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## BENIGN AND MALIGNANT NEOPLASMS IN TOXIC GOITRES

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### ABSTRACT

We found two thyrotoxic patients with cold nodules in their goitres as confirmed by hormone levels and radionuclide scans. We like to report the cases considering their rarity.

### INTRODUCTION

Graves' disease is an organ-specific autoimmune disorder characterized by the presence of stimulating auto-antibodies to the TSH receptor (TSAb) that cause hyperthyroidism.<sup>1</sup> Many authors reported that thyroid nodules and thyroid cancers are more frequently found in Graves' patients than in euthyroid controls.<sup>2</sup> Vella et al. found that surgical specimens of thyroid carcinomas express both interleukin-4R $\alpha$  and IL-4 in the majority of cases. Thyroid glands affected by Graves' disease also express IL-4. They studied a panel of eight thyroid cancer cell lines from different histotypes and found that thyroid cancer cells express high levels of IL-4R $\alpha$  although they do not express IL-4<sup>3</sup> and suggest that thyroid cancer cells receive significant protection from apoptosis by IL-4 produced in the thyroid gland by activated T lymphocytes when concomitant Graves' disease is present.

### CASE 1:

A man of 66 years with long-standing nontoxic multinodular goitre presented with a bony swelling on right shoulder and mild T<sub>3</sub> toxicosis in November/1999 (Table 1). Biopsy revealed follicular

carcinoma of thyroid metastasized to skeletal system. Bone scan (99m Tc MDP) on 25.11.99 at Institute of Nuclear Medicine (Dhaka) revealed multiple bony metastases to left 9<sup>th</sup> and 10<sup>th</sup> ribs and right scapula. He had near-total thyroidectomy on 18.12.99 and 3000 T.D. centi-Gray external beam radiotherapy in Dec. 1999 and July 2003. Due to scarcity of radioisotope in the country for many months, we gave him only 8 mCi of I-131 which was taken up avidly in the thyroid remnant and each of the bony metastases mentioned above. He experienced mild degree of sialadenitis after radioiodine therapy, however, it was self-limited. He was clinically euthyroid on 20.03.2000, and 23.04.2000, when he received 6 mCi of I-131. He was euthyroid on 03.07.2000, but he had iodophile bony metastases in right shoulder and received 75 mCi of I-131 on 8 January, 2001 (Table 2). He developed paraplegia, right sided pleural effusion and multiple bony metastases in August, 2003, received radiotherapy (Co-66) on 06-10 September, 2003, but had a bilious vomiting after eating pilau (fatty rice), developed anuria and got unconscious on 14 September and died on 15 September, 2003,

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**TABLE 1: Hormone levels of case 1**

Date	T3 NR 0.8-3.16 n mol/L	T4 NR 64.5-175 n mol/L	TSH NR 0.3-6 mIU/L
27 Nov. 99	3.9	85	0.5
11 Jan. 2000	2.9	54	3
18 Feb. 2000	--	--	1.97
20 Mar. 2000	4.14	104	3.3
2 July 2000	2.7	168	2.5
10 Dec. 2000	2.7	69	4.75
15 Apr. 2001	2.15	77	7.75

NR = Normal Range

**TABLE 2: Radioiodine therapy of case 1**

Date	Dose of I-131 (mCi)
3 Dec. 1999	1 milli Curie
9 Jan. 2000	5 milli Curies
11 Jan. 2000	2 milli Curies
23 Apr. 2000	6 milli Curies
21 Dec. 2000	4 milli Curies
8 Jan. 2001	75 milli Curies

**CASE 2:**

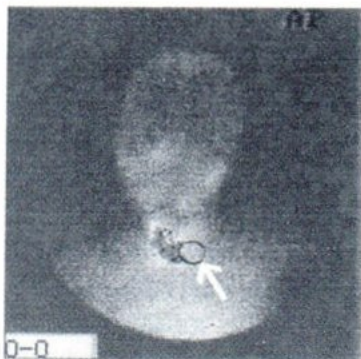
A lady of age 25 years came with the complaints of neck swelling for 1 month, insomnia and general weakness. Her thyroid hormones ( $T_3$ ,  $T_4$ ) were increased and thyrotropin (TSH) was diminished

(Table 3). Her thyroid scan showed rapid flow of radiotechnetium ( $^{99m}\text{Tc O}_4$ ), but the nodule in left lobe was cold (Fig. 1). Unfortunately the patient was lost to followup.

**TABLE 3: Hormone Levels of Case 2**

	Normal ranges
$T_3$ = 3.75 nmol/L	(0.8-3.16 nmol/L)
$T_4$ = 219 nmol/L	(64.5-152 nmol/L)
TSH = 0.25 mIU/L	(0.4-5 mIU/L)





**Fig.1** Cold nodule in left lobe of toxic goitre.

## DISCUSSION

Although the majority of Graves'-associated carcinomas are well-differentiated and belong to the papillary histotype that is usually scarcely angioinvasive, these tumors may behave aggressively and show a higher rate, of distant metastases and persisting/relapsing disease than similar tumors occurring in euthyroid patients.<sup>4,5</sup> We found a patient of follicular thyroid cancer with mild hyperthyroidism in 1999.<sup>6</sup> Edmonds and Tellez reported 9 thyroid cancer in 720 patients with hyperthyroidism.<sup>7</sup> Belfiore and colleagues examined the clinical and pathological characteristics of 22 differentiated thyroid carcinomas concomitant with hyperthyroidism; 13 were associated with Graves' disease, and 9 with autonomous thyroid nodules in a consecutive series of 359 hyperthyroid patients (132 with Graves' disease and 227 with autonomous thyroid nodules) who underwent surgery during a 6-yr. period. Serum TSH levels were suppressed in all hyperthyroid patients with thyroid cancer.<sup>4</sup> Much controversy surrounds the incidence of thyroid cancer in association with Graves' disease. It was thought that patients with hyperthyroidism have a lower incidence of thyroid cancer than euthyroid patients.<sup>8-10</sup> Subsequent reports challenging this view have shown a rising incidence of this association.<sup>11,12,13</sup> Earlier reports estimated the incidence of thyroid carcinoma in autopsy series of clinically normal thyroid to range between 0.1 % to 0.2 %, <sup>14,15</sup> while

others have reported an incidence of occult papillary carcinoma in autopsy specimens in Japan and Hawaii ranging from 13 % to 24 %.<sup>16,17</sup> In 1951, Behrs et al.<sup>18</sup> reported 14 cases of thyroid carcinoma in 3022 cases of Graves' disease, an incidence of 0.5 %. In 1954, Sokal<sup>19</sup> reviewed 10,839 patients with Graves' disease and found seven cases (0.06 %) of thyroid carcinoma. Doby's et al.<sup>8</sup> conducted a multicenter prospective study involving 10,013 patients with Graves' disease treated surgically and found a cancer incidence of 0.4 %. Later on, Behar et al.<sup>11</sup> reported an incidence of 5.2 % and Farbota et al.<sup>12</sup> 5.1 % of thyroid cancer in their series of patients treated surgically for Graves' disease. More recently, Reiger et al.<sup>20</sup> reported 0.76 % and Fong et al.<sup>21</sup> 1.5 % incidence rates of thyroid carcinoma in their series of Graves' patients treated surgically. This wide variation of incidence rates may in part be due to racial and geographical variations or possibly due to improved techniques in pathologic examination in some studies.

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