

Papillary thyroid microcarcinoma in super obese patient

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SUMMARY: Papillary thyroid microcarcinoma in super obese patient.

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Papillary thyroid microcarcinoma (PTMC) typically has an indolent behavior with a good prognosis but it is not always completely harmless. Surgical treatment varies from thyroid lobectomy to total thyroidectomy eventually associated with lymph node dissection and radioiodotherapy. The ability to identify patients with aggressive PTMCs from the majority of low risk patients is critical to planning

proper clinical management. Several studies don't report any statistically significant differences about recurrence and mortality among patients undergone lobectomy and patients undergone total thyroidectomy. Recently, higher body mass index (BMI) has been associated with aggressive pathologic features of papillary thyroid carcinoma. For differentiated thyroid cancers, an elevated BMI has been linked to a higher incidence of thyroid cancer in some cohorts. The risk factors for a more aggressiveness of PTMC don't yet clearly defined such as their biological features enable to condition the surgical treatment. In order to elucidate the precise mechanism contributing to the relationship between obesity and thyroid cancer aggressiveness, future studies must be performed.

KEY WORDS: Body mass index (BMI) - Obesity - Thyroid.

Introduction

Papillary thyroid microcarcinoma (PTMC) typically has an indolent behavior with a good prognosis but it is not always completely harmless. In fact, it is possible to observe patients with PTMC and lymph node metastases or remote metastases that have an unfavorable course. Therefore, PTMCs include at least two biologically distinct subpopulations such as indolent tumors with minimal or not potential progression, and tumors with propensity for aggressive behaviors and dissemination, so there is still no consensus on the appropriate therapy. Surgical treatment varies from thyroid lobectomy to total thyroidectomy eventually associated with lymph node dissection and radioiodotherapy. The ability to identify patients with aggressive PTMCs from the majority of low risk patients is critical to planning

proper clinical management. It does not seem possible to identify common PTMCs from those with aggressive behavior at this time. So it is not surprising the debate found in literature to come out with a common, shared strategy in the treatment of PTMC. The incidence of thyroid cancer between 1975 and 2009 in the US increased by 400% with 87% of cases with a tumor diameter less than 2 cm. and in 2013 the 39% of 60220 cases were less than a 1 cm (1). In several epidemiological studies, however, it has been noted that the exponential increase of PTMC frequency was mainly determined by an "overdiagnosis" and the less aggressive variety, the papillary tumor. Autopsy studies have shown that PTMCs between 3 and 9.9 mm were identified between 0.5% and 5.2% of examinations (2). Takebe (3) found papillary tumors in the 3.5% of women over 30 years old involved in a mass screening with ultrasound and Fnac, 75% of which were less than 15 mm big.

Matsuzo (4) studied 1088 patients with papillary thyroid cancer undergoing lobectomy with a 25-year follow-up and found 95.2% of disease-free survival.

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The conclusions were that thyroid lobectomy could represent a valid alternative to total thyroidectomy in patients under 45 years with a tumor diameter less than 4 cm and without extracellular diffusion or lymph node metastasis.

Nixon (5) studied 889 patients between 1986 and 2005 (59% total thyroidectomy and 41% lobectomy) with a 99-months follow-up. He found a survival free from disease of 98% without statistically significant differences between the two surgical techniques used. Independent variables were represented by age greater than 45 years and male sex. Recently, higher body mass index (BMI) has been associated with aggressive pathologic features of papillary thyroid carcinoma (6, 7) For differentiated thyroid cancers, an elevated BMI has been linked to a higher incidence of thyroid cancer in some cohorts (8, 9). Choi (10) found that higher BMI was associated with extrathyroidal extension in PTMC patients. The study suggests that the BMI could be considered as a prognostic factor for predicting the presence of extrathyroidal extension and it may help deciding the appropriate surgical extent for PTMC patients.

Case report

39-year-old woman patient presented a clinical-incident (2) 6-mm Tir 4 hypoechoic nodule at the right thyroid lobe with micro calcifications, without Ete and Braf V 600 E and serum Tsh 1,02. The patient with super obesity (BMI 60) and mild obstructive ventilatory deficiency, was subjected to right extracapsular lobectomy. The patient presented a regular post-operative course with discharge in the 3rd p.o. day. The definitive histology confirmed the presence of a 6 mm classical papillary carcinoma contained in the excision. Nine months follow-up shows that TSH levels were not significantly different between the preoperative data without hormone replacement treatment and ultrasound control did not show any alterations to the residual thyroid lobe or lymph node metastasis. Despite their similar small size and similar follow-up duration, non-incident papillary carcinomas demonstrated significant higher recurrence and mortality than incidental papillary carcinomas underlining the considerable differences in clinical outcome, behavior, and morbidity arising from the two conditions. These differences may reflect differences in their underlying

pathophysiology. Case report shows interest for the association of PTMC and super obesity and the choice of a lobectomy to avoid the need for a hormone replacement treatment with post-operative metabolic problem.

