

Papillary Thyroid Carcinoma: A Case Report

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Abstract: ***Introduction:** The incidence of ectopic thyroid tissue is low, which has been reported 1 in 300,000 population and when it transformed into malignant lesion, the most common histopathology is papillary carcinoma. However, case reports that discuss papillary carcinoma is still limited due to the rarity of the case. **Case Report:** We present a 55 years old woman with chief complaint of a left sided neck mass that enlarge over time with a size of a ping pong ball. Examination of the neck found a solid left sided - mass measured around 4 x 4.5 cm. Thyroid ultrasonography reported a solid enlargement of the left thyroid with cystic component, 4.1 x 4.46 x 5.28 cm in size, hypoechoic, wider than tall, smooth margin with echogenic foci punctate and concluded moderately suspicious lesion. Fine needle aspiration biopsy found active macrophage cells and hemosiderin in the cytoplasm in a background of colloid and dense erythrocytes with no visible signs of malignancy. However, the excisional biopsy of the neck revealed papillary carcinoma. Tumor extirpation was performed and the thyroid gland was preserved. After the surgery, the patient denied difficulty swallowing or voice changes. The patient was discharged after 2 days of hospitalization without. **Conclusion:** Ectopic thyroid malignancy is a rare case and when it occurs papillary carcinoma should be suspected. Patient may present with unspecific symptoms and physical examination may reveals unremarkable findings other than a nodule in the neck. Fine needle aspiration biopsy is recommended to establish diagnosis and indicated for nodules ≥ 1 cm with intermediate or high suspicion of malignancy in thyroid ultrasonography. Surgery and radioiodine remain the main management of ectopic thyroid malignancy.*

Keywords: ectopic thyroid malignancy, papillary thyroid carcinoma

1. Introduction

Ectopic thyroid could develop due to disturbance in the descent of the thyroid tissue during gestational development. [1] Ectopic thyroid rarely transformed into malignant lesion. However, when malignancy occurs the most common histopathology is papillary carcinoma. [2] The incidence of ectopic thyroid tissue is 1 in 300,000 population. [3] Ectopic thyroid malignancy is usually present as asymptomatic neck lump and incidentally found in routine imaging examination. [4] We present a case of a 55 years old woman with papillary thyroid carcinoma in the left side of the neck.

2. Case Report

A 55 years old woman came to the otolaryngologist clinic with chief complaint of a left sided neck mass for 6 months. The mass was said to enlarge over time, initially the mass was the size of a marble, but now it is around the size of a ping pong ball. Patient denied dysphagia, mass tenderness, skin discoloration, weight loss, or any other symptoms. Patient has never experienced similar symptom before. History of chronic illnesses such as diabetes mellitus and hypertension were denied. Patient has no history of taking any medications. Examination of the neck found a solid left sided - mass measured around 4 x 4.5 cm. Other physical examination showed unremarkable findings. Complete blood count and thyroid function test were within normal limits. Chest x - ray showed no metastasis to the mediastinum or lungs. Thyroid ultrasonography reported a solid enlargement of the left thyroid with cystic component, 4.1 x 4.46 x 5.28 cm in size (50.45 cc), hypoechoic, wider than tall, smooth margin with echogenic foci punctate and concluded moderately suspicious lesion. Fine needle aspiration biopsy (FNAB) found no follicular epithelial cells; the specimen contained active macrophage cells and hemosiderin in the cytoplasm in a background of colloid and dense erythrocytes. There were no visible signs of malignancy in the specimen. However, the excisional biopsy of the neck revealed papillary carcinoma

pT1pNxMx. Microscopic findings consisted of thyroid follicles various in sizes, some with widened lumen and some showing pseudo - nodular area composed of proliferative thyroid follicles of relatively monotonous size, some with papillary structures lined with cuboidal epithelial cells with a ground glass appearance. Other parts of the tissue showed areas of stroma experiencing fibrosis.

