

Concurrent Hyperthyroidism and Papillary Thyroid Cancer

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Abstract

Background: Concurrent thyroid cancer and hyperthyroidism is rare, though increasingly reported. Hyperthyroidism due to thyroid cancer is very rare and challenging.

Case presentation: We present a 35-year-old woman who had been on irregular regimen of propranolol and digoxin as treatment for worsening palpitations for 12 months. She came to our Policlinic University for her propranolol medication evaluation. We identified features of hyperthyroidism and found a left uninodular goiter with no cervical lymphadenopathy. She was referred for thyroid assessment which suggested primary hyperthyroidism and an enlarged heterogeneous left lobe with a well-defined homogenous solid mass. We restarted her on propranolol and referred her for a new course with methimazole. At the Policlinic University, she also underwent a left thyroid lobectomy. The resected lobe was sent for cytology evaluation which revealed a neoplastic nodule with features suggestive of a papillary thyroid cancer causing hyperthyroidism. The postoperative clinical progress of the patient was good and a regression of hyperthyroidism was also evidenced.

Conclusions: The historical, clinical, and laboratory findings were suggestive of hyperthyroidism due to papillary thyroid cancer. A high index of suspicion, prompt referral, and counter-referral lead to a positive outcome of such a rare case. We advocate for systematic and careful evaluation of all thyroid nodules.

Keywords: Thyroid cancer; Hyperthyroidism; Papillary thyroid cancer; methimazole

Case Report

We present a 35-year-old woman, born in Sicily (Italy) an endemic region for hyperthyroidism, who came to our outpatient department of the Policlinic University of Messina to refill her propranolol medication. She had already been taking the drug routinely for palpitations for about 12 months without any side problems before coming to our outpatient unit.

Lately she was aware of heartbeat episodes occurring recurrently and lasting several minutes each time. Heartbeats became associated with dyspnea initially moderate and then with mild exertion. After consulting at various health facilities in the north east of Italy, she was prescribed long-term, irregular, and alternate daily regimens of propranolol (40 mg) and digoxin (0.25 mg). Although the medications conferred her some relieve, she noticed a progressive weight loss over a 12-month period from 90 kg to 62 kg despite an abnormal increase in her appetite for food. She also experienced frequent watery stools (averagely 6 times daily). She complained of heat intolerance and profuse sweating resulting in sleeping with minimal clothing and noticed also spontaneous resting tremors of her hands with extended forearms. Three months before presentation at our hospital, she had also noticed a painless lump on her neck that progressively increased in size. On reviewing her medical records, we noticed a number of investigations requested by the various hospitals where she had been visited during the last 8 months preceding her visit at our hospital. These records included electrocardiographs, echocardiograms, full blood tests, fasting blood sugar and thyroid hormone assays, all of them without any relevant result except for the electrocardiography results which showed always a sinus tachycardia. As far as she knew, she did not recall any history of exposure to radiations or family history of malignancies. Physical examination revealed a chronically ill-looking middle aged woman. Eyes were normal, voice was clear, she showed fine resting tremors of her hands when her arms were outstretched. There was a left anterolateral neck mass measuring 4 × 3 cm. The mass

was mobile, non-tender, it moved when swallowing, and not fixed to overlying or underlying tissue. No bruit was heard over the mass. There was no palpable cervical lymphadenopathy. Her bmi was 20.1 kg/m². There was discrete bilateral pedal pitting oedema. The rest of the physical examination did not show any notable findings. In view of this presentation, a presumptive diagnosis of hyperthyroidism was made therefore she was prescribed propranolol (40 mg) twice daily. To confirm the diagnosis, we requested a functional serum test for T3, T4, TSH and an ultrasound of the thyroid.

Test serum level result was T3 >5.0 (high), T4=23.3 (high), TSH=0.13 (low), their normal range is (0.8-2.0) NG/mL, (5.0-13.0) mg/dl, (0.4-7.0) Miu/ML respectively.

Structural assessment of the thyroid (ultrasound scan)

The left thyroid lobe appeared enlarged, heterogeneous, with a fairly iso-echoic well-defined homogenous solid mass. The right lobe did not show any peculiar aspect. No cervical lymphadenopathy was observed. In view of these findings, we concluded on a primary hyperthyroidism most likely due to a toxic uni-nodular goiter. She was therefore placed on methimazole 60 mg daily and 4 weeks after she underwent a left thyroid lobectomy. The resected lobe was sent for cytology. The postoperative course was uneventful.

