



Metastatic Papillary Thyroid Carcinoma Arising in a Neglected Goiter: A Case Report

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Abstract

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BACKGROUND: Periodical clinical surveillance for early thyroid cancer detection among patients with diffuse goiter is a common scenario managed in the primary care setting. However, clinical palpation alone is neither sensitive nor specific in detecting the presence of nodules within a goiter. Hence, further investigation with ultrasound is key to effective surveillance for early detection of thyroid cancer.

CASE REPORT: We present a case of a stable diffuse goiter in a 51-year-old woman diagnosed 30 years ago who refused further imaging investigation. Based solely on clinical palpation, the presence of nodules within the goiter was missed. This resulted in transformation into papillary thyroid carcinoma with lung metastases. She presented with progressive hoarseness of voice and cough for 3 months. An ultrasound of the thyroid gland revealed a large heterogeneous nodule in the left lower pole with coarse calcification and internal vascularity. Further imaging with contrast-enhanced computed tomography of the neck and thorax revealed an enhancing nodule in the left thyroid lobe which extends inferiorly to the left retroclavicular region which compresses the trachea causing narrowing of its lumen at T1 and T2 vertebral levels. There were multiple lung nodules in both lungs suggestive of metastases.

CONCLUSION: A total thyroidectomy followed by radioactive iodine thyroid ablation therapy was performed. The histopathological examination revealed the surgical specimen to be papillary thyroid carcinoma.

Introduction

Papillary thyroid cancer (PTC) is the most common thyroid neoplasm constituting between 58% and 85.9% of thyroid malignancies [1]. This prevalence is similar to our local setting, where PTC accounts for 85% of all thyroid cancers [2]. Papillary thyroid cancer has a subclinical presentation with an indolent course which is frequently asymptomatic without regional cervical lymph nodes enlargement [3]. This subclinical presentation may mask malignant transformation. Using only the palpation method to evaluate the presence of nodules within a goiter can delay early cancer transformation identification as the accuracy of thyroid palpation depends greatly on the experience of the examiner [4]. Furthermore, the evaluation of thyroid nodules using the palpation method may not be sensitive in picking up nodules of <1 cm in size [5]. Hence, further imaging method such as ultrasound is needed for early clinical detection of thyroid cancer. Ultrasound is capable in picking up non-palpable thyroid nodules and

has high sensitivity in differentiating between malignant and benign nodules [6]. Thus, ultrasound becomes an important investigational tool in managing patients with diffuse goiter. Early diagnosis of PTC is essential for appropriate and timely administration of intervention. This would reduce disease progression and risk of metastasis. Herein, we report a case of a neglected, long-standing diffuse goiter in a 51-year old woman who declined further imaging investigation. The goiter later developed into metastatic PTC.

Case Report

We present a case of long-standing stable diffuse goiter in a 51-year-old woman who was diagnosed clinically, 30 years ago and presented with retroclavicular extension and local compressive symptoms. Throughout the past follow up appointments, the patient remained clinically and biochemically

euthyroid. The size and consistency of her goiter also remained stable, which was diffuse on palpation and measured approximately 3 cm × 4 cm on the left and 2 cm × 3 cm on the right. No other investigation was planned, as she was reluctant to proceed with any other investigational procedure. Although she was counseled about the need for ultrasound evaluation and potential cytological assessment, the patient remained with her decision in refusing to undergo for any further investigation. No thyroid antibody was ordered.

The patient has well-controlled hypertension and no other significant medical history. She had no



Figure 1: Revealed a mildly enlarged thyroid gland with a prominent nodule in the left anterior paramedian region of the lower neck

history of radiation exposure to her head or neck region and has no known family history of thyroid disease. She presented to her general practitioner with progressive hoarseness of voice and cough for 3 months. There were no associated symptoms of shortness of breath, orthopnoea, paroxysmal nocturnal dyspnoea, or excessive tiredness. Physical examination revealed a thin lady with a weight of 42 kg, who was clinically euthyroid. There were palpable non-tender, firm nodules, with the largest measuring 0.5 cm × 1 cm in the left thyroid lobe, fixed to the adjacent trachea (Figure 1). No thyroid bruit was noted. A small left cervical lymph node was palpable. Serum TSH was normal at 1.830 mIU/L.

This case was fast tracked to the on-site radiologist and otorhinolaryngologist. Laryngoscopic examination revealed left vocal cord palsy. Urgent ultrasound neck was scheduled which revealed an enlarged thyroid gland with several thyroid nodules. The solid nodules in the left thyroid lobe had some small hypoechoic areas within with increased central and peripheral vascularity, and one with areas of coarse calcification within (Figure 2).

