Contemporary Recognition of Primary Thyroid Lymphoma

One institution’s experience and review of current clinical knowledge

Brian L. Hendricks, BS1; Christine H. Heubi, MD2; David L. Steward, MD1,2
1University of Cincinnati College of Medicine
2University of Cincinnati Department of Otolaryngology – Head and Neck Surgery

INTRODUCTION

Primary Thyroid Lymphoma (PTL) is a rare cancer, comprising only 1-6% of all thyroid malignancies and approximately 2% of all extranodal lymphomas.1-4 Combined with the recent trend by many clinicians to begin diagnostic workup with fine needle aspiration biopsy (FNAB), little opportunity is left for many otolaryngologists to garner experience regarding the important role that surgery may still play in the identification of this disease.

In the initial workup of a rapidly growing thyroid mass, PTL and anaplastic thyroid carcinoma (ATC) must always be considered in the differential diagnosis. FNAB has more recently fallen into favor over open biopsy due to its less invasive nature, and with the introduction of adjunctive immunohistochemistry and flow cytometry, the sensitivity of FNAB has improved over time.5,6 However, it is important to recognize that FNAB has not shown consistency in its ability to reliably identify PTL even in recent years. The combination of false-negative and inconclusive tests in recent literature has resulted in a missed diagnosis rate ranging from 12.5%-40% in several studies.7-10 Patients in these studies have received diagnoses such as Hashimoto’s thyroiditis, ATC, and follicular carcinoma before further testing ultimately revealed evidence of PTL.

The aim of this review is to emphasize the importance of open biopsy when exploring a differential that includes primary thyroid lymphoma, even if initial FNAB results are negative.

METHODS AND MATERIALS

The patient database at the UC Health Otolaryngology – Head & Neck / Endocrine Clinic was reviewed to find patients who had presented with a rapidly growing thyroid mass over the past year. No specific criteria for gender, age, or racial background were used as exclusions for this study.

RESULTS

Four patients were found for inclusion in this study. All four of these patients ultimately underwent surgical biopsy in order to reach their final diagnosis. Three patients were diagnosed with PTL, while one patient was diagnosed with ATC. We present these four patients here, along with a brief literature review.

Case 1 (LK): 65-year old WM with history of radiation exposure and Hashimoto’s thyroiditis who was referred to endocrinology by his PCP for an elevated TSH and left-sided neck mass. Ultrasound revealed a right sided thyroid nodule, a 4.1 cm left-sided lymph node, and a 2.3 cm right-sided lymph node. Ultrasound-guided FNAB revealed atypical follicular cells, and the patient was subsequently referred to Otolaryngology for surgical treatment. Patient underwent partial thyroidectomy and lymph node excision. Pathology revealed diffuse large B-cell lymphoma (DLBCL) and chronic lymphocytic thyroiditis.

Case 2 (JB): 62-year old WM who presented to his PCP with a history of dysphagia, hoarseness, and occasional night sweats. CT scan revealed a thyroid mass measuring 6.3 x 4.4 cm in size, with areas of central necrosis. After discussion of treatment options, the patient elected to undergo incisional biopsy in order to reach a definitive diagnosis. Intraoperative FNA was performed and sent for analysis prior to completion of the incisional biopsy.

Pathology reported that the FNA specimen was suspicious for lymphoma, with the recommendation that incisonal biopsy be performed in order to obtain fresh tissue for flow cytometry. Subsequently, the incisonal biopsy was sent for flow cytometry which was found to be consistent with DLBCL.

Case 3 (JD): 92-year old WM who presented to the ED with history of progressive dyspnea and dysphagia. CT scan revealed a right-sided thyroid mass measuring 9.0 x 5.6 cm in size, compressing and invading the patient’s trachea (Figure 1). Despite his age, the patient was otherwise very healthy with an ECOG performance status of 1. After discussion with the patient and his family, the decision was made to perform microlyrngobronchoscopy with endotracheal biopsy for the procurement of a fresh tissue specimen. Flow cytometry of this specimen provided a diagnosis of mantle cell lymphoma. As an additional benefit, the endotracheal debulking of the tumor resulted in a more patent airway. Consequently, the patient experienced an improvement in his symptoms prior to the initiation of chemotherapy without need for further surgical treatment.

Case 4 (JW): 79-year old WM with history of dysphagia, weight loss and left-sided neck pain. FNAB performed by an outside otolaryngologist suggested poorly differentiated carcinoma, though incisional biopsy was recommended to exclude lymphoma. After discussion with the patient and his family, the decision was made to perform incisonal biopsy. Frozen histologic analysis was suggestive of anaplastic thyroid lymphoma, with flow cytometry and immunohistochemistry definitely ruling out lymphoma.

DISCUSSION

With the high rate of potential false-negative results in mind, we share the concern of other recent authors that patients who have previously been diagnosed with ATC may have been misdiagnosed cases of PTL.10 The clinical presentation of PTL is very similar to that of ATC, which is the most aggressive and deadly thyroid malignancy. Due to the high suspicion of PTL, many otolaryngologists have adopted a multimodal approach to treatment of these very different diseases, a misdiagnosis can carry significant consequences for patients with PTL. Currently, the preferred treatment for PTL is chemoradiation which has shown to have excellent results with overall 5-year survival rates ranging from 80-100% for patients with Stage IE disease 4,5,11. The high survival rates evident in early stage disease are in stark contrast to the prognosis for patients who receive a diagnosis of ATC, which has been shown to have been reported with a survival rate ranging from 4-14% 13,14. As with many diseases, higher stages of PTL correlate with worse prognosis. Overall 5-year survival rates for patients with Stage IIE PTL ranged from 36-50% 4,5,11. Those who had advanced to Stage IIE or IV disease had 5-year survival rates estimated to be between 0-36% 4,11.

Therefore, it is imperative to take the importance of early diagnosis into consideration when selecting a diagnostic approach for any patient in which PTL or ATC are in the differential.

It is our belief that FNA serves well as an initial tool for identification, having been shown to have a positive predictive value of 97.1%. However, another study revealing that FNAB allowed diagnosis of only 60% of patients who were later shown to have this rare disease 12. With the inconsistency associated with the use of FNAB in the diagnosis of PTL, several authors that advocate the use of FNAB in diagnostic workup have gone on to state that it should be used strictly as an adjunct to open biopsy rather than as a replacement.

CONCLUSIONS

High clinical suspicion of PTL must always be maintained for a rapidly growing thyroid mass, as there is a dramatic difference in the treatment and prognosis for a patient who is diagnosed with PTL rather than another malignancy such as ATC. Consequently, we recommend that every patient in whom the diagnosis of PTL is in the differential ultimately undergoes open surgical biopsy.

REFERENCES