The patient underwent isthmusectomy and lobectomy. After the surgery, the patient denied difficulty swallowing or voice changes. The patient was given antibiotics with ceftriaxone 1 gram BID, methylprednisolone 8 mg BID, tranexamic acid 500 mg TID, and an analgesic. Wound care was performed every day with the drain positioned lower than the wound, and the patient was positioned half - sitting. The drain production one day post - operation was 16 cc, and on the second day, it was 4 cc. The patient was discharged after 2 days of hospitalization without any complications. She was prescribed methylprednisolone 8 mg BID, cefuroxime 500 mg BID, and sumagesic 600 mg QID, and instructed to return for reassessment at five days post - operation.



Figure 1: A solid mass on the left side of the neck measured around 4 x 4.5 cm

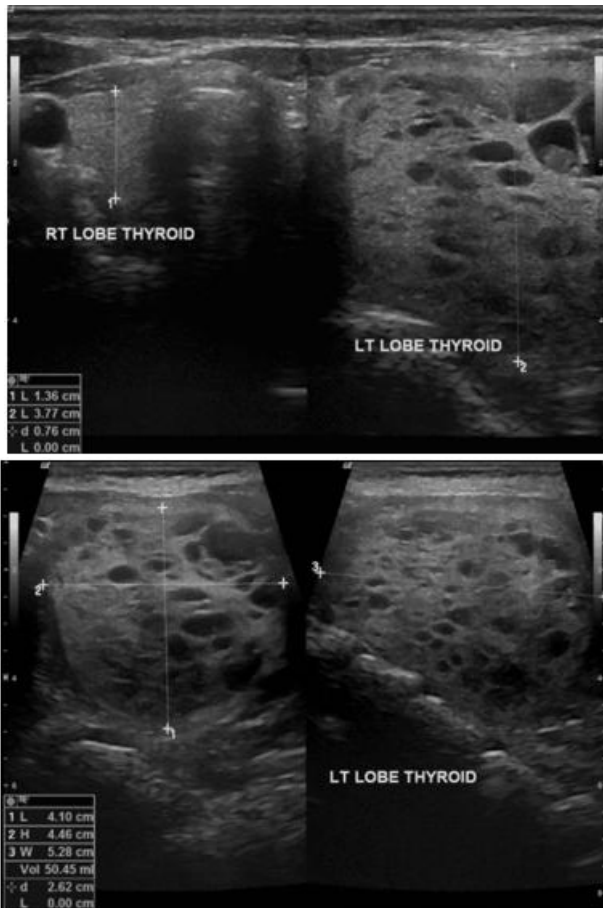


Figure 2: Thyroid USG: a solid enlargement of the left thyroid with cystic component, 4.1 x 4.46 x 5.28 cm in size (50.45 cc), hypoechoic, wider than tall, smooth margin with echogenic foci punctate



Figure 3: Chest x - ray showed no metastasis to the lung or mediastinum

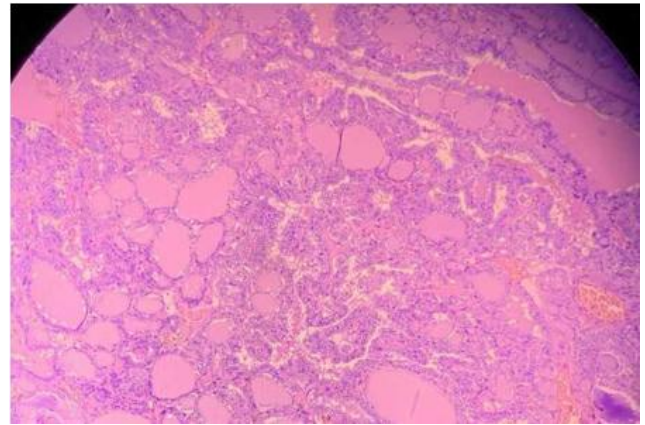


Figure 4: Histopathology of the thyroid lobes revealed papillary thyroid carcinoma

