

A Case of Miliary Nodules, Hemoptysis and Hot Thyroid Cancer: Unusual Presentation of Papillary Thyroid Cancer

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ABSTRACT

Background: Papillary thyroid carcinoma is the commonest thyroid cancer. Patients usually present with thyroid nodule and rarely with hyperthyroidism such that 2009 ATA guidelines recommended that cytological evaluation is not necessary in patients with hyperfunctioning nodules as they rarely harbor malignancy. We report a case of an unusual presentation of metastatic papillary thyroid carcinoma in a young patient.

Case presentation: A 17-year-old girl, presented to our hospital with 3 days of fever, cough and hemoptysis. Chest X-ray showed extensive miliary nodules and was treated for presumed miliary tuberculosis. Biochemical investigations revealed a hyperthyroid state (fT4 55.7 TSH < 0.02), with negative antibodies (TRAB and TSI). Radioisotope scan showed increased uptake on right lobe. She underwent bronchoscopy and biopsy which revealed metastatic papillary thyroid carcinoma.

Clinical examination revealed a small goiter with palpable cervical node at level III on the left. There were no clinical signs of Graves' disease and she had no history of previous radiation or family history of endocrine disease. Ultrasound revealed multiple hypodense thyroid nodules with microcalcification and increased vascularity. Ultrasound of the neck showed the presence of abnormal lymphadenopathy.

She underwent total thyroidectomy, bilateral central neck dissection and left lateral modified neck dissection. Histology showed 1.3 cm papillary thyroid carcinoma involving the left lobe and multifocal papillary thyroid microcarcinomas involving both lobes. Ten out of 27 nodes were involved. She was BRAF mutation positive.

She recovered well postoperatively and was rendered hypothyroid. She underwent radioiodine ablation which showed no more disease in the neck but unfortunately there was no uptake in the lung metastases.

Conclusion: Metastatic papillary thyroid cancer developing in a young patient with hyperthyroidism is extremely rare and suggests a more aggressive behavior as confirmed by BRAF mutation.

Keywords: Hyperthyroid, Papillary, Radioiodine, Thyroid cancer.

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INTRODUCTION

Papillary thyroid carcinoma is the most common thyroid cancer encountered by any endocrine surgical unit and it is usually associated with good prognosis. The patients commonly present with a thyroid nodule and rarely with hyperthyroidism such that 2009 ATA guidelines recommended that cytological evaluation is not necessary in patients with hyperfunctioning nodules as they rarely harbor malignancy.

Here, we report a case of an unusual presentation of metastatic papillary thyroid carcinoma in a young patient.

CASE REPORT

A 17-year-old girl who was previously well with no past medical history, presented to our hospital with 3 days of fever, cough and hemoptysis. Initial chest X-ray showed extensive miliary nodules (Fig. 1). Sputum was sent for staining and culture for acid fast bacilli. She was treated for presumed miliary tuberculosis with anti-mycobacterial drugs. During the course of treatment as she was noted to be persistently tachycardic, further blood investigations were performed.

Biochemical investigations revealed a hyperthyroid state (fT4 55.7 TSH < 0.02), with negative antibodies (TRAB and TSI). She did not have any clinical or serological features of Graves' disease. Radioisotope scan (Fig. 2) showed slightly increased uptake on right lobe. She was started on carbimazole and propranolol for hyperthyroidism likely secondary to toxic thyroid nodule and discharged well.

Upon further review in clinic, CT scan of the thorax (Figs 3A and B) was performed in view of poor resolution of symptoms and showed multiple miliary nodules scattered in random distribution in both lungs with the largest nodule measuring up to 3.5 mm. There were prominent left axillary lymph nodes, measuring up to 11 mm. The sputum culture results were found to be negative for mycobacterial infection. She underwent a

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bronchoscopy and biopsy of right middle lobe of lung which revealed metastatic papillary thyroid carcinoma. Immunohistochemical staining was positive for TTF-1, CK-7 and thyroglobulin. She was thus referred to our endocrine surgery unit for further review.

Clinical examination revealed a pleasant girl who was clinically euthyroid and had a small goiter with no obvious nodules. There was a 1 cm palpable cervical node at level III on the left. There was no history of previous radiation or family history of endocrine disease. Ultrasound and CT scan of the neck revealed multiple thyroid nodules with microcalcification and increased vascularity, with the largest nodule seen at the left thyroid

upper pole measuring 15 mm. This was associated with prominent cervical lymph nodes, at levels III, IV, V and VI on the left and level VI on the right. Serum thyroglobulin level was 26.5 and anti-thyroglobulin antibodies were undetectable.

