy was performed and was read as anaplastic carcinoma. A decision was made for the patient to undergo surgery to alleviate the obstructive symptoms and provide definitive diagnosis.

Upon admission a computed tomography (CT) scan of the neck was performed which revealed a  $12 \times 10$  cm solid mass displacing the trachea and esophagus to the left. Numerous matted lymph nodes were noted beneath the sternocleidomastoid muscles on both sides, extending to the posterior triangles of the neck (Fig. 1). Further studies revealed no other organ involvement or distant metastasis.

The patient underwent preoperative risk assessment and was eventually scheduled for surgery (Fig. 2). The patient underwent total thyroidectomy with modified radical neck dissection on the right and functional neck dissection on the left. Findings during the procedure included an enlarged right thyroid lobe with size of  $12 \times 10$  cm with matted lymph nodes at level II-V. The isthmus was enlarged to  $6 \times 4$  cm, with the left thyroid lobe measuring  $5 \times 4$  cm (Fig. 3). Both recurrent laryngeal nerves were identified and preserved. Neck nodes at levels II, III, IV and V were harvested with sparing of the sternocleidomastoid and right spinal accessory nerve. On the left side, slightly enlarged lymph nodes were noted and a functional neck dissection was performed. There were no intraoperative complications.



**Fig. 2.** Lateral view of the neck demonstrating preoperative bulging of the tumor.

Biopsy of the thyroid mass showed diffuse large B cell lymphoma. Immunohistochemical staining was positive for CD 45+ and CD 20+, confirming the diagnosis (Figs. 4–6).

The patient was discharged with noted relief of the obstructive symptoms and kept on close follow up by the medical oncology and endocrinology services. She underwent chemotherapy with Cyclophosphamide, Doxorubicin, Vincristine and Prednisone. She was likewise subjected to adjuvant radiotherapy and remains disease free 3 years from surgery.

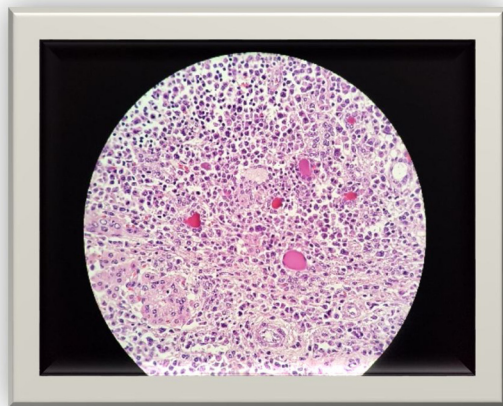
### 3. Discussion

PTLs are rare and comprise only 2% of all thyroid malignancies. It is found in only 2% of all extranodal non Hodgkins lymphoma [1,2].

