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Thyroid Papillary Carcinoma in a Patient with Hyperthyroidism: A Case Report and Review of Literature

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Abstract. Thyroid carcinoma in hyperfunctioning thyroid is a rare entity and a rare clinical condition, but should be suspected as there is rising trend in these cases. While subtotal thyroidectomy is an adequate treatment for incidental small focus of malignancy, hyperfunctioning thyroid malignancy requires more aggressive treatment. This report presents a case of 41-year-old hyperthyroid man who was found to have papillary thyroid cancer with hyperplastic goiter; consistent with toxic goiter based on postoperative histopathology. This case shows the importance of proper evaluation of the thyroid to exclude malignancies even in hyperfunctioning thyroid patients. Thyroid cancer should be considered in the differential diagnosis of hyperthyroid goiter and Graves' disease despite the rare association between them. Careful history and physical examination should be carried out. Although hot nodules in iodine or technetium scan may suggest a benign condition, malignancy should be always ruled out with histopathology examination.

Keywords: Hyperthyroidism, Carcinoma thyroid.

Introduction

Hyperthyroidism and malignancy were considered mutually exclusive for a long time but association of these two conditions is being increasingly

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recognized[1]. In a study carried in 2003 in Italy, thyroid cancer was diagnosed in 1.65% of 425 hyperthyroid patients[2]. Thyroid carcinomas usually are clinically euthyroid and appear as cold nodules on scintigraphy[1]. However, thyroid carcinoma is presented with hyperthyroidism in this case report.

Case Report

A 41-year-old male patient was referred to King Abdulaziz University Hospital in 1999 with a history of neck swelling for 2 years. The problem started as a diffuse thyroid swelling, which got bigger with time. This was associated with thyrotoxic symptoms like palpitations, weight loss, heat intolerance, tremor, sweating and blurred vision. There were also mild pressure symptoms like difficulty with swallowing, shortness of breath and change in voice. No history of head and neck irradiation in the past. The patient had unremarkable past medical history. Socially, he is married and an ex-smoker for more than 15 years. There was no similar problem in his family. On examination, there was a gross exophthalmos with bilateral redness, lid lag and lid retraction, and diffuse enlargement of gland. There were no enlarged lymph nodes in the neck. Pulse, blood pressure (BP) and respiratory rate were normal. (Patient was under treatment).

Investigations

No abnormality found in chest X-ray and abdominal ultrasound.

Thyroid function test showed high level of T4 and low level of thyroid-stimulating hormone (TSH), high level of anti-microsomal and thyroglobulin antibodies. Thyroid scan with technetium showed enlargement in both lobes with homogeneous high tracer uptake. Ultrasound reported as diffuse homogeneous enlarged gland. A computed tomography (CT) scan of both orbits showed an increase in retrobulbar fat and symmetrical enlargement of extra ocular muscles, which was consistent with bilateral thyroid orbitopathy.

Patient's hyperthyroidism was controlled by carbimazole and beta blockers. He underwent subtotal thyroidectomy. During surgery, the gland was soft and in some parts, cystic. Specimen was examined postoperatively; macroscopically consisted of multiple grayish masses measuring 9 cm in aggregate. The largest one on gross section revealed

homogeneous surface. Microscopically, the sections revealed variable sized thyroid follicles lined by cubical to columnar lining. There was focal stratification and peripheral scalloping of the light colloid. Multiple foci of papillary carcinoma were seen. The complex malignant papillae were covered by malignant follicular cells having ground glass nuclei, focal intranuclear inclusions and nuclear cleavage. Numerous psammoma bodies were seen. Extensive fibrosis surrounding occasional malignant foci was seen. The malignant cells showed crowding with egg basket appearance. Histopathological final diagnosis was papillary adenocarcinoma, hyperplastic goiter consistent with toxic goiter.

The patient was discharged and readmitted again 2 months later for radioiodine whole body scan and ablation. Since then, the patient follows up in the general surgery clinic regularly and the patient has been doing fine. Thyrotoxic symptoms improved. He is on 200 microgram of thyroxin. Whole body scans after 10 years and still normal.

Discussion

Hyperthyroid patients used to be considered at low risk to have a thyroid malignancy. Recently, there was an increase in the number of studies and cases that report the association of hyperthyroidism and thyroid cancer. In a retrospective study done by Gabriele *et al.*[2] the incidence of thyroid cancer in 425 hyperthyroid patients was analyzed. Thyroid cancer was diagnosed in 7 (1.65%) hyperthyroid patients. Papillary carcinoma was found in 5 cases and follicular carcinoma in 2 cases. This was confirmed by histological examination. Although 64 cases of the 425 patients had Graves' disease (15%), none of them had thyroid cancer[2].