3. Discussion

The thyroid has widespread impact on nearly every organ system through the hormone it produces, primarily by increasing their metabolism and function. [5, 6] The thyroid gland is a butterfly - shaped endocrine gland located anterior to the trachea below the neck. [7] This gland originates at the base of the tongue between the first and second pharyngeal pouches, usually aligning with the C5 - T1 vertebral levels. It consists of two lobes joined by the isthmus, which spans the midline of the upper trachea at the second and third tracheal rings. Positioned behind the sternothyroid and sternohyoid muscles, the thyroid wraps around the cricoid cartilage and tracheal rings. The normal thyroid gland appears to have symmetrical lateral lobes with the isthmus located on the middle side. The thyroid gland is known to have a wide variety of morphological variations. Studies have suggested that abnormal thyroid anatomy is associated with clinically relevant surgical considerations. [5]

In terms of size, the anteroposterior and transverse dimensions of the lateral lobe of the thyroid gland range from 1.3 - 1.8 cm in adults. [8] Based on studies, the relationship between the anatomy of the thyroid gland and its potential for enlargement is closely related to the risk of thyroid cancer, which can affect the structural and functional aspects of the thyroid gland. Thyroid gland enlargement can be caused by various factors. Enlargement of the thyroid structure can occur due to cellular hyperplasia or the formation of nodules which are abnormal growths in the thyroid. Enlargement leading to malignancy can be seen in the size of the nodule, irregular borders, and increased vascularity. [9, 10] Increased vascularization is also an important part of thyroid anatomy and physiology. In the case of thyroid carcinoma, not only is the size enlarged, but also the changes in the vascularization pattern. Vascularization in the malignant thyroid can have an irregular and chaotic pattern. This is due to the expression of vascular endothelial growth factor (VEGF) as angiogenesis - promoting factors that contribute to aggressive tumor growth and metastasis. [11]

The primary hormones produced by the thyroid gland are thyroxine (T4) and triiodothyronine (T3). The process of thyroid synthesis involves five main steps: the creation of thyroglobulin, absorption of iodide, iodination of thyroglobulin, storage, and the discharge of thyroid hormones

by thyrocytes into the fenestrated capillary network. Through coordinated action, thyrotropin - releasing hormone (TRH) from the hypothalamus, thyroid - stimulating hormone (TSH) from the anterior pituitary gland, and T4 ensure balanced feedback mechanisms and overall homeostasis that is known as the hypothalamic - pituitary - thyroid axis. [6] Furthermore, thyroid receptors serve as transcription factors capable of binding to both T3 and T4. However, their affinity for T3 is significantly greater, rendering T4 relatively inactive in comparison. [12] Free T3 and T4 circulating in the circulation can be taken up by peripheral cells at any time. Either T3 or T4 can quickly detach from the carrier protein to increase the amount of free hormone when needed. [13] In addition to T3 and T4, the thyroid also produces the hormone calcitonin through c - cells. The role of the hormone calcitonin is to help regulate calcium levels in the blood although the general role is carried out by the parathyroid hormone. Calcitonin plays a role in inhibiting the release of calcium from bones which can affect bone metabolism. [14]

Ectopic thyroid tissue is defined as tissue located outside its normal anatomic position, anterior to the laryngeal cartilages. Based on its structure, many cases of ectopic thyroid tissue present with an underdeveloped or incomplete capsule. The enlargement of this mass may invade adjacent structures. [15] Ectopic thyroid could develop due to disturbance in the descent of the thyroid tissue. (1) The proliferation of endodermal cells of the primitive pharynx begin during day 20 - 24 of gestation and form thyroid diverticulum. The thyroid diverticulum then descends throughout the midline, running through the hyoid bone and laryngeal cartilage anteriorly. During the 5th week of gestation, the thyroid divides into left and right lobes and arrived in the neck during the 7th week of gestation, and the disturbance in this descent phase may cause ectopic thyroid. [16] Other causes of ectopic thyroid are metastases from thyroid cancer and improper tissue implantation after thyroid surgery. Ectopic thyroid may transformed into malignant in less than 1% of cases and the most common histopathology is papillary carcinoma. [2] Thyroid carcinoma refers to cancer that develops in the cells of the thyroid gland. Based on its pathophysiology, in most cases, ectopic thyroid tissue experiences quantitative deficiency, resulting in increased TSH expression which causes hyperplasia in the ectopic tissue and enlargement as a manifestation. [17]