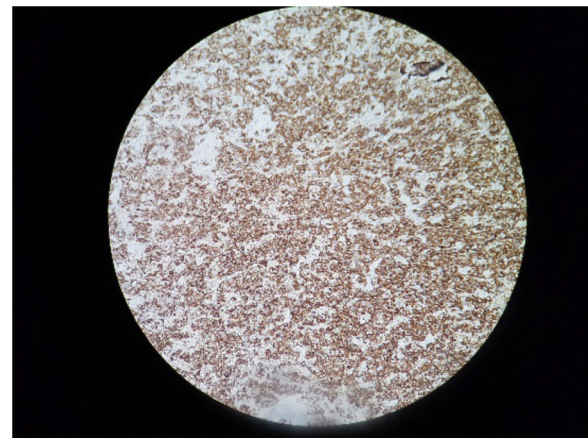




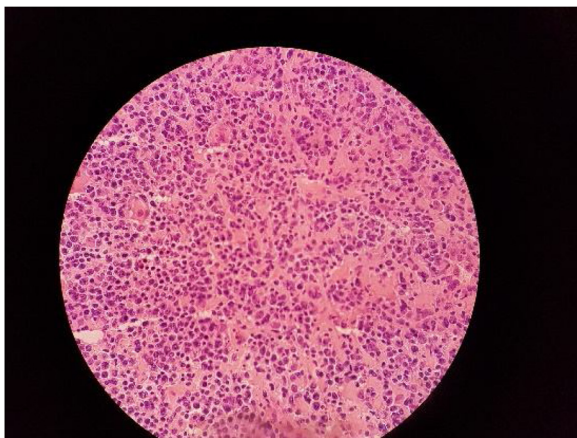
**Fig. 3.** images of the intraoperative appearance of the thyroid lobes upon excision of the right thyroid lobe (right) and of the left thyroid lobe (left).



**Fig. 4.** Follicles with diffuse infiltration by large atypical lymphoid cells (H&E, ×40).



**Fig. 6.** Malignant cells diffusely immunoreactive to CD 20 (×40).



**Fig. 5.** Diffuse infiltration by lymphocytes (H&E, ×40).

Of all PTLs which are of the extranodal non Hodgkins type, most are either of the diffuse large B cell lymphoma (DLBCL) type or the mucosa associated lymphoid tissue (MALT) lymphoma type. The most common subtype is the DLBCL which comprise 70% and the

MALT marginal zone B cell lymphoma which is present in 15–30% of cases [4–6]. In local Philippine literature, only 8 cases of PTL have been reported and only 3 so far of this subtype, the DLBCL [2]. In this patient, the presence of lymphomatous disease elsewhere has been ruled out preoperatively. PTLs must be differentiated from lymphomas that secondarily involve the thyroid, since treatment and prognosis is markedly different. Thyroid involvement from a disseminated lymphoma has worse outcomes as compared to localized primary thyroid lymphomas.

This patient being reported is consistent with the literature, where it has been noted that female patients are more commonly affected than males by a ratio of 4:1. Our patient presented at an earlier age than those reported previously (average of 67 years) [4,5,7]. Patients with these tumors usually present with a progressively enlarging asymptomatic anterior neck mass [1,2]. In more advanced cases, patients may present with signs and symptoms of airway compromise, including cough, dyspnea, stridor and hoarseness. Some may develop dysphagia and superior vena cava syndrome [4,5,7,8]. The biological behavior of the tumor may be compatible with an anaplastic carcinoma of the thyroid, which was the preoperative diagnosis in our patient. Hashimoto's thyroiditis, diagnosed in this patient 3 years prior to surgical referral, has been a well-established risk factor for the development of PTL. It has been theorized that chronic antigenic stimulation in Hashimoto's

thyroiditis leads to the development of intrathyroidal lymphoid tissue. The lymphoid tissue develops under pathological conditions to evolve into non-Hodgkin lymphoma of B cell origin [9–11].

The diagnostic confirmation of PTL is complex and some cases may require surgery for a definitive diagnosis. In terms of systemic symptoms, those classically associated with B lymphomas such as night sweats, fever and weight loss are present in only 10% of patients [12–14]. Imaging studies like ultrasonography, CT, and magnetic resonance imaging (MRI) may reveal a diffusely enlarged thyroid gland or a nodular thyroid gland with solitary or multiple thyroid nodules. Most appear as cold nodules on thyroid scanning [15]. CT scan or MRI will help determine extent and location of the tumor but are usually unable to distinguish from inflammatory or colloid nodules. Although these radiographic studies are not diagnostic, they are useful in defining the extent of disease, planning therapy, and monitoring the response to treatment. CT and MRI are superior to ultrasonography for evaluating local extent because of their greater ability to detect tracheal invasion, substernal extension, and involvement of cervical, mediastinal, or abdominal nodes [16–18]. In cases where a disseminated lymphoma or carcinoma is considered, imaging of the other organ systems is necessary.