Discussion

Sugitani (2) identifies 3 different PTMC presentation modes: "pathological" PTMCs diagnosed after histological examination after surgery for benign lesions, "clinical incidental" PTMCs detected during instrumental exams (eco, Fnac), "clinical symptomatic" PTMCs which manifest with symptoms such as cord paralysis or lymph node or distance metastasis (occluded PTMC). A fourth type of PTMC that could fall into the first two groups is the microcarcinoma detected at the autopsy.

Mehanna (11) found an average 70-month follow-up rate of 0% relapse in the incidental PTMC and 7.9% among non- incidental, with a mortality of 0% between incidental and 0.1% among non-incident in a meta-analysis of 3523 PTMCs (2669 non-incident and 854 incidental).

By SEER Cancer Database data, Yu (12) has detected that age over 45 years old represents a risk factor for recurrence. Xu (13) instead reports that age under 45 years old is a risk factor for recurrence, such as Roti (14). By an observational study of PTMC Ito (24) reports that patients under 40 years old have more possibilities of tumor growth than patients over 60 years old.

In a study about 2070 patients with PTMC Noguchi (15) reports that in PTMC with diameter greater than 6 mm the rate of recurrence at 35 years is about 14% compared to 3% of tumours smaller than 6 mm.

Lai (16) highlights that PTMC smaller than 5 mm have less aggressive features, while Wu (27) suggests total thyroidectomy of PTMC bigger than 5 mm.

Several studies have identified in the extracapsular spread (ETE) a risk factor for local recurrence. Chen (17) links Ete, male sex, age under 45 years old, multifocality to the possible progression of the disease. Lin (18) reports a correlation between Ete and lymph node metastases. In a metaanalysis of 19 studies with 8345 PTMC (16 study with central compartment's prophylactic lymphectomy) reports a correlation between Ete, male sex, age under 45

years old, smaller than 6 mm diameter, multifocality as risk factors for central compartment's lymph node metastases. The US criterion for predicting extrathyroidal extension was contact with the adjacent thyroid capsule along more than 25 % of the perimeter of the tumor. Preoperative staging US is known to be helpful in the prediction of extrathyroidal extension and presence of lateral lymph node metastasis, thus it can help determine the appropriate surgical extent of thyroid cancer.

BrafV 600 E's frequency/attendance in PTMC is attested between 30% (Xing) (19) (Lee) (20) and 62,5% in Korea (Kim) (21). In a metaanalysis about 63 studies with 20764 enrolled patients Chunping (22) has reported that Braf 600V E is related to Ete, lymph node metastases and recurrence but not to distance metastases. Lu (23) confirmed that Braf 600V E is related to Ete, lymph node metastases, thyroiditis and worse prognosis.

In "Controversy session at the 58th annual cancer symposium of the society of surgical oncology" in Atlanta (U.S.) (24) in March 2005 about the most appropriate treatment of the differentiated thyroid cancer, Udelsman supported total thyroidectomy for the following reasons: substantial frequency of bilateral tumours even in the PTMC (30-85%), reduction of recurrences, reduction of mortality in patients at high risk, reduction of re-operations with increase of morbidity however low in the TT, possibility of immediate radioiodine therapy if necessary, easier follow up through dose of thyroglobulin. Shaha, in support of lobectomy for these tumours with a good prognosis, reported similar outcome about recurrence and mortality in comparison as TT, with lower complication's percentage, without necessity of replacement post-operative therapy, yet in absence of precise data about these tumours' biology. Reporting a Cady's (25) citation: "an operation that is not worth doing is not worth", it's clear that discussion is open and, above all, it needs a multidisciplinary approach to avoid overtreatment and legal conflicts. In 12469 PTMC Hay (26) didn't report substantial differences about survival between TT and LT, such as Lin (27) and Lee (20) didn't too.

Conclusions

The risk factors for a more aggressiveness of PTMC don't yet clearly defined such as their biolog-

ical features enable to condition the surgical treatment. Several studies don't report any statistically significant differences about recurrence and mortality among patients undergone to lobectomy and patients undergone to total thyroidectomy (28-30). Moreover, prophylactic lymphectomy of the central compartment is not able to reduce recurrence's percentage (31, 32). It would have been better to select patients with PTMCs which show more aggressive features and to program more demolitive operations in patients with higher risk. A higher BMI is related to extrathyroidal extension, higher serum Tsh and advanced stage. It is unclear whether it will directly affect the long-term outcome of thyroid cancer, such as recurrences and survival. In order to elucidate the precise mechanism contributing to the relationship between obesity and thyroid cancer aggressiveness, future studies must be performed.

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