

## Diagnostic Challenges of Primary Thyroid Lymphoma: A Case Report

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### ABSTRACT

Primary Thyroid Lymphoma (PTL) requires a pathology confirmatory test to conclude the definitive diagnosis. Concerns arise when insufficient pathology specimen collection results in nonspecific pathological conclusion, in spite of the fact that the patient's clinical and radiological presentation strongly suggests a diagnosis of PTL. Patient with complaint of a painless lump in the neck that has been progressively getting bigger since a month ago. He also reported shortness of breath, intermittent fever, decreased appetite, weight loss of 5 kilograms, and general weakness. Physical examination showed a single and immobile palpated mass measuring  $\pm 10 \times 10 \times 10$  centimeters in the neck with hard consistency. Imaging concluded that the patient had a suspected malignant tumor with bilateral lymphadenopathy and cervical thoracic spondyloarthritis. Rapidly growing neck mass leads to heterogeneous diagnosis. Primary Thyroid Lymphoma (PTL) is suggested prominently in progressive thyroid mass expansion. The presented case was a male patient with clinical presentation showing a rapidly growing neck mass with an airway compression. While working on confirmatory testing of pathology examination (to define the type and immunohistochemistry characteristic of the tumor), the patient was treated adequately with supportive treatments. Supportive treatments for suspected PTL patients are important in securing airway patency, adequate fluid and nutritional intake, and prevent aspiration while working on confirmatory test. Diagnostic challenges of PTL not only limited to insufficient sample collection leading to unspecified pathologic results. Repetitive testing may result in delayed treatment and increase risk of complications.

**Keywords:** Neck mass, primary thyroid lymphoma, diagnostic challenge, supportive treatment

## INTRODUCTION

Rapidly growing neck mass leads to heterogeneous diagnosis. Primary Thyroid Lymphoma (PTL) is suggested prominently in progressive thyroid mass expansion along with Anaplastic Thyroid Cancer (ATC). Both diseases have differences in treatment responsiveness and clinical outcomes. Primary Thyroid Lymphoma (PTL) shows a higher treatment response and better outcome compared to ATC. In common, patients with rapidly growing neck mass may report neck discomfort, decreased range of movement, hoarseness, dysphagia, shortness of breath, or even recurrent bleeding. Those clinical presentation makes it a dilemma for clinicians to provide precise treatment without knowing the definitive diagnosis.<sup>1,2</sup>

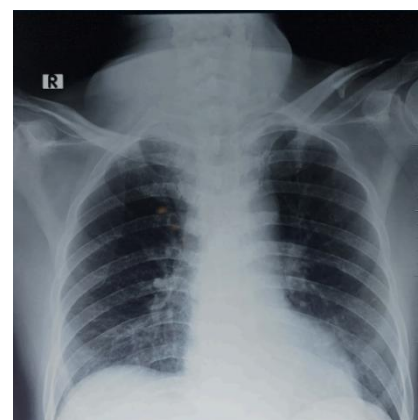
The path towards the definitive diagnosis is a true challenge to overcome. Despite a well-developed algorithm for establishing a diagnosis, clinicians remain hard to implement the common bias found in specimen collections to get the pathology reports, the ultimate diagnostic gold standard.<sup>1,2,3</sup> This case report was conducted to describe the challenges faced by internal medicine professionals at Dr. Zainoel Abidin General Hospital, Banda Aceh, in assessing the diagnosis of suspected Primary Thyroid Lymphoma (PTL). The challenges are mainly related to the progressiveness of the disease and the uncertainty result of the pathology tests.

## CASE ILLUSTRATION

A 69-year-old male was admitted to the emergency room with chief complaint of a painless lump in the neck that has been progressively getting bigger since a month ago. He also reported shortness of breath, intermittent fever, and decreased appetite. Patient had 5 kg weight loss during the last month. Patient also experienced asthenia (complete weakness, no energy). Patient had a history of long-standing hypertension and dyspepsia.

