Hyperfunctioning Papillary Carcinoma Of Thyroid: A Case Report And Brief Literature Review

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Citation

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Abstract

Hyperfunctioning thyroid carcinoma is a rare clinical condition. Coexisting carcinoma and hyperthyroidism implying a focus of malignancy in a hyperfunctioning thyroid gland is more common. Absence of hyperplastic thyroid tissue on histology in the former differentiates the two conditions. While subtotal thyroidectomy is an adequate treatment for incidental small focus of malignancy, hyperfunctioning thyroid malignancy requires more aggressive treatment. We present a case of papillary carcinoma of thyroid presenting with hyperthyroidism. This case emphasizes the need for thorough evaluation of thyroid to exclude malignancy even in a clinical setting of hyperthyroidism.

INTRODUCTION

Hyperthyroidism and malignancy were considered mutually exclusive for a long time. But association of these two conditions is being increasingly recognised. A 6.9% incidence of concurrent carcinoma in patients of hyperthyroidism has been reported by cakir et al [1]. Cytological examination of nodules detected either clinically or by ultrasound in a patient with hyperthyroidism is suggested to exclude malignancy [2]. Thyroid carcinomas are clinically euthyroid and appear as cold nodules on scintigraphy. Thyroid carcinoma presenting with hyperthyroidism is rare. We report a case of differentiated thyroid carcinoma presenting with clinical and biochemical features of hyperthyroidism. Histological examination of the gland revealed papillary carcinoma and there was no evidence of hyperfunctioning thyroid gland.

CASE HISTORY

A 50 year old female presented with symptoms of neck swelling, palpitations and weight loss. She did not have dyspnoea or hoarseness of voice. She had undergone tonsillectomy 3 years back. There was no history of irradiation to head and neck. On examination, the patient had a staring look, a resting pulse rate of 112/minute and BP of 130/80mmHg. Both lobes of thyroid were enlarged, were soft to firm in consistency with no palpable nodules. There was no cervical lymphadenopathy. Clinical examination of chest and abdomen was normal.

Serum TSH was 0.03microIU/mL (normal 0.5-5.0microIU/mL). Serum total T4 was 19.08microgram/dL (normal 5-12microgram/dL), total T3 was 350ng/dL (normal 80- 180ng/dL). Ultrasonogram of the neck showed a right lobe 4.8 x 3.4 x 2.2cm with altered echo pattern and a 1.0x 0.8cm lesion with well defined hypo echoic boundaries in the right lobe. The left lobe was 3.2x 2.4 x1.4 cm with altered echo pattern. No lymph nodes were detected. Microsomal and thyroglobulin antibody levels were elevated. X-ray chest was normal. In view of diffuse enlargement of the thyroid gland with features of hypervascularity and clinical and biochemical evidence of hyperthyroidism, radio isotope studies were not considered and FNAC was not performed.

The patient underwent surgery after control of hyperthyroidism with carbimazole and propranolol. At surgery, the gland was found to be hypervascular with both lobes enlarged and nodular. Three small lymph nodes in the pretracheal region were found to be enlarged and frozen section examination revealed metastases from papillary carcinoma. Total thyroidectomy with excision of the enlarged lymph nodes was done. Histopathology of the thyroidectomy specimen showed a right lobe 5x3.5x2.5cm and left lobe 3.5x2.5x1.8cm with multiple grey white poorly circumscribed areas in the right lobe and a single grey white nodule in the left lobe. Microscopy of the specimen showed papillary carcinoma with infiltration into both lobes of the thyroid. There was no evidence of thyrotoxicosis in the

thyroid gland. Pretracheal lymph nodes showed metastases.

The patient became euthyroid following surgery.