A chest X-ray showed several small nodules in both lower lobes with increased soft tissue density on the left side of the neck, causing narrowing of the trachea, as illustrated in Figure 3a.

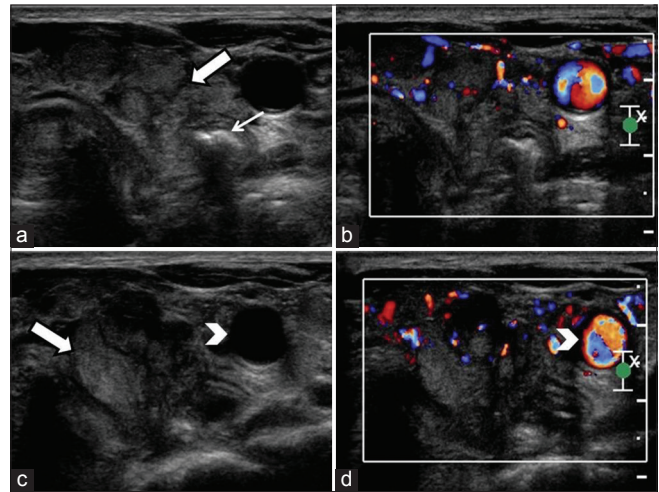


Figure 2: Transverse view of an ultrasound of the left lower pole of the thyroid gland revealed several solid heterogeneous nodules (a and c) (white arrow), some with hypoechoic areas and coarse calcification (thin white arrow) within, and increased internal vascularity in (b and d). There was encasement of the left common carotid artery (arrowhead) at this level; however, the left common carotid artery was patent

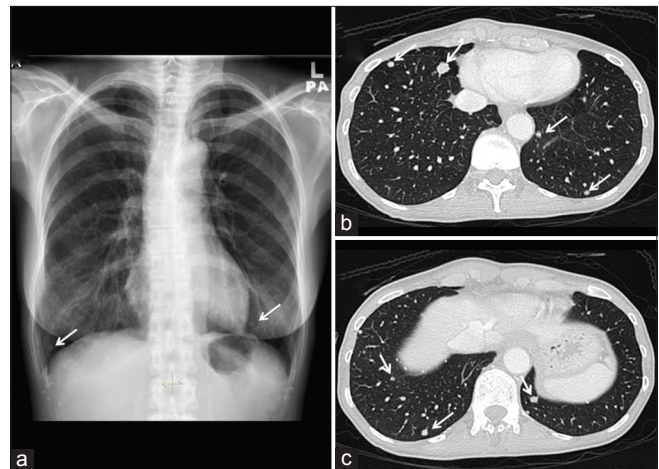


Figure 3: Chest X-ray (a) revealed two lung nodules in both lower lobes. Contrast-enhanced computed tomography thorax in lung window showed multiple lung nodules in both lower lobes of varying sizes in (b) and (c) in keeping with metastases

Subsequently, a contrast-enhanced computed tomography (CT) scan of the neck and thorax revealed an enlarged heterogeneously enhancing lesion in the inferior aspect of the left thyroid lobe measuring 2.9 cm × 3.7 cm × 3.4 cm (AP × W × CC) which extends to the left retroclavicular region. The mass was seen to compress the trachea on the left side, displacing it to the right with evidence of luminal narrowing at T1 and T2 vertebral level (Figure 4).

The CT scan also revealed multiple lung nodules in both lungs (Figure 3b and 3c).

The ultrasound-guided fine-needle aspiration cytology (FNAC) of the left thyroid nodule reported a follicular lesion of undetermined significance (Bethesda category 3). The cytological smear was hypocellular and showed minimal colloid and a few follicular cells