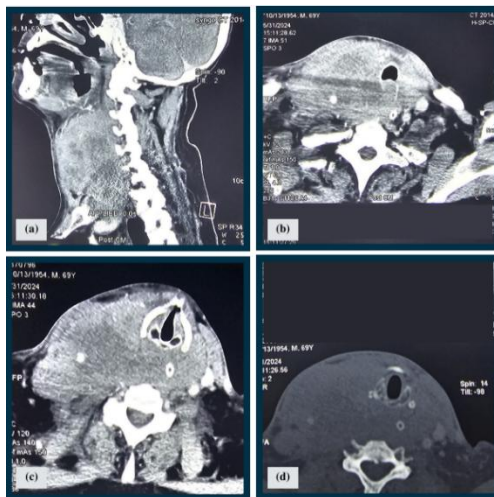
Vital signs examination showed that blood pressure 176/94 mmHg, heart rate 42 rates per minute, respiratory rate 29 times per minute,

oxygen saturation 87%, axillary temperature 36.6° Celsius. Oropharyngeal inspection showed that no significant findings on the oropharyngeal lumen, retropharyngeal walls, uvula, tonsils, and its surrounding tissues. However, there are multiple mouth ulcers with leukoplakic areas and erythematous lesions suspecting for oral candidiasis in the whole oral cavity. Neck examination showed a single immobile palpable mass measuring  $\pm 10 \times 10 \times 10$  centimeters with hard consistency. We then conducted an ultrasonography on the neck which found bilateral thyroid nodules and lymph nodes enlargements. Further imaging studies were needed to determine the anatomical abnormality related to the mass. Below are photograph and imaging reports showing the clinical condition of the patient's neck (See Figure 1).



**Figure 1.** (Left) Clinical presentation of a patient showing a lump in his neck. No signs of inflammation were observed. (Right) Chest X-ray showing soft tissue mass in the right and left side of the neck (VC4-VT 2).

CT scan of the nasopharynx revealed a lobulated solid mass (40 HU) with a partially indistinct margin, measuring  $\pm 11.15 \times 13.06 \times 9.9$  centimeters in the right thyroid with contrast enhancement (84 HU). The mass affected the right thyroid muscle, hypopharynx, inferior constrictor muscle of the pharynx, longus muscle of the right-left neck, and right sternocleidomastoid muscle. Below are the CT scan findings in this patient (see figure 2).



**Figure 2.** CT scan of the nasopharynx revealed a lobulated solid mass (40 HU) with a partially indistinct margin ( $\pm 11.15 \times 13.06 \times 9.9$  centimeters) with contrast enhancement (84 HU). The mass in the isthmus shifted the airway lumen to the left side and narrowed the lumen (narrowest width was  $\pm 0.63$  centimeters) at the level of the VT 1.

Mass in the isthmus shifted the airway lumen to the left side and narrowed the lumen with the narrowest width of  $\pm 0.63$  centimeters at the level of the thoracic vertebrae 1. Multiple lymph node enlargements were obtained in the right-left neck and submandibular region with the largest diameter of  $\pm 1.08$  centimeters. Cervicothoracic osteophytes were also obtained with narrowing of the intervertebral space of cervical 6-7, cervical 7 - thoracic 1, thoracic 1-2, and thoracic 2-3. Based on the imaging findings it was concluded that the patient had a suspected malignant tumor with bilateral lymphadenopathy and cervical thoracic spondyloarthritis. Below is the result of a blood test on the 1<sup>st</sup> and 7<sup>th</sup> days of hospitalization. Blood test also included thyroid function test.

**Table 1. Result Blood Test Parameter**

| Blood test parameter                               | Result (Day 1)  | Result (Day 7)   |
|----------------------------------------------------|-----------------|------------------|
| Hemoglobin                                         | 13,4 g/dL       | 12,8 g/dL        |
| Hematocrit                                         | 40%             | N/A              |
| Leucocyte                                          | 7,57 $10^3$ mcL | 10,62 $10^3$ mcL |
| - Eosinophil                                       | 2               | 1                |
| - Basophil                                         | 1               | 0                |
| - Banded neutrophil                                | 0               | 0                |
| - Segmented neutrophil                             | 71              | 81               |
| - Lymphocyte                                       | 20              | 9                |
| - Monocyte                                         | 5               | 9                |
| Thrombocyte                                        | 233 $10^3$ mcL  | 324 $10^3$ mcL   |
| Erythrocyte                                        | 5. $10^6$ mcL   | 6. $10^6$ mcL    |
| - Mean corpuscular volume (MCV)                    | 91 fL           | 91 fL            |
| - Mean corpuscular hemoglobin (MCH)                | 31 pg           | 31 pg            |
| - Mean corpuscular hemoglobin concentration (MCHC) | 34 g/dL         | 34 g/dL          |
| Lactate dehydrogenase (LDH)                        | N/A             | 693 U/L          |
| Erythrocyte sedimentation rate (ESR)               | N/A             | 130 mmph         |

