

# Microscopic papillary thyroid cancer as an incidental finding in patients treated surgically for presumably benign thyroid disease

Sakorafas GH, Stafyla V, Kolettis T, Tolumis G\*, Kassaras G, Peros G

Departments of Surgery and \*Endocrinology, 251 Hellenic Air Force Hospital, Athens, Greece

Correspondence:  
George H. Sakorafas,  
E-mail:  
georgesakorafas@yahoo.com

## ABSTRACT

**Background:** Papillary thyroid microcarcinoma (PTMC) is a relatively common entity in the general population. **Aim:** To present our experience with papillary thyroid microcarcinoma of the thyroid as an incidental finding in patients treated surgically for presumably benign thyroid disease. **Settings and Design:** Histology reports of patients treated surgically with a preoperative diagnosis of benign thyroid disease were reviewed to identify patients with PTMC. Patients with a preoperative diagnosis of thyroid cancer were excluded from this study. **Materials and Methods:** The files of 380 patients who underwent surgery for presumably benign thyroid disease in our hospital from 1990 to 2002 were reviewed. Data regarding patient's demographics, pathology findings, management and outcomes, were retrieved. **Statistical Analysis Used:** The findings are expressed as absolute numbers and as percentages (with reference to the total number of patients of this study). **Results:** Twenty-seven patients with PTMC diagnosed incidentally following thyroid surgery for presumably benign thyroid disease (27/380 or 7.1%) (multinodular goiter = 20 patients, follicular adenoma = 6 patients, diffuse hyperplasia of the thyroid = 1 patient) are presented. Mean diameter of PTMC was 4.4 mm. In 11 patients (40.7%) the tumor was multifocal and in about half of them tumor foci were found in both thyroid lobes. In two patients the tumor infiltrated the thyroid capsule. Total/near-total thyroidectomy was performed in all these patients (in three as completion thyroidectomy). All patients received suppression therapy and 20 of them underwent adjuvant radioiodine therapy. Follow-up (mean 4.56 years, range 1-12 years) was completed in 25 patients; all these patients were alive and disease-free. **Conclusions:** PTMC is not an uncommon incidental finding after surgery for presumably benign thyroid disease (7.1% in our series). The possibility of an underlying PTMC should be taken into account in the management of patients with nodular thyroid disease; total/near total thyroidectomy should be considered, at least in selected patients with presumably benign nodular thyroid disease.

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Papillary thyroid microcarcinoma (PTMC) is defined as papillary thyroid cancer measuring less than 10 mm in its greatest diameter.<sup>[1]</sup> It represents the most common form of thyroid cancer and frequently remains clinically occult. A common clinical scenario is the incidental diagnosis of PTMC on histology of the resected thyroid following surgery for a presumably benign thyroid disease. Some controversy still persists regarding the optimal management of these patients. We present our experience in the management of patients with

PTMC incidentally diagnosed following surgery for a presumably benign thyroid disease.

## Materials and Methods

Histology reports of all 380 patients who underwent thyroidectomy during a 12-year period (Feb 1990-Feb 2002) for a presumably benign disease were reviewed. All these patients were referred for surgery by the managing endocrinologist. The evaluation of these patients included a complete clinical examination, imaging of the thyroid (routine use of ultrasonography, selective use of thyroid scintigraphy and very exceptional use of computed tomography, mainly to determine the extent of substernal extension of a massively enlarged thyroid gland), and laboratory investigation (TSH, thyroxine and triiodothyronine levels, antithyroid peroxidase/

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antithyroglobulin antibody levels and selective measurement of serum thyroglobulin and calcitonin levels). To exclude thyroid malignancy, fine-needle aspiration cytology (FNAC)—often under ultrasonography guidance—was deliberately used, especially in patients with solitary thyroid nodules or when risk factors for the presence of underlying malignancy were present. Such risk factors included findings from history and clinical examination (i.e., development of hoarseness, progressive dysphagia or shortness of breath, rapid growth of the thyroid nodule, especially if observed under thyroid hormone suppressive therapy or presence of cervical lymphadenopathy) or suspicious findings on preoperative imaging evaluation. Preoperative diagnosis included multinodular goiter, solitary nodule, Hashimoto's thyroiditis and diffuse hyperplasia of the thyroid. Based on current therapeutic recommendations, we do not perform prophylactic cervical lymph node dissection, even in patients with preoperatively diagnosed thyroid cancer. Patients with cytologically-proven (by using fine-needle aspiration cytology [FNAC]) preoperative diagnosis of thyroid malignancy were excluded from this study. We identified patients with a postoperative, histologically proven diagnosis of PTMC as an incidental finding unexpectedly diagnosed following thyroidectomy in patients with a presumably benign thyroid disease. Histopathological examination of the resected specimen was performed as usual (i.e., with the serial sectioning technique, sections of 1 mm). Patient's demographics, pathology findings, management and outcomes are discussed.