Figure 1

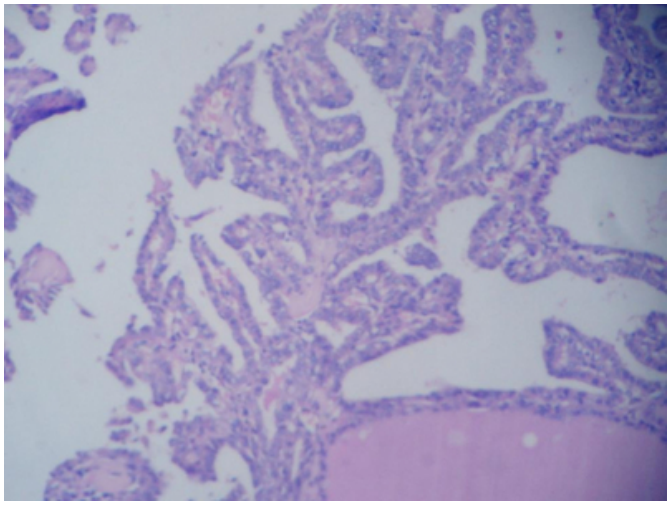


Figure 2

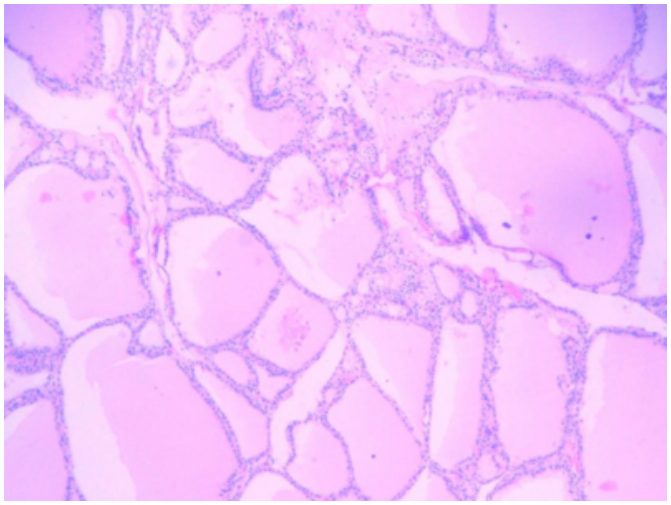
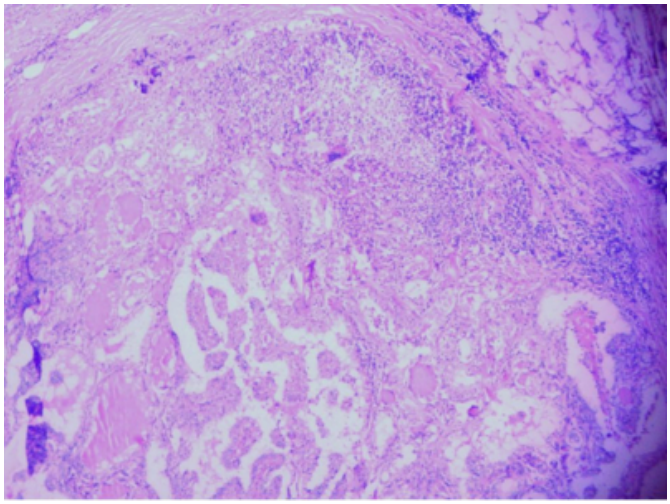


Figure 3



DISCUSSION

The risk of thyroid malignancy in a clinically hyperthyroid patient was considered quite low. But this interesting coexistence of hyperthyroidism and thyroid malignancy is being increasingly recognized. This association can be either in the form of an incidental focus of malignancy in the thyroid gland of otherwise clinically hyperthyroid patient or a carcinoma of thyroid presenting with hyperthyroidism with the former being much more common. Diaconescu described these two clinically and pathologically distinct groups. The first category was represented by one case of follicular thyroid cancer with clinically and biologically confirmed hyperthyroidism. The second group included ten patients with thyrotoxicosis and associated unsuspected occult or nodular carcinoma [$_3$].

