

Nonocult Differentiated Thyroid Cancer Exhibits Aggressive Behavior in Graves' Disease

Pellegriti G, et al.

cinomas. In the present study, 21 nonocult DTCs were compared with 70 DTCs occurring in matched euthyroid patients. All patients with DTCs included in this study underwent total or near-total thyroidectomy plus central compartment lymph-node dissection. Serum TSH-receptor antibodies (TSHR-Abs), antimicrosomal antibodies, and/or antithyroglobulin antibodies were obtained before surgery.

After 14 years of patient follow-up, the disease-specific mortality in patients with Graves' disease is alarming (6 of 21 [28.6%]) as compared with the euthyroid patients (2 of 27 [2.9%]). At the end of the study, the percentage of disease-free patients was 57.1% in the DTC-GD group versus 87.1% in the control group. There was no statistical difference between the groups in age, sex, the papillary histotype, or tumor size. There was a trend toward a higher frequency of high-stage tumors in the DTC-GD group, but the difference did not reach statistical significance. By applying multivariate Cox analysis, the authors found that only two variables, stage and GD, were significantly and independently associated with relapses and with cancer-specific deaths. In patients with stage III–IV cancer, but not in those with stage I–II cancer, relapses were significantly more frequent ($P = 0.0062$) in patients with GD than in euthyroid control patients.

Circulating TSHR-Abs were present in all patients in whom a recurrence developed, and they persisted as long as signs of disease were evident. Only one patient had a negative titer before surgery. The authors discussed the potential role of TSHR-Abs in thyroid cancer initiation and progression, and the mitogenic and anti-apoptotic effects elicited by both TSH and TSHR-Abs in thyroid follicular cells.

According to the authors, only two other studies have used a control group of euthyroid patients (2, 3). Both these studies did not show a worse outcome of DTCs associated with GD. The authors speculated that the difference between the studies could be due to the inclusion of a large proportion of occult cancers incidentally found at the postsurgical pathology examination and the fact that the authors' study was performed in eastern Sicily, a region including a volcanic area and whose population has a high incidence of thyroid cancer.

This study has important implications for clinicians who care of patients with Graves' disease, among them: (a) performing a careful physical examination to detect the presence of nodules in these patients, and (b) determination of TSHR-Abs before surgery and regularly during postsurgical follow-up.

References

1. Spaulding SW. How important are preexisting comorbidities and genetic proclivities in explaining the increased risk of mortality in hyperthyroidism? *Clin Thyroidol* 2013;25:37-9.
2. Pellegriti G, Belfiore A, Giuffrida D, Lupo L, Vigneri R. Outcome of differentiated thyroid cancer in Graves' patients. *J Clin Endocrinol Metab* 1998;83:2805-9.
3. Yano Y, Shibuya H, Kitagawa W, et al. Recent outcome of Graves' disease patients with papillary thyroid cancer. *Eur J Endocrinol* 2007;157:325-9.
4. Hales IB, McElduff A, Crummer P, et al. Does Graves' disease or thyrotoxicosis affect the prognosis of thyroid cancer. *J Clin Endocrinol Metab*. 1992;75:886-9.