In view of the findings, she was underwent a total thyroidectomy, bilateral central neck dissection and left lateral neck dissection. Histology showed 13 mm papillary thyroid carcinoma involving the left lobe and multifocal papillary thyroid microcarcinomas involving both lobes. Ten out of 27 lymph nodes were involved. She was also found to be BRAF mutation positive.

She recovered well postoperatively and was rendered hypothyroid. Subsequently, she underwent radioiodine ablation which showed no more disease in the neck. However, despite the proven lung metastases, there was no radioiodine uptake in the lung metastases suggesting that the tumor may have dedifferentiated. This was further confirmed on PET-CT (Fig. 4) which showed varying degrees of FDG uptake compatible with metastases. She was started on thyroxine replacement with the aim for TSH suppression. She continues to well with no further complications, with plans to start tyrosine kinase inhibitors if metastases continue to grow.



Fig. 1: Chest X-ray showing multiple miliary nodules in the lung fields

DISCUSSION

Papillary thyroid cancer is the most common thyroid malignancy and clinically manifests as a thyroid nodule, discovered on clinical examination or incidentally on

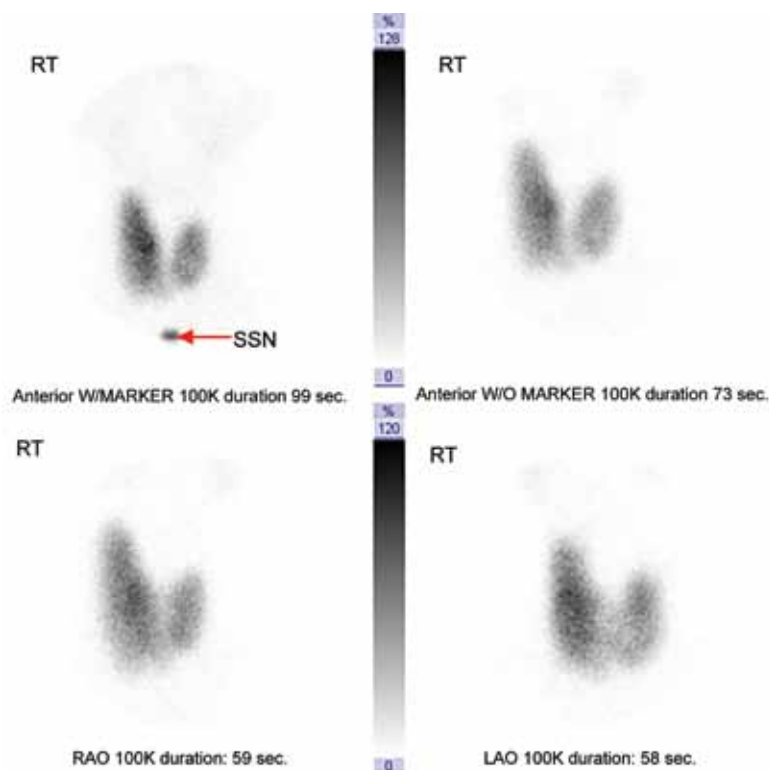
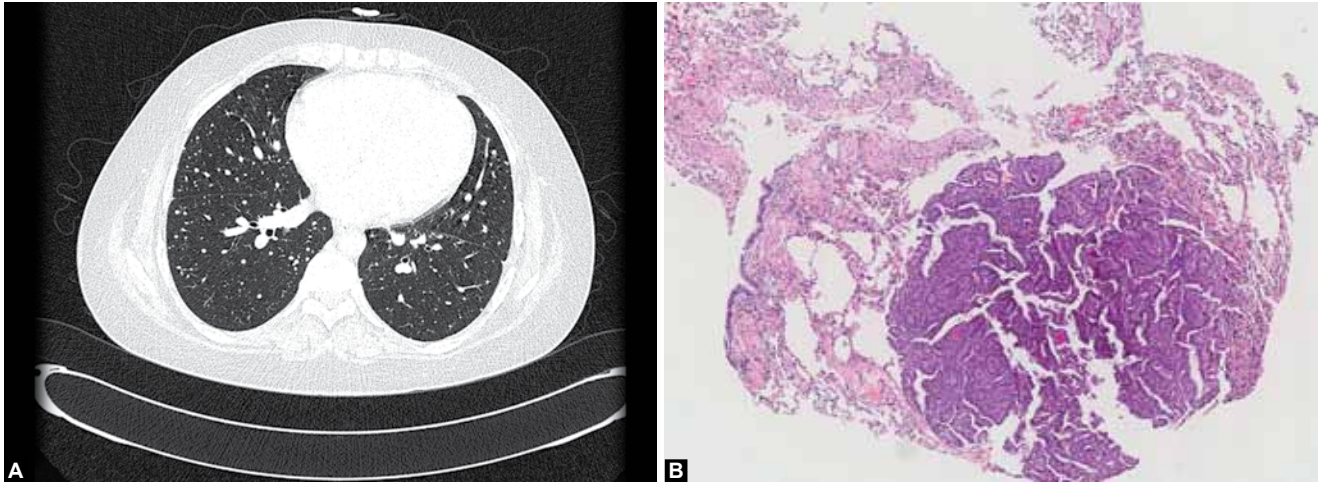