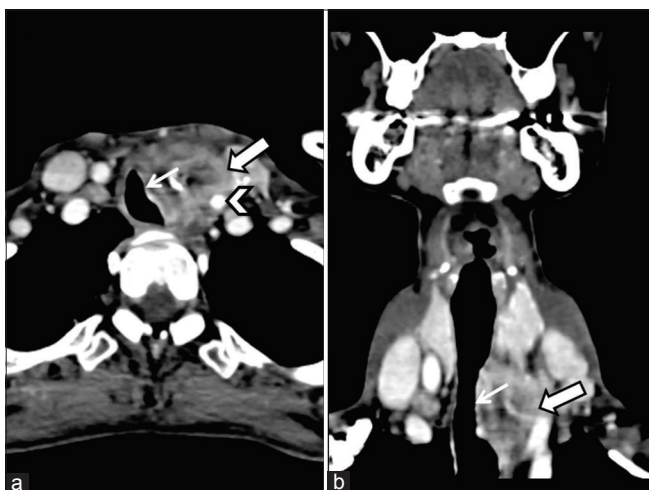


Figure 4: (a and b) Contrast-enhanced computed tomography of the neck showed an enlarged thyroid gland with multiple nodules. The largest nodule in the left lower pole (white arrow) showed heterogeneous enhancement with foci of coarse calcification and mass effect to the adjacent trachea (thin white arrow), causing narrowing of its lumen. There was encasement of the left common carotid artery (arrowhead) by this mass

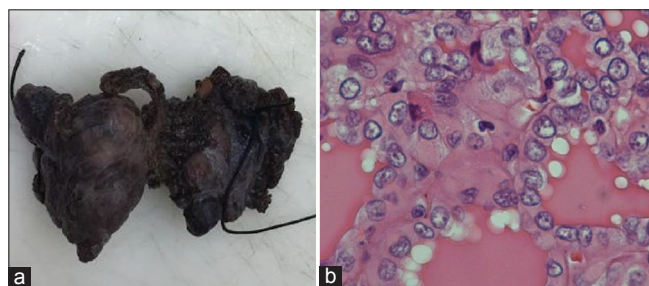


Figure 5: (a) Macroscopic examination of the resected thyroid gland (anterior view) shows 2 nodules, each in the right and left lobes, measuring 12 mm × 10 mm × 10 mm and 20 mm × 10 mm × 20 mm, respectively. (b) Microscopic examination of the thyroid nodules show characteristic nuclear features of papillary thyroid carcinoma such as nuclear clearing, grooving, molding and overlapping (H&E, 400×).

which displayed mild nuclear atypia with no evidence of PTC. The patient was staged at T3N1bM1. The patient underwent a total thyroidectomy. Intraoperatively, there was a hard mass which measured 6 cm × 5 cm in the left thyroid lobe, extending to the isthmus and part of the right thyroid lobe which adhered to the upper trachea. The mass also infiltrated the overlying strap muscles and pretracheal lymph nodes. The mass was resected, as shown in Figure 5a, and histopathological examination confirmed PTC (Figure 5b). However, the hard matted paratracheal and pretracheal lymph nodes were unresectable and were left *in situ*. The patient received her first post-operative radioactive iodine ablation therapy the following 2 months to ablate the residual unresectable paratracheal and pretracheal lymph nodes.

The patient is currently under follow-up from the multidisciplinary team which includes the oncologist, ENT specialists, speech therapy, and wound care. At 6 months follow-up post-surgery, a tracheostomy is still maintained *in situ* as a precautionary plan to secure the airway should laryngoedema occur following radioactive iodine therapy.

The patient is due to have her second ^{131}I radioiodine in June 2020. After a reducing dose of levothyroxine, she is now on a stable dose of levothyroxine at 75 mcg OD. The thyroxine will be lifelong. Her latest blood tests showed an FT4 of 23 ng/dL, thyroid-stimulating hormone (TSH) of 0.091 mU/L, and corrected calcium of 2.26 mmol/L. As for now, there is no conclusive management plan as yet.

Discussion

Papillary thyroid cancer (PTC) is the most frequent histological subtype of thyroid cancer, accounting for 58–85.9% of the cases [1]. Papillary thyroid cancer is a well-differentiated type of cancer, occurring more frequently in women among their 5th decade of life. Many cases of PTC are subclinical. Most patients initially present with an asymptomatic slow-growing goiter or nodule in the anterior neck. Papillary thyroid cancer is commonly associated with low risk of distant metastasis, but when metastasis has occurred, it usually spreads through the lymphatic system or hematogenously to the lungs and bones. When identified early, PTC has a favorable prognosis, but distant metastasis is usually associated with an increased risk of mortality. Advanced stage IV metastasis is rare, accounting for 1% of patients [3]. This case report is a confirmed case of stage IV papillary thyroid cancer evident by CT and histopathological results.