## Results

A series of 27 patients (7.1% of the total number of patients, 19 females and eight males) with incidental PTMC is presented. These patients were treated surgically for presumably benign thyroid disease (multinodular goiter = 20 patients, follicular adenoma = 6 patients, diffuse hyperplasia of the thyroid = 1 patient). Chronic lymphocytic thyroiditis (Hashimoto) was also present in four of the patients with multinodular thyroiditis. Mean age at the time of surgery was 45.2 years (38.37 for males and 48 for females). Based on the results of preoperative evaluation (mainly ultrasonography) and intraoperative findings, cervical lymphadenopathy was not found in any of the 27 patients of this study.

Mean diameter of PTMC was 4.4 mm (range, 1-10 mm). In 11 patients (40.7%) the tumor was multifocal (two tumor foci in seven patients, three tumor foci in three patients and four tumor foci in one patient). Multifocal tumors were located at the same lobe in five patients, while in the other six patients the tumor foci were found in both thyroid lobes. In two patients (7.4%), the thyroid capsule was infiltrated by the tumor, probably as a result of the peripheral location of the PTMC within the thyroid parenchyma.

Total or near-total (leaving no more than 3 g of thyroid tissue) thyroidectomy was the most commonly performed surgical procedure. In 24 patients, total/near-total thyroidectomy was performed at the time of initial surgery. Two patients

underwent lobectomy/isthmusectomy, while in another patient a total ipsilateral lobectomy/isthmusectomy and subtotal contralateral lobectomy was performed. In these three patients who underwent less than total or near-total thyroidectomy, a completion total thyroidectomy was performed at a second time when the final pathology analysis was completed. Mortality was zero and there was no significant morbidity, except transient hypocalcemia in four patients, probably as a result of ischemia of the parathyroid glands. Following surgery, adjuvant radioiodine therapy was given in 20 patients, at a dose of 80-100 mCi, usually four to six weeks following thyroid surgery. Patients were selected for radioiodine therapy based mainly on the presence of multifocal PTMC and infiltration of the thyroid capsule and after an extensive discussion about the prognosis of PTMC and the advantages/disadvantages of radioiodine adjuvant therapy.

In our practice, following thyroid surgery most patients (including those with thyroid cancer) are seen every six months for two years postoperatively and then yearly. Follow-up visits include measurement of the serum thyroglobulin level, a chest X-ray and a repeat <sup>131</sup>I scan after temporary (four to six weeks) deletion of hormonal replacement. Postoperative follow-up was completed in 25 patients by regular examination, which included periodic clinical examination, thyroglobulin (Tg) measurements and neck ultrasonography (when indicated). Mean duration of follow-up is 4.56 years (range, 1-12 years). All these patients were alive and disease-free at the time of the completion of the follow-up.

## Discussion

PTMC is a common type of papillary thyroid cancer. In this study, PTMC was diagnosed in 7.1% of patients with presumably benign thyroid disease. It may be possible that this is an underestimate of the true incidence, because we have not used the serial sectioning technique. In autopsy studies, the incidence of PTMC ranges from 3-36%.<sup>[2,3]</sup> Because of this high incidence, Harach *et al.* from Finland concluded that "...occult papillary thyroid carcinoma are so common in Finland ... that they can be regarded as a normal finding".<sup>[3]</sup> Similarly, in surgical studies, incidental foci of PTMC were found in a large percentage of patients after thyroidectomy for a presumably benign thyroid disease, ranging from 2-24%.<sup>[4,5]</sup> In our study, PTMC was diagnosed in 7.1% (27 of 380) of patients who were treated surgically for presumably benign thyroid disease. Multifocality is common in PTMC and is observed in 20-46% of cases (~ 41% in this study).<sup>[2,5,6]</sup> Interestingly, lymph node metastases (usually micrometastases) can be detected in a significant percentage of patients with PTMC (up to 40%) and, in a small percentage of patients, these metastases may precede the clinical evidence of the primary tumor.<sup>[7]</sup>