Fig. 2: Radioisotope scan showing a slight increased uptake in a right lobe (SSN: Suprasternal notch)



Figs 3A and B: (A) Computed tomography thorax showing multiple miliary nodules in keeping with metastasis and (B) histology of transbronchial lung biopsy showing nodule of metastatic papillary thyroid carcinoma (Courtesy: Dr Seet JE, Department of Pathology, NUHS)

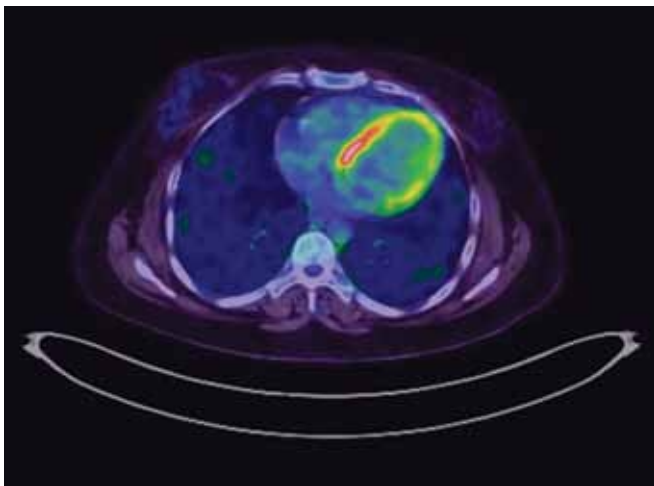


Fig. 4: Positron emission tomography CT showing lung metastases

imaging. It is not uncommon to diagnose cancers following total thyroidectomy for either Graves' disease or nodular goiter.¹⁻³ However, for thyroid cancer to present with hyperthyroidism in the absence of diagnosis of Graves' disease or toxic nodular goiter is uncommon, as is the case with our patient. Even more uncommon is the fact that the patient presented with hemoptysis secondary to the extensive bilateral lung metastases instead of the primary.

Historically, it was believed that hyperthyroid state protects against thyroid malignancy⁴ and the incidence of cancers reported in patients undergoing surgery for Graves' disease was up to 2.5%.^{5,6} However, more recent series have shown the rates to be much higher at 1.6 to 21%.⁷ A recent 4-year population-based cohort study showed an increased risk of thyroid cancer (6.8 fold over patients with normothyroid state) and the risk increased with duration of hyperthyroidism.⁸ The difference in outcomes of thyroid cancers in patients who present with hyperthyroid states in comparison to the euthyroid states is poorly studied.

Patients with hyperthyroid state are investigated with a radioiodine uptake scan and in the presence of cold nodules, needs further imaging with an ultrasound scan along with a needle biopsy. The use of ultrasound in Graves' disease may lead to early detection of nodules not felt by clinical examination⁹ and characterize the nodules as malignant in the presence of echogenicity, ill-defined borders, absence of a peripheral hypoechoic rim, no cystic changes, increased intranodular blood flow, and punctate calcifications^{10,11} as seen in our patient.

Distant metastasis is seen in 1 to 7% of patients with differentiated thyroid cancer, with lung being the most common site followed by bone.¹²⁻¹⁴ The patients present with hemoptysis or dyspnea at rest or upon exertion in the presence of lung metastasis. The radioiodine avid lesions in the lungs are usually treated with radioactive iodine (RAI) ablative therapy, but in some cases it may be difficult to completely eradicate with radioiodine therapy.¹⁵ In absence of effective ablation with radioiodine therapy of lung metastasis one has to consider the possibility of dedifferentiation.

This case highlights the importance of carefully evaluating patients with hyperthyroid state in the presence of thyroid nodules. The earlier belief that 'hot nodules' are unlikely to be malignant is no more true. To conclude, the detection of the rare truly hot thyroid carcinomas remains a clinical challenge.

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