| Blood test parameter                         | Result (Day 1) | Result (Day 7) |
|----------------------------------------------|----------------|----------------|
| Prothrombin time (PT)                        | N/A            | 0,86 second    |
| Activated Partial Thromboplastin Time (aPTT) | N/A            | 1,03 second    |
| D-dimer                                      | N/A            | 3390 ng/mL     |
| Electrolyte                                  |                |                |
| - Natrium (Na)                               | 145 mmol/L     | 137 mmol/L     |
| - Kalium (K)                                 | 4,1 mmol/L     | 3,3 mmol/L     |
| - Chloride (Cl)                              | 102 mmol/L     | 94 mmol/L      |
| Calcium (Ca)                                 | N/A            | 8,5 mg/dL      |
| Blood Glucose                                | 90 mg/dL       | N/A            |
| - Ureum                                      | 38 mg          | N/A            |
| - Creatinine                                 | 1,25 mg/dL     | N/A            |
| Thyroid-Stimulating Hormone (TSH)            | 85,4 uIU/mL    | N/A            |
| Thyroxine (T4)                               | 5,4 ng/dL      | N/A            |

**Abbreviation:**

g: gram; dL: desiliter; N/A: not applicable; mcl: microliter; fl: femtoliters/cubic microns; pg: picogram; U: unit; mmPH: milliliter per liter; ng: nanogram; mmol: millimole/one-thousandth of a mole; mg: milligram; uIU: micro-international units; mL: milliliter.

The first pathological tissue examination of the neck mass concluded an unspecified metastasis from undifferentiated carcinoma and tuberculous lymphadenitis. The sample was collected by fine needle aspiration biopsy (FNAB). We suggested another pathological examination conducted in the future. We also planned to perform ultrasonography (US) and thoracic CT scan with and without contrast. While working on a confirmatory test for definitive diagnosis, the patient was treated adequately with supportive treatments. Patient laid down in a semi fowler position, given 8 to 10 liters of oxygen per minute using a simple mask, 200 mL ketogenic enteral nutrition every four hours using a nasogastric tube. Patient also received infusions of 500 mL isotonic sodium chloride (0,9%) every eight hours. Patient received 10 milligrams amlodipine and 80 milligrams valsartan to reduce hypertension, both given orally once daily.

## DISCUSSION

The presented case was a male patient with clinical presentation showing a rapidly growing neck mass causing airway compression. Imaging studies confirmed respiratory tract complications with a suspected malignant tumor, bilateral lymphadenopathy, and cervical thoracic spondyloarthritis. Further testing was required to define the type and immunohistochemistry characteristic of the tumor. Core/Fine Needle Aspiration Biopsy (FNAB) with US or CT scan guided procedure may be feasible options to collect the specimen.<sup>1,2,3</sup> However, due to inconclusive findings of the pathological examination, the patient was then planned for further testing and received supportive treatments. The blood test including thyroid function test showed a non-specific finding of strongly suggested on-going systemic inflammation with alteration in thyroid functions (hypothyroidism). The blood test cannot rule out the possibility of other diagnosis such as tuberculosis and metastatic process. Thus, we planned to conduct further tests such

as ultrasonography and thoracic CT scan with and without contrast.<sup>1,2,3</sup>

The above-mentioned supportive treatments were to ensure airway patency, adequate fluid and nutritional intake, and to prevent aspiration during hospitalization. Patient also received anti-hypertensive drugs to lower his stage II hypertension. The confirmatory testing was undergone and took several days to complete. The repetition of specimen collection and testing should not become a reason to postpone any emergency treatment.<sup>1,2,3</sup> Additionally, the abnormal thyroid function should also be a priority in treating this patient. For instance, patient may be admitted to the hospital with contrary thyroid functions. Some may present with hypothyroid profile, while others present with hyperthyroid. These profiles are beneficial in determining the most possible cause.<sup>1,2,3</sup>

