Papillary Thyroid Microcarcinomas: Experience at a Single Institute

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Purpose: Papillary thyroid microcarcinomas (PTMCs) have the same histological features as papillary thyroid cancer, but they are 1.0 cm or less in diameter. They can metastasize to the regional lymph nodes and distant sites, but its ability to cause significant morbidity and mortality has been questioned. Because of this reason, the role of papillary thyroid tumor resection remains an issue of controversy. This study is aimed at identifying the statistically significant factors that are associated with recurrence and we also wanted to devise an appropriate surgical treatment plan for PTMC patients.

Methods: The retrospective review (350 cases, 1990.1~2004. 11) was obtained from Seoul National University Hospital (SNUH). The median age at the time of diagnosis was 46.5±11.0 (yrs) (range: 12~75). The mean overall length of follow-up was 37.70±36.03 months (range: 1~169). The PTMCs were treated with total and subtotal thyroidectomy or lobectomy. The invasiveness and lymph node metastasis (LNM) from 350 PTMCs were analyzed according to tumor size, multiplicity, bilaterality of the tumor and the perithyroidal invasion. Fishers exact test and the exact logistic regression test were used for the stratified analysis.

Results: 350 of the 2187 papillary carcinoma were PTMCs. There were 296 females (84.6%) and 54 males (15.4%) in the study. Invasion into the perithyroidal tissue was common (128/336, 38.1%). There were 68 patients with LNM among the 312 total patients (21.7%). The group with either perithyroidal invasion or LNM showed a significantly higher recurrence rate than those group having neither one (4.8% vs. 10.9%, 4.5% vs. 19.1%, respectively). Even for tumor smaller than 1 cm, a larger-sized tumor resulted in a poorer prognosis.

Conclusion: PTMC is an early stage carcinoma with the capability of tissue invasion, lymph node metastasis and multiplicity. Based on this study, total thyroidectomy is recommended for significant portion of the PTMCs. Furthermore, more careful imaging studies (such as neck ultrasonography or neck CT scan) are needed to detect contralateral lesions or neck lymph node metastasis (Korean J Endocrine Surg 2006;6:63-67).

Key Words: Papillary thyroid microcarcinoma, Invasiveness, Lymph node metastasis

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INTRODUCTION

Papillary thyroid microcarcinomas (PTMCs) are detected incidentally with a high prevalence in autopsy studies and histopathological examinations of resected specimens.(1-6) This variant, also known as occult papillary carcinoma, latent papillary carcinoma, small papillary carcinoma, non-encapsulated thyroid tumor, or occult sclerosing carcinoma,(7,8) is an extremely common condition and is often regarded as ‘a normal finding’ on autopsy.(8)

The majority of these are not palpable and are clinically unappearing. In the past, many PTMCs were found on pathology specimens from thyroids removed for benign diseases, such as multinodular goiter, follicular adenoma, and Graves’ disease. These small cancers have also been commonly found on autopsy in patients who died of non-thyroid-related diseases.

With the increasing use of thyroid ultrasound, many nonpalpable thyroid nodules have been detected.(9) The management of these clinically unappearing thyroid tumors (thyroid inciden-
talomas) is controversial. Those that are suspicious usually undergo fine-needle aspiration (FNA) biopsy under ultrasound guidance. If papillary cancer is found on FNA, thyroidectomy is usually performed. We undertook this study in patients with PTMCs who received total/subtotal thyroidectomy or lobectomy. In this study, we analyzed several factors associated with recurrence to establish an appropriate treatment strategy.

**MATERIALS AND METHODS**

Three hundred fifty patients who underwent thyroidectomy and/or neck node dissection for PTMC at SNUH between Jan. 1990 and Nov. 2004 were analyzed retrospectively. The mean overall length of follow-up was 37.7 ± 36.03 months (range 1–169). When indicated, radioactive iodine ablation (RAI) was performed. All patients underwent TSH suppression.

We undertook size-based analysis (≤0.5 vs. >0.5 cm). We also studied several factors possibly associated with recurrence such as age, sex, perithyroidal invasion, LNM, multiplicity bilaterality, and type of operation.

Results are expressed as mean ± standard deviation (S.D.). Statistical analysis was performed using the Fisher’s exact test by univariate analysis, where appropriate.

