Toxic thyroid carcinoma: A new case

Sir,

Differentiated thyroid cancer may coexist with hyperthyroidism. Cancer cell mass is less functional and appears as cold nodule in thyroid scintigraphy. Cancer cell mass rarely becomes site of excess hormone production. When thyroid cancer cell mass occupies a scintigraphically hot, functionally autonomous thyroid nodule and if thyrotoxicosis is attributable exclusively to this nodule, as shown by clinical and histologic correlation, a toxic thyroid carcinoma is diagnosed.[1] We are reporting case feature which coincides well with the above mentioned diagnosis.

A 38-year-old male patient was evaluated for an incidentally detected thyroid nodule of 3 months duration. He experienced weight loss (3 kg), episodes of palpitation, and sweating during last 6 months. Clinical examination showed apparently healthy person (BMI 24.8) with tachycardia (>90/minute) and fine tremors of upper limbs. There was a 3-cm size hard solitary nodule in the right lobe with palpable deep cervical lymph nodes on the right side.

Laboratory investigations revealed thyrotoxicosis [Table 1]. Technetium 99 thyroid scintigraphy showed hyperfunctioning thyroid nodule involving entire right lobe of the thyroid gland [Figure 1]. The lymph nodes did not concentrate the isotope. Ultrasound examination showed 3.8 × 2 cm hypoechoeic nodule with scattered microcalcifications in the right lobe, which corresponded to hyperfunctioning region. There were multiple deep

Table 1: Laboratory investigations

	F T4	F T3	T S H	Anti-TPO antibody	TSHR antibody
Case	2.90 ng/dl (0.93–1.71)	6.12 pg/ml (1.71–3.71)	0.003 μIU/ml (0.27–4.2)	5.3 U/ml (<35)	Not detected

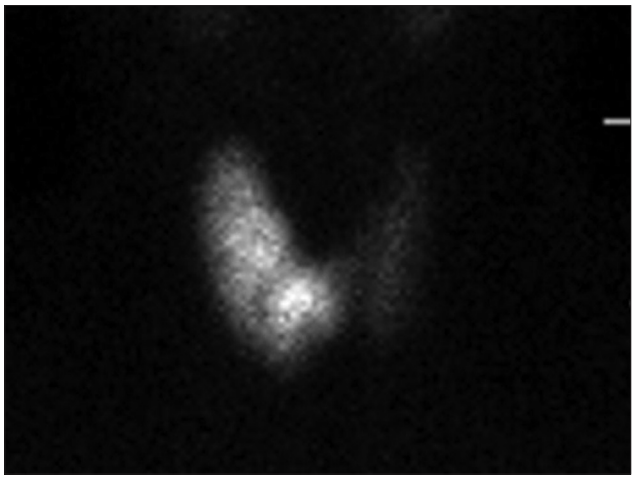

Figure 1: Technetium 99 thyroid scintigraphy: hyperfunctioning thyroid nodule involving entire right lobe

cervical lymph nodes with microcalcifications and loss of fatty hilum.

Patient was treated with carbimazole (30 mg daily) and was reassessed after 6 weeks. He was taken up for total thyroidectomy, central compartment, and right-side lateral neck dissection. The right lobe showed adhesions to soft tissue, strap muscles, and trachea. The soft tissue and lymph nodes in the central compartment were removed *en bloc* with thyroid gland preserving the parathyroid glands. Lymph nodes in Level II A and B, III, IV, and V were removed. The accessory nerve was preserved after clearing the nodes around it. Lymph nodes in the central compartment and lateral neck showed adhesions to the soft tissue and occasional matting.

Thyroid gland weighed 38 g with an ill-defined mass lesion of 3 × 2 cm in the right lobe. Histological features were suggestive of papillary thyroid cancer with capsular and lymphovascular invasion. The rest of the right lobe was studded with multiple papillary microcarcinomas. Left lobe and isthmus showed features suggestive of Hashimoto's thyroiditis. Eight nodes in central compartment (8/10) and six nodes in lateral neck dissection (6/32) showed metastasis with perinodal spread.

The patient received 4181 MBq of I-131 after 4 weeks of operation. The follow-up whole-body scan showed concentration of isotope in the residual thyroid tissue only. Serum stimulated thyroglobulin level was found high after 6 months [Table 2]. I-131 whole-body scan showed a metastatic lymph node toward level II region on right side. US-guided aspiration cytology confirmed metastasis. Patient opted radioiodine ablation and so second dose of 4329 MBq of I-131 was administered. Serum stimulated thyroglobulin level was still found high after 1 year [Table 2] and FDG

Table 2: Thyroglobulin values on follow-up visits

Date	Thyroglobulin	Antibodies	TSH
6th month	83.68 ng/ml	45.28 IU/ml (<4.11)	>100
1 year	88.61 ng/ml	18.38 IU/ml (<4.11)	99.7

PET scan showed active metastatic nodes. Patient was offered operation but preferred to remain under observation now.

