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Case Series
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Differentiated Thyroid Carcinoma Associated with Graves' Disease: A Series of Six Cases and Review of the Literature

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Abstract

Introduction: Graves' disease is an autoimmune disorder characterized by hyperthyroidism related to the presence of thyroid-stimulating hormone receptor antibodies. Long considered protective against thyroid cancer, it is now recognized as potentially associated with differentiated thyroid carcinomas, mainly papillary carcinoma.

Objective: To describe the clinical, histological, therapeutic, and outcome characteristics of thyroid carcinomas occurring in patients with Graves' disease.

Patients and Methods: A retrospective descriptive study including six patients followed for Graves' disease who underwent total thyroidectomy, in whom histopathological examination revealed differentiated thyroid carcinoma.

Results: The mean age of the patients was 38.2 years, with a male predominance (5 men, 1 woman). Cervical ultrasound showed multinodular goiter in four patients, a suspicious nodule classified as EU-TIRADS V in one patient, and a simple goiter in one patient.

Histological examination revealed five papillary carcinomas (83.3%) and one follicular carcinoma (16.7%). TNM staging showed predominantly localized forms. All patients underwent total thyroidectomy, associated with central lymph node dissection in one case. Radioiodine ablation was performed in five patients. Outcome was favorable in all cases, with no recurrence or distant metastasis.

Conclusion: Graves' disease does not exclude the occurrence of thyroid cancer. The presence of nodules, even in a hyperthyroid context, should raise suspicion of associated malignancy. The prognosis of differentiated thyroid carcinomas associated with Graves' disease is generally favorable, provided appropriate management.

Keywords: Graves' Disease; Papillary Carcinoma; Follicular Carcinoma; Hyperthyroidism; Thyroid Cancer

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Introduction

Graves' disease is the most common cause of autoimmune hyperthyroidism. It is characterized by the production of thyroid-stimulating hormone receptor antibodies (TRAb) responsible for diffuse stimulation of the thyroid gland [1].

For several decades, hyperthyroidism was considered a protective factor against thyroid cancer due to TSH suppression. However, more recent data have challenged this concept, demonstrating a non-negligible association between Graves' disease and differentiated thyroid carcinomas [2, 3].

The incidence of thyroid cancer in patients with Graves' disease is estimated to range between 2% and 10%, with a predominance of papillary carcinoma [4]. This association raises important pathophysiological, diagnostic, and therapeutic questions.

Patients and Methods

Study Design

Retrospective descriptive study.

Population

Six patients followed for Graves' disease and operated on between 2018 and 2024.

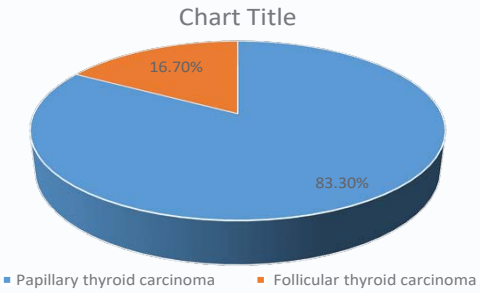

Figure 1: Distribution of histological types of thyroid carcinomas in patients with Graves' disease.

Data Analyzed

- Clinical and biological data
- Cervical imaging (ultrasound ± scintigraphy)
- Histopathological findings
- TNM classification
- Surgical and adjuvant treatment
- Clinical outcome

Results

Clinical and Radiological Data

- Mean age: 38.2 years
- Sex: 5 men, 1 woman
- Multinodular goiter: 4 cases
- Suspicious nodule EU-TIRADS V: 1 case
- Simple goiter: 1 case

Histological Findings

The distribution of histological types showed:

- Papillary carcinoma: 5 cases
- Follicular carcinoma: 1 case

TNM Staging

- pT1a N0: 1 case
- pT1b N1a: 1 case
- pT2 N0: 4 cases

Management and Outcome

All patients underwent total thyroidectomy.

Radioiodine ablation (100 mCi) was performed in five patients.

Suppressive therapy with levothyroxine was initiated in all patients.

No recurrence or metastasis was observed after a satisfactory mean follow-up period.

Discussion

The association between Graves' disease and thyroid carcinoma, long considered exceptional, is now well documented [3–5]. Papillary carcinoma is the most frequently encountered histological type, accounting for more than 80% of cases, as observed in our series [6].

Pathophysiology of the Graves' Disease–Thyroid Cancer Association

Several hypotheses have been proposed to explain this association. Thyroid-stimulating hormone receptor antibodies (TRAb) may play a direct role in thyroid carcinogenesis by stimulating cell proliferation through activation of adenylate cyclase and the MAPK and PI3K pathways [7].

Furthermore, the thyroid hypervascularization observed in Graves' disease may promote tumor growth and local dissemination [8].

Role of Thyroid Nodules

The presence of nodules in a patient with Graves' disease is a key element that should raise suspicion of associated carcinoma [9]. Cold or hypofunctioning nodules on scintigraphy, as well as nodules classified as EU-TIRADS IV or V on ultrasound, are particularly suggestive [10].

Impact of Antithyroid Drug Therapy

Some authors suggest that the progressive normalization of TSH levels under antithyroid drugs may remove the initial inhibitory effect of hyperthyroidism on previously occult tumor foci [11].

Prognosis

Contrary to some older series suggesting a more aggressive behavior, recent data indicate that differentiated thyroid carcinomas associated with Graves' disease have a comparable, or even favorable, prognosis when managed early [12–14].

In our series, the absence of recurrence or extension confirms these findings.

Conclusion

Graves' disease does not protect against thyroid cancer. Any nodular abnormality in a hyperthyroid patient should be thoroughly investigated. Total thyroidectomy allows both control of hyperthyroidism and oncological treatment. The prognosis of differentiated thyroid carcinomas associated with Graves' disease is generally favorable, provided appropriate management.

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