The lobe weighed 33.5 g, it was received in formalin as two grey-tan

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Received June 04, 2016; **Accepted** November 30, 2016; **Published** December 05, 2016

Citation: Gagliano E, Sturniolo G, Querci A, Milone A, Paparo D, et al. (2016) Concurrent Hyperthyroidism and Papillary Thyroid Cancer. J Health Educ Res Dev 4: 203. doi: [10.4172/2380-5439.1000203](https://doi.org/10.4172/2380-5439.1000203)

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soft tissue fragments. Cutting demonstrated a red tan cut surface with a 3 x 2.3 x 2 cm nodule inside the bigger piece. Microscopic examination of representative sections of the large fragment with a full thickness section of the nodular structure revealed a nodular proliferation of enlarged pale cells with marginated chromatin and overlapping nuclei. Pink "bubble-gum"- like colloid was focally noted. The lesion was partially encapsulated and displayed areas with fibrosis and more follicular appearance of the aggregates. Based on these findings, a histological diagnosis of papillary thyroid cancer (T2N0Mx) was made.

We monitored the patient through scheduled regular visits and referrals. We observed a progressive decline in hyperthyroid symptoms and signs: palpitations regressed as well as diarrhea and polyphagia, heat intolerance regressed and one month postoperatively, her weight increased from 62 kg to 72 kg.

Discussion

We report a fortuitous finding of concurrent hyperthyroidism and papillary thyroid cancer. A challenge to manage.

Grave's disease, although the most common cause of hyperthyroidism, is less likely identifiable when goiter is not diffuse, eyes are normal and no pretibial myxedema is present [1].

Therefore, a hyper functioning thyroid nodule took precedence as the probable etiological diagnosis, with a toxic adenoma being the most likely etiology [2]. Since the patient's TSH levels were low, the most appropriate step would have been a thyroid scintigraphy to determine if the nodule is hot [3].

That notwithstanding, even if the hyperthyroidism was due to a hyper functioning nodule, such kind of nodule very rarely has malignant potentials, thus it is seldom biopsied after scintigraphy. In the management of this case although cytologic evaluation can be carried out on a resected lobe through fine needle aspiration, cytology is advisable for proper planning of the surgical approach to be used.

This is just because it is suggested that toxic thyroid cancers are best treated by total thyroidectomy, whereas incidental carcinomas can be managed by subtotal thyroidectomy or lobectomy [4]. Histopathology revealed a papillary thyroid cancer [5]. Given the partial encapsulation of the neoplastic nodule in this case, the lesion could be further classified as an encapsulated variant of the papillary thyroid cancer [6]; the differential diagnosis also included follicular adenoma with papillary hyperplasia but the extensive nuclear changes observed were typical of a papillary thyroid cancer (pT2N0Mx), this case is again unusual in that most malignant thyroid tumors associated with papillary hyperthyroidism as so far reported are papillary thyroid micro-carcinomas (nodule <1 cm or pt 1) [7]. The many follicular cells observed in the neoplastic lesion were suggestive of follicular hyperactivity which is seen in toxic thyroid cancer [8]; if hyperthyroidism is due to a tumor cell mass, demonstrated in most cases by clinical-histopathological correlation, a toxic thyroid cancer is diagnosed [9]. An ambiguity, however, remains because a scintigraphically hot nodule was not confirmed. Concomitant thyroid cancer and hyperthyroidism can either be in the form of a fortuitous malignancy in the thyroid gland of a clinically hyperthyroid patient or as a thyroid cancer presenting with hyperthyroidism with the latter being rarer [10]. These two can be distinguished via cytological examination even when there is lack of hyperplastic thyroid tissue suggesting a hyper functioning thyroid cancer as in the case presented

[11]. Again, with retrospect to the lack of ultrasound findings of an increase in vascularity and a diffuse enlargement of the thyroid tissue, further belief is lent to the autonomous nature of the tumour mass [7]. In terms of risk factors, based on the study by Mirfakhtaee et al. [1], patients with malignant hot nodules seem more likely younger and females as in the case the patient we presented. Hyperthyroidism due to thyroid cancer is explained by somatic mutations in the TSH receptor genes of the cancer cells. These mutations lead to constitutive activation of intracellular cyclic adenosine monophosphate (cAMP) cascade which induces hormonogenesis and thus hyperthyroidism [11].

Conclusions

We can therefore conclude that in any case suspicion arises due to presence of anomalous findings, such as T3, T4, TSH and a thyroid nodule it is advisable to carry out every needed procedure to find out what is the cause for that. The historical, clinical and laboratory findings of the case we report concurred with hyperthyroidism due to papillary thyroid cancer. A high index of suspicion should be the attitude towards every thyroid nodule [12]. A good referral and counter-referral system can lead to a positive outcome. We advocate and suggest in any case for a systematic and careful evaluation of all thyroid nodules [13,14].

Consent

Written informed consent was obtained from the patient for publication of this case report.

Competing Interest

The authors declare that they have no competing interests.

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