The high incidence of PTMC in autopsy studies suggests that most of them have a relatively "benign" biological behavior. These studies showed that a significant percentage of patients (up to 36%) who died of diseases other than thyroid cancer had PTMC that remained asymptomatic throughout their

lives.<sup>[3,8]</sup> The discordance between the prevalence of PTMC and population estimates of death from cancer further support that PTMC is an indolent disease.<sup>[9,10]</sup>

The diagnosis of PTMC is usually based on a combination of clinical examination, laboratory investigations and specialized radiological techniques. However, PTMC is often clinically undetectable because of its small size and usually remains clinically silent, discovered as an incidental finding at autopsy or in specimens of thyroid removed for other reasons. However, with the advent of improved methods of diagnostic evaluation (usually neck ultrasonography and image-guided FNAC), the diagnosis can now often be made preoperatively. Nowadays, tumors between 1 and 2 mm in diameter can be detected with the use of high-resolution transducers.<sup>[11]</sup> It was the recognition of this fact that has led Salvadori *et al.* to question the term “occult”, frequently used in the past to describe PTMC.<sup>[12]</sup> Most authors recommend ultrasound-guided FNAC for thyroid nodules larger than 10 mm.<sup>[13]</sup>

A limitation of the present study is the lack of a control group treated by a less aggressive therapeutic protocol. However, the aim of this study is not to compare different treatments in the management of incidental PTMC in patients with presumably benign thyroid disease, but to emphasize the problem that both the clinician and the patient face in this clinical scenario. The findings of this study could serve as an additional factor in favor of a more radical and aggressive therapeutic management in patients with presumably benign nodular thyroid disease. Despite continuing controversy, in our clinical practice, because of many theoretical advantages, we consider total or near-total (leaving < 3 g of thyroid tissue behind) thyroidectomy as the procedure of choice for the management of nodular thyroid disease, including patients with PTMC; however, we acknowledge that this remains a controversial issue. Others have proposed a more selective therapeutic approach, i.e., a less radical treatment in patients without adverse risk factors, indicating a less aggressive disease. In experienced hands, however, total/near-total thyroidectomy can be performed with a very low and acceptable morbidity. The advantages of this procedure include the elimination of the frequently observed multifocal/bilateral PTMC, thereby reducing recurrence rates, the avoidance of the rare possibility of transformation of the in-thyroid-recurrence from well-differentiated to undifferentiated.<sup>[14,15]</sup> Performing total/near-total thyroidectomy at the time of the initial surgery avoids the risk of reoperation which is associated with an increased morbidity; obviously, the avoidance of a second procedure is preferable for both the patient and the surgeon. Additional advantages of total/near-total thyroidectomy are the possibility of better monitoring of treated patients by scintigraphic scan and thyroglobulin measurements to detect residual or recurrent disease and the increase of the yield of postoperative radioactive iodine therapy.<sup>[2,13]</sup> Interestingly, hormone replacement therapy will be required in most patients (> 50%) following more limited thyroid resections (i.e., lobectomy plus isthmusectomy and/or subtotal thyroidectomy), thereby eliminating the theoretical advantage of less radical thyroid surgery. The management of PTMC incidentally diagnosed following a

limited thyroid resection (i.e., lobectomy/isthmusectomy or subtotal thyroidectomy) for presumably benign thyroid disease should be completion (total or near-total) thyroidectomy.<sup>[2,16]</sup> Others, however, have suggested that completion thyroidectomy is not indicated in selected patients with incidental PTMC, such as patients with well-differentiated tumor and with no enlarged lymph nodes.<sup>[17]</sup> Due to the high prevalence of incidental PTMC we also favor total/near-total thyroidectomy as the procedure of choice during the initial surgery for all nodular thyroid disease (multinodular goiter or dominant, presumably benign nodules).<sup>[18]</sup> This avoids the need for reoperation for patients with incidental PTMC. This seems particularly reasonable because other groups have previously reported a risk for benign contralateral nodule growth requiring reoperation after lobectomy for nodular goiter.<sup>[19,20]</sup> Surely, this is the clinical experience of many endocrine surgeons. Routine use of thyroxine to suppress TSH secretion is recommended in the management of PTMC.<sup>[21]</sup> Central neck or modified neck lymph node dissection is indicated in the presence of cervical lymphadenopathy and is preferred over the “berry picking procedure”.<sup>[22,23]</sup> Adjuvant radioiodine therapy is indicated at least in selected patients with PTMC, based on the presence of adverse prognostic factors, such as tumor multicentricity, positive lymph nodes, capsular or vascular invasion; prognostic scoring systems (such as the AMES) may be used to select patients for radioiodine therapy.

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