Multivariate analysis was made by exact logistic regression test. Differences were considered significant when P < 0.05.

**RESULTS**

350 of the 2,187 papillary carcinomas were PTMCs. The mean age at diagnosis was 46.5 years of age (12–75 years old). 296 patients were women (84.6%) and 54 were men (15.4%). Incidentaloma was identified in 6 cases.

Perithyroidal invasion was investigated in 336 patients except patients who had unacceptable pathologic report. Similarly, LNM and bilaterality was analyzed in 312 and 327 patients. Perithyroidal invasion was identified in 128 cases (38.1%). Lymph node metastasis was identified in 68 patients (21.7%). Single lesion vs. multiple lesions was 270 (77.4%) and 79 (22.6%), respectively. Bilaterality was discovered in 46 of 327 cases (14.1%) (Table 1).

There were 227 total thyroidectomies, 54 subtotal thyroidectomies, and 19 lobectomies. 41 patients underwent total thyroidectomy with ipsilateral or bilateral modified radical neck dissection (MRND). Another 9 patients underwent either lobectomy with ipsilateral MRND (5 patients) or ipsilateral lobectomy with contralateral hemilobectomy (4 patients) (Fig. 1). We performed modified neck dissection when LNM was suspicious on preoperative neck sonogram or CT scan. In addition, 18 patients out of 41 MRND cases (43.9%) was pathologically confirmed as cervical LN metastasis.

The overall recurrence rate was 7.4% (26/350). There were two cases of thyroid bed recurrence and recurrence in neck lymph node was observed in 16 cases. Distant metastasis without local recurrence was also found in 8 cases, 5 in the mediastinum, 3 in the lung.

The size distribution of the PTMCs is depicted in Fig. 2. We subdivided PTMCs into two subgroups using 0.5 cm as a

<table>
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<tr>
<th>Table 1. Factors associated with recurrence</th>
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<td>Age</td>
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<td>≤45</td>
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<tr>
<td>≥45</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Multiplicity*</td>
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<td>Bilaterality*</td>
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<td></td>
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<tr>
<td>Operation†</td>
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<td></td>
</tr>
<tr>
<td>Perithyroidal invasion</td>
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<tr>
<td></td>
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<tr>
<td>Tumor</td>
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<td></td>
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<td>Lymph node*</td>
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*Perithyroidal invasion was investigated in 336 patients except those who had unacceptable pathologic report. Statistics of lymph node metastasis, bilaterality, and multiplicity were analyzed in 312, 327, and 349 patients, respectively. †300 operations were investigated. Among the total 350 operations, total thyroidectomy with ipsilateral or bilateral MRND (n=41) and miscellaneous operations, such as lobectomy with ipsilateral MRND (n=5), ipsilateral lobectomy with contralateral hemilobectomy (n=4) were excluded in the analysis.
cutoff. The larger-sized group (>0.5 cm) showed more aggressive clinical behavior than the smaller-sized group (≤0.5 cm). The group larger than 0.5 cm metastasized to the lymph node more readily, invaded perithyroidal tissues more frequently, and recurred more frequently (P=0.0037). But there is no significant difference of multiplicity or bilaterality (Fig. 3).

The younger age group (<45) showed higher recurrence rates than the old age group (≥45), but was not statistically significant. There was no difference in sex-related recurrence rates. Also, multiplicity and bilaterality had no significant effect on recurrence (Table 1).

Invasion into perithyroidal tissue can be characterized by a) gross invasion by intraoperative finding and b) microinvasion by pathologic reports. Because gross invasion can be vague due to surgeon’s subjective judgement, it is limited to the invasion into strap muscles. Perithyroidal invasion significantly elevated recurrence rates (P=0.048, Table 1).

The node-positive and node-negative groups of patients were compared. Recurrence rates without LNM was 4.5%, but with LNM the rates were 19.1% (P-value < 0.0001, Table 1).

Contrary to our initial expectations, the type of operation had no statistical significance on PTMC recurrence. Only 19 lobectomies were performed in SNUH and the recurrence rate was 10.5% (Table 1). It seems there are differences between total and lobectomy group, but the P-value was determined to be 0.318 with the Fisher’s Exact test (Table 1).