FNAB has been proven to be an essential tool in the evaluation of thyroid nodules and masses. In PTL however, FNAB has provided inconsistent results. In one series, FNAB was able to correctly diagnose 70–80% of patients with thyroid lymphoma. In another, FNAB was suggestive but not diagnostic in 50–60% of patients [19]. In a report published in the Philippines, sensitivity was lower, with only 1 out of the 8 cases diagnosed accurately by FNAB [2]. PTL should be strongly considered when the aspirated specimen predominantly consists of lymphocytes. In our patient, FNAB was not able to provide a diagnosis. Core needle biopsy was performed which was read as anaplastic carcinoma. Unfortunately, no immunohistochemical studies were performed. Ancillary procedures such as immunohistochemical staining and molecular genetic testing can increase diagnostic accuracy and could have distinguished PTL from anaplastic carcinoma [20,21]. The resected specimen established the definitive diagnosis in our patient.

The role of surgery in the management of PTL remains highly controversial due to the effectiveness of non-surgical options and the attendant morbidity to radical surgery. Some suggest that surgery is appropriate for the management of localized intra-thyroidal lymphoma. Surgery may likewise be necessary for tumors causing obstruction or when diagnosis is uncertain [22–24]. Whenever surgical resection is deemed incomplete, margins are compromised, or tumor is purposely left behind, adjuvant external beam radiation therapy should be considered. The decision to perform outright surgery for our patient was influenced by the pre-operative diagnosis of anaplastic carcinoma and the progression of the obstructive symptoms.

Chemotherapy as a stand-alone treatment for PTL is not recommended, as better results have been demonstrated when combining it with radiotherapy. Thus, most of the PTL subtypes, including DLBCL are treated with the combination even at early stages [25–27]. The combined therapy is associated with a significantly lower risk of disseminated disease in locally advanced tumors as compared to patients treated only with radiotherapy. The conventional chemotherapeutic regimen consists of cyclophosphamide, doxorubicin, vincristine and prednisone. A rapid response has been noted in most cases using this treatment protocol. Rituximab has recently been proven effective when used in elderly patients with diffuse large B-cell lymphoma of thyroid [15].

Radiation therapy is given after 3–6 courses of chemotherapy. There is evidence supporting radiation therapy for local control of the disease. An effective strategy is the use of chemotherapy to control systemic dissemination of the disease and radiation therapy to achieve local control of the lymphoma [25,26,28,29].

As in other malignancies, patient outcomes depend on the histologic subtypes and the tumor stage. Patients with DLBCL or mixed histological subtypes have a more aggressive clinical course compared to other subtypes like the MALT lymphomas. This is because patients with MALT lymphoma have more favorable response rates to treatment than those with DLBCL of comparable stage. Overall 5-year survival rates of PTL ranges between 50 and 60% [8,28–31]. Our patient remains disease free 3 years after undergoing combination treatment.

#### 4. Conclusion

Primary thyroid lymphomas are rare tumors that may present similarly with some types of thyroid malignancies. It must be a differential diagnosis in patients presenting with large tumors in the background of Hashimoto's thyroiditis. The diagnostic approach to thyroid lymphomas may be more complex than the well differentiated thyroid malignancies. However, an accurate diagnosis is important because non-surgical treatment options like combination chemotherapy and radiotherapy may be effective while sparing the patient from unnecessary radical surgery. A multimodal approach to this rare disease will give the best possible outcome in most cases. In this case, surgery was deemed necessary to ascertain diagnosis and alleviate airway and digestive obstruction. Adjuvant chemotherapy and radiotherapy rendered this patient disease free 3 years after surgery.

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Declaration of Competing Interest

The authors report no declarations of interest.

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#### Ethical approval

This was registered in the UP PGH ethics office as a case report.

#### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Author contribution

Anthony R. Perez: Study concept, writing the paper.  
Mary Ellen Perez: Data collection, study design.  
Cristostomo Arcilla Jr.: Writing and editing the paper.

#### Registration of research studies

NA.

#### Guarantor

Anthony R. Perez.

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