In this report, patient was admitted with hypothyroidism. It is commonly caused by Hashimoto Thyroiditis. The clinical presentations of the patient in this report were not fully linear to the findings of hypothyroid profile. Patient experienced intermittent fever, decreased appetite, weight loss, and complete weakness. The unreported findings were hoarseness, dry skin, and bradycardia. Patient was unaware of the latest symptoms. On the other hand, patient may present with hyperthyroidism. But this is less likely to occur and reported only in a small number of cases.<sup>3,4</sup> The team was working on defining the definitive diagnosis, as it was highly suspected as a Thyroid Lymphoma. Thyroid lymphoma may present either primarily or secondarily. Primary Thyroid Lymphoma (PTL) is diagnosed when thyroid glands firstly impacted and then spread to loco-regional lymph nodes and/or other organs. On the other hand, Secondary Thyroid Lymphoma (STL) is lymphoma originated from outside of thyroid glands which later affect the thyroid glands.<sup>3</sup>

The diagnosis of PTL is established by an integrative approach of comprehensive examination. A well-conducted history taking, detailed physical examination, and further confirmatory tests including blood test, imaging,

and pathology should be done. Our team found it was challenging to establish the definitive diagnosis due to unspecified findings in pathology test from FNAB.<sup>5</sup> To confirm the diagnosis of Primary Thyroid Lymphoma (PTL), immunohistochemical testing is essential. Key findings include a solid proliferation of lymphoid cells expressing the B-cell marker CD20 and for lymphomas with plasma cell differentiation demonstrating light chain restriction with kappa and lambda antibodies is helpful. Cytokeratins are used to highlight lymphoepithelial lesions, while follicular dendritic cell markers (CD21 or CD23) indicate follicular colonization. Additionally, Hans' classification markers like BCL6 and MUM1 are utilized by some institutions. Therefore, the minimum immunohistochemical panel for diagnosing PTL should include B-cell markers, T-cell markers, light chains, cytokeratins, and follicular dendritic cell markers.<sup>5,7</sup>

In general, Primary Thyroid Lymphoma (PTL) belongs to the category of B-cell non-Hodgkin lymphomas. It accounts for up to 98% for all cases of PTL.<sup>6</sup> The subtype of PTL in the most prevalent order are Diffuse Large B-cell Lymphoma (DLBCL), Mucosa-associated Lymphoid Tissue (MALT) Lymphoma / Extranodal Marginal Zone Lymphoma, Follicular Lymphoma, Small Lymphocytic Lymphoma, Chronic Lymphocytic Lymphoma, and Mantle Cell Lymphoma. The prevalence of the subtype may be different in studies conducted widespread. A well-defined diagnosis of PTL may direct the future treatment of patient. A DLBCL patient may receive a combination of chemotherapy and radiotherapy, as it is beneficial for the clinical improvement especially in early stages of DLBCL.<sup>7</sup> Chemoimmunotherapy is suggested in patient with advanced stages (IIIE or IV) of DLBCL in conjunction with chemotherapy.

On other pathological findings such as MALT and follicular lymphoma, patients in early stages are treated by radiotherapy with or without chemoimmunotherapy. In late stages (IIIE or IV) patients are treated by chemoimmunotherapy with or without chemotherapy. The selective monoclonal

antibody of rituximab is the first line therapy in patients undergoing chemoimmunotherapy treatment in DLBCL, MALT, and follicular lymphoma. This agent is selectively binding the CD20 and the pre-mature to mature B cell lymphocytes.<sup>7,8</sup>

## CONCLUSION

Supportive treatments for suspected PTL patients are important in securing airway patency, adequate fluid and nutritional intake, and prevent respiratory aspiration while working on confirmatory tests. Diagnostic challenges of PTL mostly due to inconclusive pathologic results. Repetitive sampling and testing may result in delayed definitive treatment and increase risk of further complications.

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