In contrast, there was several cases reported thyroid cancer in Graves' disease patients. Bałdys-Waligórska *et al.*[3] reported a 39-year-old man with clinical features of hyperthyroidism associated with exophthalmos and the goiter was diagnosed as Grave's by elevated thyroid-stimulating antibodies. Near total thyroidectomy was performed. Histologically, papillary microcarcinoma was found[3]. Kinkel *et al.*[4] also reported a 41-year-old woman presented with hyperthyroidism and diagnosed as Graves'. After 12 months of thyrostatic medication, recurrence occurred and a thyroidectomy was performed. Histologically, a papillary cancer was found and postoperative radioiodine therapy was added[4]. Another

study of a 65-years-old gentleman who presented with classical features of Graves disease was reported by Al-Omari *et al*.[5]. Technetium 99 scintigraphy revealed diffuse goiter with a cold nodule, which suggests thyroid cancer. The malignancy was proven by fine needle aspiration biopsy of this nodule and the diagnosis was confirmed by histopathology of thyroid specimen after total thyroidectomy[5].

By definition, a hot nodule is a nodular region of the thyroid gland that takes up large amounts of radioactive iodine relative to the rest of the thyroid gland. Although mostly benign, thyroid cancer has been detected in a small percentage of hot nodules, generally in less than 5% of reported cases, but up to 10% in some series. This can be difficult to diagnose, since fine needle aspiration biopsy of hot nodules will often show follicular thyroid cells, and may not be suggestive of thyroid cancer even if this turns out to be the final diagnosis. Persistently, enlarging nodules, or nodules that are irregular or large should prompt a higher suspicion for the presence of thyroid cancer in the setting of a hot nodule[6].

Harach *et al.*[7] described the pathologic findings of 73 clinically and scintigraphically confirmed hot nodules. Malignancy was observed in six cases (8.2%). A young woman with a thyroid papillary carcinoma behaving as an autonomously hyperfunctioning nodule was described by De Rosa *et al.*[8]. According to them, only 17 similar patients have been seen in the past 25 years. It is emphasized that hyperthyroidism does not exclude malignant disease in hot nodules[8]. As for our presenting case, the thyroid technetium scan showed high total uptake. Both lobes were enlarged and showed homogeneous tracer uptake.

The basis of this interesting association of malignancy and hyperthyroidism has been investigated. Initially, hyperthyroidism was attributed to a sheer increase in the volume of thyroid tissue even in the face of decreased function associated with malignancy[9]. A rare case of hyperthyroidism in the presence of a functioning bone metastasis secondary to an occult thyroid cancer was reported by Ikejiri *et al.*[10] . In a 59-years-old woman, there was pelvic bone metastasis much too extensive and hypervascular to permit resection. The patient also had vertebral metastasis and required methimazole to prevent thyrotoxicosis[10]. In Al-Omari *et al.* case, metastatic work up revealed pulmonary and liver metastasis[5]. In our case, there was no evidence of

local or distant metastasis by whole body iodine scan. Mssrouri *et al*. studied 547 patients who underwent subtotal thyroidectomy for gravis disease and he found six (1.1%) cases of thyroid cancer of which half were papillary carcinoma[11]. Sahin *et al,* studied 333 patients of hyperthyroidism who underwent surgery and histopathology showed thyroid cancer in 13 (2.1%) patients[12].

The cause of hyperthyroidism in thyroid cancer is believed to be due to an activating mutation of thyroid hormone receptor gene through activation of cAMP signal transduction[13]. According to Niepomniszcze *et al.* a combination of mutations of TSH receptor and Ki-RAS was found to be responsible for hyperfunction of the tumor, and the carcinogenic process in an autonomously functioning thyroid follicular carcinoma[14].

Conclusion

Thyroid cancer should be considered in the differential diagnosis of hyperthyroid goiter and Graves' disease despite the rare association between them. Careful history and physical examination should be carried out. Although hot nodules in iodine or technetium scan may suggest a benign condition, malignancy should be always ruled out with histopathology examination.

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سرطان الغدة الدرقية في مريض مصاب بزيادة إفراز الغدة الدرقية

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المستخلص. سرطان الغدة الدرقية في غدة زائدة النشاط نادرة الحدوث ولكن يجب توقعها في بعض الحالات، حيث أن هناك زيادة في نسبة حدوثها مؤخرا. إن استئصال معظم الغدة في وجود سرطان صغير يكون كافيًا أغلب الأحيان ولكن في حالة زيادة النشاط يجب أن يكون الاستئصال كاملاً. ونحن هنا نقدم حالة لرجل في العقد الخامس من عمره مصابًا بزيادة إفراز الغدة الدرقية وبعد استئصالها وتحليلها وجد أنها تحتوي على ورم سرطاني حليمي بالإضافة إلى زيادة في نشاط وحجم الخلايا. وهذه الحالة تبين أهمية الفحص الإكلينيكي والمخبري والنسيجي لأي مريض يعاني من نشاط الغدة الدرقية لاستبعاد وجود أورام خبيثة.