

Differentiated Thyroid Cancer: New Strategy of Treatment

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Abstract

Differentiated thyroid cancer is the most frequent endocrine tumor, more frequent in young females and increasing in all countries. The prognosis is very good in relationship with age and gender and the recurrences are very rare. The treatment expected is the surgery (partial or total thyroidectomy). After surgery the histological examination permit to have a new strategy in relationship to the new TNM staging to decide if radiodine therapy is necessary or not. In the majority of cases after surgery the treatment ends. However some authors prefer to use radioiodine therapy after total thyroidectomy using low activities after adjuvant therapy with recombinant human TSH to reduce the recurrences and to better follow the patient using Tg in the blood as a marker.

Keywords: *Differentiated Thyroid Cancer; Radiodine Therapy; TNM Thyroid Staging*

Introduction

Differentiated thyroid cancer (DTC), although rare, is the most frequent endocrine tumor diagnosed especially in females and young adults [1]. In 2014, approximately 63,000 new cases were diagnosed in the US [2], about twice as high as in 2009, probably in relation to greater use of diagnostic tools such as neck ultrasound. The prognosis is generally very good with a survival of about 98% [3] in relationship with histology, age and gender and the recurrence's percentage is very low [4]. The DTC includes both the papillary form (PTC) and the follicular form (FTC). Papillary carcinoma accounts for about 90% of DTCs with histological variants that characterize the degree of risk (classical, follicular, tall cell, solid, trabecular, etc). Recently encapsulated follicular variant of papillary thyroid cancer (EFVPTC) has been reclassified into noninvasive follicular thyroid neoplasm [5].

Treatment

Until a few years ago the treatment of DTC was classically the total or subtotal thyroidectomy followed by the radioiodine therapy, regardless of the histological shape and the aim was to ablate the post-surgical residual tissues in order to follow the patient with the measurement of thyroglobulin in the blood (Tg) [6].

Recently the American Thyroid Association published guidelines [7] and stratified patients with DTC in: a) high-risk (with extrathyroid extension, incomplete tumor resection, distant metastases or metastatic lymph nodes > 3 cm), b) intermediate-risk (aggressive histology, lower extrathyroidal extension, vascular invasion or metastatic lymph nodes but with a diameter of up to 3 cm), c) low risk (intrathyroid tumor and/or micrometastasis in less than 5 lymph nodes with diameters < 0.2 cm.).

Finally, the recent review of the staging of thyroid cancer (8th edition of the AJCC staging system [8] and the recent publication of its review [9] further delimited the choice of post-surgical treatment.

Total thyroidectomy is recommended for widely invasive follicular DTC or papillary aggressive variants. Lymph node dissection is recommended when lymph node metastases are detected before or during surgery. For papillary thyroid cancer > 1 cm and/or for all

metastasized or microscopically invasive PTC, total thyroidectomy is recommended [7,10]. Lobectomy can be performed in patients with intrathyroidal CDT and without evidence of lymph node metastasis both before and during surgery and when histology shows non-aggressive forms.

After surgery, histology and staging are essential for deciding the next therapy.

The new TNM clinical staging (AJCC staging 7th and 8th edition) [8,9] indicate:

- pTx primary tumor cannot be assessed;
- pT0 no evidence of thyroid tumor;
- pT1 (tumor 2 cm or less) limited to thyroid, 1a tumor 1 cm or less, 1b tumor more than 2 cm limited to thyroid;
- pT2 tumor than 2 cm but not more 4 cm limited to the thyroid;
- pT3 tumor more than 4 cm in greatest dimensions, limited to the thyroid or with gross extrathyroidal extension invading only strap muscles (sternohyoid or omohyoid muscles); T3a tumor more than 4 cm in greatest dimension, limited to the thyroid gland, T3b tumor of any size with gross extrathyroidal extension invading strap muscles (sternohyoid, sternothyroid, or omohyoid muscles);
- pT4 tumor extends beyond the thyroid capsule and invading any of the following: subcutaneous soft tissue, larynx, trachea, esophagus, recurrent laryngeal nerve.

In consequence of that the use of adjuvant radiiodine therapy was changed and limited only when aggressive variants or if lymph nodes are present, independently to the pT, or in case of pT4 or if distant metastases are documented. In the other cases the ATA and BTA guidelines [7,11] suggest to don't use radioactive iodine therapy as adjuvant therapy but only recommended surveillance.

Others authors as Schlumberger [12] and Schmidbauer [14], Hilo Study (Great Britain) and the ESTIMABL study (France) [13] continue to suggest to use radioiodine therapy after rhTSH stimulation using low activities (1110 MBq) in patient with low-risk carcinoma.

Conclusions

Differentiated thyroid cancer represents a rare tumor but over the years seems to be increasing in many countries. The classic therapeutic approach was total or subtotal thyroidectomy and then radioactive iodine therapy. The latest ATA guidelines suggest performing lobectomy in microcarcinomas or in case without evidence of lymph nodes metastases. However using this technique we lose the possibility to follow a patient for Tg level measurement. In the other cases total thyroidectomy and lymph nodes dissection, if local metastases are documented, was preferred. After surgery, the histological examination becomes fundamental for the subsequent therapeutic choice. In the majority of cases with total thyroidectomy, the therapeutic procedure ends. Only for patients with aggressive variants of DTC (tall cells, columnar cell, and hobnail variants) independently to pT, or in cases with locoregional lymph node metastases or in pT4 or if distant metastases are documented, radioiodine therapy was recommended. On the contrary many authors publish some papers in which they prefer to continue to use adjuvant radioiodine therapy with low activity after rhTSH, in the majority of patients (a part a microcarcinoma or pT1 without evidence of metastatic involvement) independently to the age and gender both to reduce the incidence of recurrence both to following the DTC trend with Tg levels.

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