Coexisting thyroid cancers are not rare in Graves' disease. A multicenter study noted that 3.8% of Graves' disease contained focus of cancer, and 15% of cold nodules in Graves' disease were malignant.[2] As high as 25% of patients with palpable nodules in Grave's disease contained papillary cancers.[3] Thyroid cancers generally appear as cold nodules in hyperfunctioning thyroid gland. Differentiated cancer cells have decreased expression of Na/I symporter and so compete less efficiently with normal follicular cells. Thyroid cancer cell mass, expressing exaggerated capacity to synthesise thyroxin, is rarely encountered. Autonomously functioning thyroid nodules are common in iodine-deficient regions. Hot nodules are generally considered benign and so routine cytology studies are not mandatory (American Thyroid Association Guidelines, 2009).[4] Somatic point mutations activating TSH receptor were first described by Parma and colleagues.[5] In different studies, the prevalence of somatic mutations of TSHR and members of G protein family has been reported to vary from 8% to 82%, respectively.[6] These mutations are not known to initiate malignant transformations. Genetic changes that cause constitutive activation of the RAS/RAF/MEK/ERK/MAP pathway have been suggested as a key mechanism during tumor initiation and progression in thyroid follicular cells. Genetic background of toxic thyroid cancer is uncertain. Niepomniszcze *et al.* recently had noted an activating point mutation of TSHR along with mutation of *Ki-RAS* (G12C) genes in a toxic hyperfunctioning follicular carcinoma of thyroid.[7]

Thyroid cancer in association with toxicity was not considered to have separate prognosis. Tzu-Chieh Chao noted patients with thyroid cancer with higher serum concentrations of T_3 or T_4 before antithyroid treatment have an aggressive tumor course when compared with those with lower concentrations.[8] Als *et al.* noted relative poor prognosis of 19 toxic thyroid cancers compared with differentiated carcinoma in general. But he also feels that higher dose I-131 ablation likely improves the outcome.[1]

Our patient, who did not show residual disease following first sitting of radioremnant ablation, developed a lymph node metastasis after 6 months indicating aggressive nature of the disease.

C. Gopalakrishnan Nair, Pradeep Jacob, Misha Babu, Riju Menon

Department of Surgery, Surgical Endocrinology Division, Amrita School of Medicine, Kochi, Kerala, India

Corresponding author: Dr. C. Gopalakrishnan Nair, Department of Surgery, Surgical Endocrinology Division, Amrita School of Medicine, Kochi, Kerala, India.
E-mail: gopalakrishnannair@aims.amrita.edu.

References

1. Als C, Gedeon P, Rösler H, Minder C, Netzer P, Laissue JA. Survival analysis of 19 patients with toxic thyroid carcinoma. J Clin Endocrinol Metab 2002;87:4122-7.
2. Kraimps JL, Bouin-Pineau MH, Mathonnet M, De Calan L, Ronceray J, Visset J, *et al.* Multicenter study of thyroid nodules in patients with Graves's disease. Br J Surg 2000;87:1111-3.
3. Stocker DJ, Foster SS, Solomon BL, Shriver CD, Burch HB. Thyroid cancer yield in patients with Grave's disease selected for surgery on the basis of cold scintiscan defects. Thyroid 2002;12:305-11.
4. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, *et al.* Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. The American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid 2009;19:1167-214.
5. Parma J, Duprez L, Van Sande J, Cochaux P, Gervy C, Mockel J, *et al.* Somatic mutations in the thyrotrophic receptor gene cause hyper functioning thyroid adenomas. Nature 1993;365:649-51.
6. Krohn K, Führer D, Bayer Y, Eszlinger M, Brauer V, Neumann S, *et al.* Molecular pathogenesis of euthyroid and toxic multinodular goitre. Endocr Rev 2005;26:504-24.
7. Niepomniszcze H, Suárez H, Pitoia F, Pignatta A, Danilowicz K, Manavela M, *et al.* Follicular carcinoma presenting as autonomous functioning thyroid nodule and containing an activating mutation of the TSH receptor (T620I) and a mutation of the Ki-RAS (G12C) Genes. Thyroid 2006;16:497-503.
8. Chao TC, Lin JD, Jeng LB, Chen MF. Thyroid cancer with concurrent hyperthyroidism. Arch Surg 1999;134:130-4.

Access this article online	
Quick Response Code:	Website: www.ijem.in
	DOI: 10.4103/2230-8210.98047