According to the 2022 WHO classification of thyroid carcinoma, several diagnosis of thyroid carcinoma include benign follicular cell - derived thyroid tumours, differentiated high - grade thyroid carcinoma, anaplastic thyroid carcinoma, and squamous cell carcinoma of the thyroid. [18] These groups encompass various types of thyroid neoplasms with distinct histological and molecular characteristics, aiding in their classification and management. Among this classification, papillary thyroid carcinoma is the most common type of thyroid cancer, accounting for about 80% of cases, typically grows slowly and has a good prognosis. It is characterized by papillary growth patterns and nuclear atypia and is classified in the WHO 2022 classification of thyroid tumours as a distinct type of thyroid carcinoma originating from follicular cells. The subtypes of papillary thyroid carcinoma listed in the WHO classification include classic variant, infiltrative follicular variant, tall cell, columnar cell,

hobnail, solid, diffuse sclerosing, Warthin - like, and oncocytic variant. [19] Each subtype has unique histological characteristics and may have different clinical implications in terms of prognosis and treatment. [4] According the Surveillance, Epidemiology, and End Results (SEER), the incidence of papillary thyroid carcinoma from 1973 to 2006 has increased 3.2 - fold and mostly affect the middle - aged population with median age of 50 years old. [19, 20]

Ectopic thyroid carcinoma may occur at any part of the body and clinical manifestations are related with the affected structure. Based on its anatomy, the most common location for ectopic thyroid tissue is in the head and neck, especially the lingual. However, in some rarer cases, the location can be in the esophagus, mediastinus, intra trachea, visceral organs, and submandibular region. [21] Ectopic carcinoma in head and neck may manifest into several symptoms such as headache, dysphagia, head and facial swelling, cough, vomiting, dyspnoea, hoarseness, and snoring. (22) However, papillary thyroid carcinoma could also present as painless neck lump, which may or may not accompanied by enlarged cervical lymph nodes. Physical examination of the neck presents a fixed, nontender mass measured less than 5 cm with irregular borders. [4] Our case presents a 55 years old woman with chief complaint of a left sided neck mass that enlarge over time since 6 months ago. Patient denied dysphagia, mass tenderness, skin discoloration, weight loss, or any other symptoms. Examination of the neck found a solid left sided - mass measured around 4 x 4.5 cm. Judging from the normal anatomical size of the thyroid, this enlargement is a clinical condition that needs further evaluation because it can develop into carcinoma.

Other than history taking and physical examination, some further evaluations are also needed to support the diagnosis of papillary thyroid carcinoma. Laboratory test such as thyroid function test is mostly within normal limit in patients with papillary thyroid carcinoma. Ultrasonography of the mass reveals a solid nodule with ill - defined margin that is hypoechoic or isoechoic, taller - than - wide, disorganised internal vascularity, and accompanied with microcalcifications. [4] Thyroid ultrasonography reported a solid enlargement of the left thyroid with cystic component, 4.1 x 4.46 x 5.28 cm in size (50.45 cc), hypoechoic, wider than tall, smooth margin with echogenic foci punctate and concluded moderately suspicious lesion. According to the American Thyroid Association, the sonographic appearance of intermediate suspicion of malignancy is a hypoechoic solid nodule, well - defined margin, with no microcalcifications, extrathyroidal extension, or taller than wide shape. Fine needle biopsy is need to rule out malignancy in ≥ 1 cm nodule. [23] In addition, based on the anatomy of vascularization of thyroid cancer, papillary thyroid carcinoma tends to have an irregular vascularization pattern. This condition is also in accordance with the findings of the results that found disorganized internal vascularity in cases of papillary thyroid carcinoma. [11]

