The association between Graves' disease and thyroid cancer: coincidence or causality? Case report

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INTRODUCTION

Graves` disease (GD) has been related to a higher incidence of thyroid cancer. Thyroid nodules found in GD seem to have a higher risk for malignancy. The prognosis of thyroid cancer may be aggravated by the association with GD. We present a rare case of simultaneously diagnosed GD and thyroid cancer.

CASE REPORT

N.I., 56 year old woman, 2 months follow-up after the initial diagnosis of "toxic nodular goitre"

Medical history:

- 2007: Multinodular goitre;
- 2014 (2 months before the patient's visit to our endocrinology department):
  - Overt hyperthyroidism;
  - Carbimazole 40 mg/d and Propranolol 80 mg/d;
- Average smoker.

On current admission complains of:

- marked weight loss (11 kg in 2 months),
- palpitations,
- fatigability,
- recent swelling of the neck.

Clinical examination:

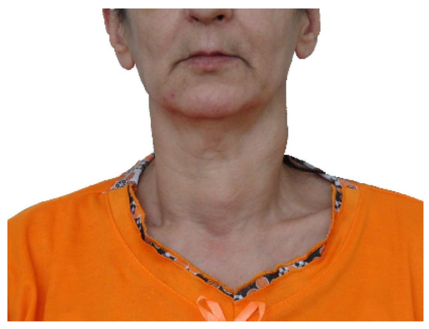

Fig. 1:Painless large goitre

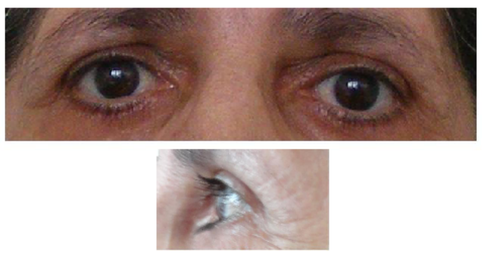

Fig. 2: Mild exophthalmia

Fig. 3: Massive enlargement of left cervical lymph node

Laboratory investigations:

Table 1: Laboratory investigations in our department

Blood test	Value	Normal range
TSH	**0.013 uUI/ml**	**0.4-4**
FT4	0.957 ng/dl	0.89-1.76
TSAb	**2.04 UI/l**	**< 1**
Calcitonin	<2 pg/ml	0-11.5
CEA	0.557 ng/ml	Smoker: 0-4.9
ESR	**38 mm /hr**	**2-10**

Graves' disease

Subclinical hyperthyroidism (under Carbimazole 40 mg/d)

Thyroid ultrasound:

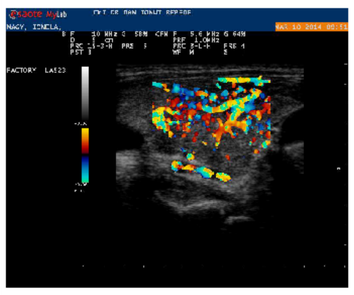

Fig. 4: Right thyroid lobe

Right lobe:
- ill-delimitated, hypoechoic mass (volume= 5ml);
- background: hypervascular goitre;

Left lobe - large conglomerate mass:
- occupies the entire lobe (volume= 18 ml);
- microcalcifications;
- minimal internal vascularization.

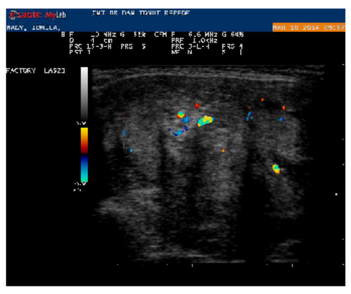

Fig. 5: Left thyroid lobe

Fine needle aspiration-biopsy from left lobe mass:

Cytology highly suspicious of malignancy (Bethesda V).

Thyroid surgery:

Intraoperative: malignant mass within left thyroid lobe, with invasion of the infrahyoid muscles, trachea and larynx.

Total thyroidectomy was performed: "shave excision" (residual microscopic remnant tissue at the level of the larynx).

Histopathology report:

Invasive papillary thyroid carcinoma follicular variant pT3N0G2

Background: typical findings of Graves' disease

Post-operative management: Graves' disease and thyroid cancer Radioiodine (I-131) therapy

Table 2: Laboratory investigations 3 weeks after surgery (June 2014)

Blood test	Value	Normal range
TSH	**46.92 uUI/ml**	0.27-4.2
Thyroglobulin antibodies (TGAB)	**1059 UI/ml**	<115
Thyroglobulin (Tg)	**244.5 ng/ml**	Athyroid patients: <0.04

Table 3: Laboratory investigations in October 2014

Value	Normal range
64.27 (L-T4 withdrawal for 2 weeks)	0.27-4.2
>4000 UI/ml	<115
9.82 ng/ml	Athyroid patients: <0.04

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Tg levels diminished to 1.4 ng/ml (normal range: <0.04 in athyroid patients) under unsuppressed TSH but they **cannot be interpreted due to very high titres of TGAB** (> 4000 UI/ml, normal range: <115).

I-131 administration: 70 mCi

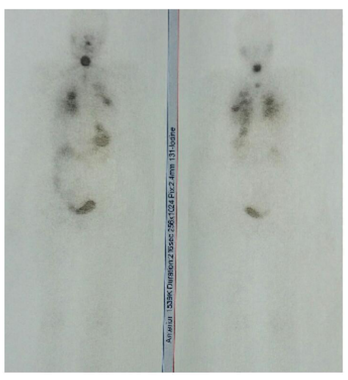

Fig. 6: Post-therapy whole-body radioiodine scintigraphy (WBS): remnant thyroid tissue and multiple iodine-avid lung metastases.

126.5 mCI

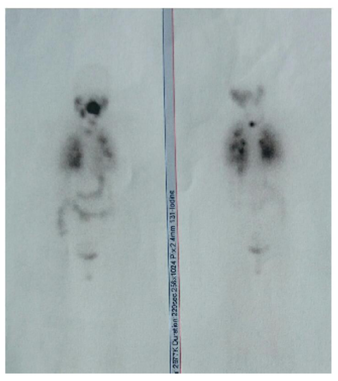

Fig. 7: Post-therapy WBS: Discrete radiotracer fixation at cervical level but otherwise diminished (positive effect) Persistent multiple lung metastasis.

136 mCI

Post-therapy WBS is stationary.

CONCLUSIONS

1. In this rare case of simultaneously diagnosed GD and thyroid carcinoma, the tumor had a rather invasive and aggressive phenotype, in contrast to histopathology: rapid growth with lung metastases at the moment of diagnosis.
2. The evolution of this patient is in accordance with studies proposing GD as a negative prognostic factor in thyroid cancer.
3. This may be explained by TSAb stimulation of thyroid cells, which could be responsible for the onset of an oncogenic mutation. Also, immunological disturbance associated to cancer development may lead to TSAb production. TSAb enhance cell proliferation in already established thyroid carcinoma, promoting a rather aggressive evolution.
4. We suggest managing patients with thyroid cancer and GD according to high-risk protocols.
5. We recommend a closer ultrasound follow-up for nodules in GD and the performance of FNAB when nodules are found.

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Clinical Cases - thyroid/others

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