Histopathology can differentiate these two conditions as lack of hyperplastic thyroid suggests a hyperfunctioning thyroid carcinoma [$_4$]. In the present case histopathology revealed papillary carcinoma and there was no evidence of hyperfunctioning thyroid tissue.

Incidence of hyperthyroidism in patients with thyroid carcinoma is 2.8%. Gulcelik et al found 12 cases of hyperthyroidism among 422 patients of thyroid carcinoma. Nine patients with papillary carcinoma, 1 patient with follicular carcinoma and 2 patients with follicular variant of papillary carcinoma presented with hyperthyroidism. None of the patients had Graves' disease [$_5$].

The incidence of concurrent cancer in patients with hyperthyroidism is higher at around 5%. Zanella et al reported an incidence of 5.3% of thyroid cancer in a series of 202 patients of Graves' disease who underwent

thyroidectomy. [6] Thyroid carcinoma was found in 5.8% of patients of hyperthyroidism in Terzioglu's series of 138 patients. Concurrent carcinoma was more frequent in patients with toxic adenoma (8 %) than in those with Graves' disease (6 %) and toxic nodular goiter (5 %).Papillary carcinoma was more common than follicular carcinoma. (7 vs. 1) [7]

Thyroid scintigraphy is used to determine the functional status of thyroid nodules and 'hot' nodules on scintigraphy are generally considered benign. But, autonomously functioning thyroid nodules (AFTN) on scintigraphy were found to be histologically malignant emphasizing that not all hot nodules are necessarily benign [8]. A carcinoma associated with hyperthyroidism is rarely diagnosed before surgery [12] .This is largely due to the fact that the majority of the patients had an occult microcarcinoma defined as a tumor of less than 1cm.

Recently a case of papillary carcinoma in an autonomously functioning nodule was described by José Ulisses M confirming that the presence of hot thyroid nodule does not exclude the concomitance of well differentiated thyroid carcinoma [9].

dell'Erba et al found that a malignant nodule can trap technetium pertechnate and appear hot on technetium scan but may appear cold on radioiodine scan. They advise thyroid scintigraphy with radio iodine scan in a sonographically suspicious nodule even if it appears hot on technetium scan [10]. But Fine needle biopsy revealed a papillary carcinoma in a hyper functioning nodule on thyroid scintigraphy with I123 in another case described by Rubenfeld and Wheeler [11]. Scintigraphy was not performed in our case.

The basis of this interesting association of malignancy and hyperthyroidism is being investigated. Initially hyperthyroidism was attributed to sheer increased volume of thyroid tissue even in the face of decreased function associated with malignancy [13]. Bulky metastasis in some cases was considered responsible for hyperthyroidism. A rare case of hyperthyroidism in the presence of a functioning bone metastasis secondary to an occult thyroid cancer is reported [14]. In the present case there was only moderate enlargement of thyroid gland and small lymph nodes detected at operation. Thyroid auto-antibodies are considered responsible for hyperthyroidism and cancer progression in cases of Graves' with concurrent carcinoma [15].

Activating mutation of thyroid hormone receptor (TSH-r) gene has been demonstrated in a hyperfunctioning differentiated cancer. This mutation through activation of cAMP signal transduction is believed to cause hyperthyroidism [16].In an autonomously functioning thyroid follicular carcinoma, a combination of mutations of TSH receptor and Ki-RAS was found to be responsible for hyperfunction of the tumor and the carcinogenic process [17].

Hyperfunctioning thyroid carcinoma should be considered in the differential diagnosis of thyrotoxicosis / hyperthyroidism. This association of hyperthyroidism and malignancy has considerable therapeutic significance. Functioning thyroid carcinomas require total thyroidectomy whereas incidental carcinomas, because of their small size can be adequately treated with subtotal thyroidectomy. This case emphasizes the need for thorough evaluation of thyroid to exclude malignancy even in a clinical setting of hyperthyroidism.

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