We performed multivariate analysis with factors showing a significant effect on recurrence. Lymph node status was the most significant factor associated with PTMC recurrence (Table 2).

**DISCUSSION**

The principal treatment of thyroid papillary microcarcinoma is surgical resection. In many prospective studies, total thyroidectomy versus lobectomy and isthmcotomy are controversial. Hay et al. (10) performed a multivariate analysis of 535 PTMC patients with a mean follow-up of 17.5 years (of whom 27 had recurrence) and individualized two risk factors for locoregional recurrence, namely, initial lymph node metastases and extent of initial thyroid surgery. These authors concluded that a bilateral lobar resection seemed to be the treatment of choice for these patients. Also, studies revealed total or near-total thyroidectomy is associated with reduced recurrence rates.

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**Table 2. Multivariated analysis of influencing factors with recurrence**

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<th>Predictor</th>
<th>Odds ratio</th>
<th>P-value</th>
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<tr>
<td>Lymph node</td>
<td>4.048</td>
<td>0.0033</td>
</tr>
<tr>
<td>Size &gt;0.5 cm</td>
<td>2.849</td>
<td>0.0824</td>
</tr>
<tr>
<td>Microinvasion</td>
<td>1.383</td>
<td>0.6407</td>
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compared with lobectomy and isthmectomy (5% vs. 20%) due to possibility of multifocality.(11,12) Moreover, performing total or near-total thyroidectomy at the time of diagnosis avoids the risk of reoperation.(13) A few retrospective studies have shown that distant metastases causing mortality were occasionally observed in PTMC patients.(14)

Lobectomy with isthmectomy is the less aggressive method of surgical management for PTMC. Proponents of this method emphasize the minimal morbidity associated with this procedure, which is performed for a disease with a relatively benign biological behavior.(15-17) Ito et al.(18) concluded that no specific treatment was necessary for this type of tumor except simple excision. They added that PTMC has few clinical characteristics of carcinoma with regard to preoperative diagnosis, treatment and prognosis.

Overall, there is general agreement that the loco-regional recurrence rate after lobectomy significantly exceeds that seen after total thyroidectomy - 20% and 5%, respectively, at 20 years.(19) In patients with unfavourable prognostic factors, total thyroidectomy improves survival.(19)

We analyzed the results of 350 patients with PTMC to determine factor associated with recurrence and establish the optimal strategy for management in these patients.

The optimal treatment strategy for patients with papillary thyroid cancer involves complete surgical resection of clinically and radiographically evident disease within the neck, the selective use of adjuvant radioiodine therapy, and postoperative thyroid-stimulating hormone suppression.(20-22)

In this study, 68 patients (21.7%) showed metastatic lymphadenopathy. They had significantly higher recurrence rates (Table 1, Table 2). Moreover, the smaller the size of PTMC, the lower the recurrence rate. Kasai and Sakamoto(23) proposed a further subdivision of PTMC; the terms “tiny” referring to 5–10 mm diameter foci, and “minute” for foci of 5 mm diameter or less were suggested because of different incidences of lymph-node metastases (59% vs. 13%) and extrathyroidal extension (10% vs. 3%).

Even our study did not prove that total thyroidectomy decreases recurrence rates, we suggest more aggressive treatment of PTMC due to metastatic capacity and PTMC invasiveness. We suggest a modified surgical strategy based on the results of this study (Fig. 4).

According to our strategy, if preoperative imaging study show a tumor larger than 0.5 cm (tiny PTMC), total thyroidectomy would be the more appropriate treatment. In the cases of smaller than 0.5 cm (minute PTMC), completion thyroidectomy is recommended, if perithyroidal invasion is proved by pathology.

Further long-term and multicenter trial should be followed to evaluate this strategy.

CONCLUSION

PTMC is an early stage carcinoma with the capacity to a) invade surrounding tissue, b) metastasize and c) present with more than one nodule. Total thyroidectomy is recommended in the case of tiny PTMC, presence of LNM and microinvasive based on this study. Furthermore, careful imaging studies such as neck ultrasonography or neck CT scan are needed to detect contralateral thyroid lesions or LNM.

REFERENCES

2) Fink A, Tomlinson G, Freeman JL, Rosen IB, Asa SL. Occult