Changes of papillae and nucleus are the main histopathologic features of papillary thyroid carcinoma. Fine needle aspiration biopsy (FNAB) is mainly used as initial examination in thyroid abnormalities. The FNAB may reveal enlarged tumor cells with eosinophils in its cytoplasm and

papillary structures in watery or thick colloidal background accompanied by macrophages, debris, stromal fragments. [12] In our case, FNAB reveals no follicular epithelial cells; the specimen contained active macrophage cells and hemosiderin in the cytoplasm in a background of colloid and dense erythrocytes. There were no visible signs of malignancy in the specimen. However, the excisional biopsy of the neck revealed papillary carcinoma (pT1pNxMx). Microscopic findings consisted of thyroid follicles various in sizes, some with widened lumen and some showing pseudo-nodular area composed of proliferative thyroid follicles of relatively monotonous size, some with papillary structures lined with cuboidal epithelial cells with a ground glass appearance. Other parts of the tissue showed areas of stroma experiencing fibrosis. Given the various types of thyroid cancer that can occur, the characteristics of papillary thyroid carcinoma should be distinguished from others. Papillary thyroid carcinoma will show a large picture, overlapping nuclei with ground glass appearance, pseudo inclusions, and intranuclear grooves that can distinguish it from other types of thyroid cancer. [24] These results are in accordance with research that found ground glass appearance as one of its characteristics.

As previously mentioned, the thyroid gland can produce the hormones thyroxine (T4) and triiodothyronine (T3). Studies have shown that T4 at physiological concentrations can stimulate cancer cell proliferation, cancer angiogenesis, and platelet coagulation. The prothrombotic activity of T4 on platelets is postulated to support cancer-like blood clotting and tumour cell metastasis. Studies have found that differentiated thyroid cancer cells respond to physiological T4 levels with increased proliferation. [25] On the other hand, TSH examination can be used as a predictor of thyroid malignancy and is often performed. The risk of malignancy increases with increasing TSH. Previous studies have found that the TSH has a significant relationship with papillary thyroid carcinoma and lymph node metastasis. [26] In this study, unfortunately, the assessment of T3, T4, and TSH hormone levels was not carried out so that the association between hormone levels and thyroid cancer could not be done. Unlike T3 or T4 hormones, other hormones, namely calcitonin, are said to have no further role in the progression of papillary thyroid carcinoma. So this examination is not implied as a biomarker of papillary thyroid carcinoma. [27]

According to the American Thyroid Association, the management of papillary thyroid carcinoma depends on tumor size and staging. Tumor with less than 4 cm in size and no metastasis in the lymph nodes or distant organ should be considered lobectomy. Total thyroidectomy and primary tumor removal should be considered if the tumor size is >4 cm, or clinical T4, or metastases to the lymph nodes (N1) or distant organ (M1). To ablate the remnant thyroid tissue, adjuvant radioiodine is the first treatment of choice after thyroidectomy. Other indications of radioiodine therapy are as follows: 1) Tumor >2 cm in size accompanied with several risk factors including extrathyroidal extension, older than 45 years - old, metastases to lymph node and distant organ; 2) Tumor <2 cm in size and metastases to distant organs. [4, 28] Our patient underwent tumor extirpation, and the thyroid gland was preserved. This management was in line with the recommendation due to large size in the tumor (4.1 x

4.46 x 5.28 cm in size). After the surgery, the patient denied difficulty swallowing or voice changes. The patient was given antibiotics, analgetics, and corticosteroid to control post-surgery inflammatory reaction and prevent infection. She was discharged after 2 days of hospitalization without any complication.

4. Conclusion

Ectopic thyroid malignancy is a rare case and when it occurs papillary carcinoma should be suspected. Patient may present with unspecific symptoms and physical examination may reveal unremarkable findings other than a nodule in the neck. Fine needle aspiration biopsy is recommended to establish diagnosis and indicated for nodules ≥ 1 cm with intermediate or high suspicion of malignancy in thyroid ultrasonography. Surgery and radioiodine remain the main management of ectopic thyroid malignancy.

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