Clinical examination of patients with goiter remains an important component in cancer risk assessment. All patients presenting with goiter should be periodically monitored by assessing for the occurrence of nodules, change in the characteristic of pre-existing nodules with regards to size, consistency, and association with pain, as these changes may suggest possible malignant transformation [4]. However, solely relying on physical examination, as illustrated in this case, to detect new nodules or changes in the size of the nodules are highly inaccurate. While palpation is a clinically relevant method of examination of the thyroid gland, it has low sensitivity (10–41%) to pick up thyroid nodule size of <1 cm. Ultrasound, on the other hand, can pick up nodules as small as 3 mm. The concordance rate between the palpation and ultrasonography methods in finding results in the assessment of goiters is low at 58% [5]. This suggested an important clinical implication. There is a limitation to clinical examination among clinicians in detecting discrete thyroid nodules, and thus, ultrasonography is a required tool for more accurate detection of significant non-palpable nodules.

Ultrasound remains the gold standard procedure in the assessment of all patients presenting with goiter, especially among patients with thyroid nodules. The usefulness of ultrasound covers three important domains: (1) As a tool to identify the presence of nodules that are

not clinically palpable; (2) to clinically evaluate nodules that require a diagnostic procedure such as FNAC; and (3) to provide baseline information in monitoring the progression of thyroid nodules [6]. Once thyroid nodules are identified, the major challenge for clinicians is to determine if these nodules require further assessment.

Based on clinical practice guidelines [7], [8], the risk of malignant transformation is determined by a combination of factors. These include data from the patients' medical history such as a history of head and neck radiation exposure, family history of thyroid cancer, presence of compressive symptoms, and examination findings of the character of the nodules which may be hard, firm, or fixed nodule(s) with the presence of cervical lymphadenopathy. In addition, thyroid hormone levels, scintigraphy, and FNAC findings provide valuable information in coming to a possible diagnosis.

In this case, the patient refused further imaging evaluation of her long-standing goiter due to the lack of concern, as the size of her goiter remained static and that she was clinically asymptomatic. Thus, the clinically stable goiter which was diagnosed 30 years ago was clinically monitored without any imaging studies. Monitoring of stable goiter for early cancer detection in the absence of initial imaging evaluation proved to be a great challenge, as discussed earlier. Several blood tests to support the presence of thyroid cancer have been proposed, but its evidence as a modality for early thyroid cancer detection is lacking. Serum thyroglobulin (Tg) and calcitonin are not recommended for routine or initial evaluation of thyroid nodules as evidence of their accuracy was insufficient [7].

Ideally, surveillance for thyroid cancer is best to be done clinically with an ultrasound performed at 6–12-month intervals [4]. Surveillance using ultrasound should be emphasized to the patient as it plays a major role in the early detection of thyroid cancer. The plan of management and the reasoning behind surveillance for thyroid cancer should be discussed with the patient at the initial stage and reemphasized throughout the follow-up sessions. Discussion between doctor and patient is vital for good decision-making and perhaps was lacking in this case. Doctors ought to provide patients with adequate information and take sufficient time to explain the diagnosis, prognosis, and any potential uncertainties that may arise during the course of the illness. They should also discuss the need for further investigations if required. The decision not to undergo further investigations should not be encouraged, as the probability of malignant transformation, although rare, is a possibility.

Cytological examination findings reported based on Bethesda's system is recommended for the diagnosis of thyroid cancer. Surgery for near-total thyroidectomy or total thyroidectomy is the mainstay treatment for papillary thyroid cancer (PTC) with a tumor of more than 1 cm in diameter. Evaluation of post-operative status is usually done using serum Tg. Tg is secreted by cancerous thyroid cells and hence, detectable serum Tg is highly suggestive of thyroid remnant, residual, or recurrent

tumor. The ^{131}I radioiodine can also be considered for post-operative status assessment, but the use of ^{131}I ablation to ablate potential thyroid tissue remnant following surgery is not commonly done. However, in this case, ^{131}I radioiodine therapy is needed to ablate the residual unresectable paratracheal and pretracheal lymph nodes. The maintenance level for an initial TSH depends on the serum Tg level. The target TSH is between 0.5 and 2.0 mU/L for serum Tg of <0.2 ng/ml and a TSH between 0.1 and 0.5 mU/L for serum Tg of ≥ 0.2 ng/ml. The evaluation of levothyroxine therapy is commonly assessed using serum Tg and ultrasound methods [4].

The patient, in our case, had a total thyroidectomy and ^{131}I radioiodine and has been followed up by a multidisciplinary team.

Conclusion

Appropriate thyroid carcinoma surveillance procedures to include ultrasound investigation should be practiced in managing patients with long-standing and stable diffuse goiter. This case highlights a chronic, neglected stable diffuse goiter which developed into PTC with distant metastases. This case report discusses and highlights the importance of combining clinical examination with ultrasonography findings as a periodical surveillance measure for early detection of thyroid cancer as a basis of follow-up management of patients with goiter.

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