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Clinical characteristics of papillary thyroid carcinoma arising from the pyramidal lobe

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Purpose: Papillary thyroid carcinoma (PTC) arising from the pyramidal lobe is rare; therefore, clinicopathologic evaluation is lacking. In addition, the rate of occult malignancy in the pyramidal lobe after thyroid surgery is unclear. This study is to evaluate the clinical characteristics of PTCs that involve the pyramidal lobe.
Methods: The study enrolled 1,107 patients who underwent thyroid surgery for PTC at Seoul National University Hospital from 2006 to 2015. Pyramidal lobe status in pathologic reports was clear in all cases. "Pyramidal lobe-dominant PTC" was defined as single pyramidal lobe cancer or multifocal cancer with larger pyramidal lobe tumor. "Incidental pyramidal lobe PTC" was defined as occult cancer identified after thyroidectomy or as multifocal cancer with smaller pyramidal lobe tumor.
Results: Ten patients were included in the pyramidal lobe-dominant PTC group. The mean age was 58 ± 12.5 years, and the mean tumor size was 0.7 ± 0.7 cm. Cervical lymph node metastasis was found in 5 patients (50%). Three patients had microscopic lymphatic invasion, and 7 had advanced American Joint Comitee on Cancer (AJCC) stage disease (5 with stage III and 2 with stage IV). Compared with conventional PTC (n = 1,058), pyramidal lobe-dominant PTC was significantly associated with lymphatic invasion (P = 0.031) and advanced AJCC stage (P = 0.022). The prevalence of incidental pyramidal lobe PTC was 3.56%.
Conclusion: Pyramidal lobe PTC is relatively small in size; however, the rate of extrathyroidal extension and lymph node metastasis is high. Preoperative evaluation of nodal status is important, and the extent of surgery should be determined in accordance with the preoperative diagnosis.
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Key Words: Thyroid, Pyramidal, Papillary thyroid carcinoma, Lymphatic metastasis, Thyroid neoplasms

INTRODUCTION

The pyramidal lobe of the thyroid gland is a remnant of the inferior part of the thyroglossal duct [1]. It is usually connected to the isthmus of the thyroid gland but can be linked to the right and left thyroid lobes [2]. The pyramidal lobe is thought to be present in 15%–75% of the general population [2,3].

Papillary thyroid carcinoma (PTC) arising mainly from the pyramidal lobe is extremely rare. Indeed, only 5 case series have been reported worldwide [4-8]. Thus, the clinical and pathological characteristics of pyramidal lobe PTC are not fully understood. A recent study suggests that pyramidal lobe thyroid

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cancer should be classed as an upper neck papillary thyroid cancer (UPTC), which includes Delphian node metastasis and thyroglossal duct cyst (TGDC) carcinoma [8]. In these cases, the need for concurrent thyroid resection is different from that of pyramidal lobe cancer, which requires orthotopic thyroidectomy.

Another clinical issue with respect to the pyramidal lobe is the possibility of hidden malignancy after thyroid surgery to treat cancer identified in the other lobes of the thyroid. A previous study reported the incidence of occult malignancy in the surgically resected pyramidal lobe as 2% [7]. Occult pyramidal lobe malignancy is important to endocrine surgeons, not only in terms of the decision to completely remove the thyroid tissue, but also with respect to remnant cancer in the operating field.

Therefore, the aim of this study was to examine the clinical and pathologic characteristics of pyramidal lobe PTC. We also examined the rate of occult pyramidal lobe malignancy after thyroid surgery at Seoul National University Hospital.

METHODS

This was a retrospective, single center study performed at Seoul National University Hospital, Seoul, Korea. Patient data were retrieved from electronic medical records. The study enrolled 1,107 patients who underwent thyroid surgery from January 2006 to December 2015 and had a clear description of "pyramidal lobe" status in the final pathologic report. Patients were divided into 2 groups as follows: "Pyramidal lobe-dominant PTC", defined as single pyramidal lobe cancer or multifocal cancer in which pyramidal lobe tumor is the largest, and "Incidental pyramidal lobe PTC," defined as occult cancer identified after thyroidectomy or multifocal cancer in which pyramidal lobe tumor is not the largest one.

Clinical and pathologic data were retrospectively reviewed by 2 surgeons. Data collected from pathologic reports included greatest tumor size, extrathyroidal extension, lymphatic invasion, microvascular invasion, surgical margin status, and thyroiditis. Somatic $BRAF^{V600E}$ mutation status was confirmed by immunohistochemistry or targeted SANGER sequencing. TNM and American Joint Comitee on Cancer (AJCC) stages were based on the AJCC thyroid cancer staging system (7th edition). Data regarding age, gender, surgical extent, and follow-up duration were obtained from clinical records.

Statistical analysis was performed using R program version 3.2.4 (R Core Team 2016. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria). Mean values between groups were compared using an unpaired t-test, and Fisher exact test was used for cross table analysis. This study was approved by the Institutional Review Board of Seoul National University Hospital (H-1607-008-772).

RESULTS

Forty-nine patients had PTC in the pyramidal lobe; of these, ten were assigned to the "Pyramidal lobe-dominant PTC" group and 39 to the "Incidental pyramidal lobe PTC" group. The clinical and pathologic characteristics of those with pyramidal lobe-dominant PTC are listed in Table 1. The mean age was 58 ± 12.5 years, which is older than the 45 years used as the prognostic cutoff for differentiated thyroid cancer, and 80% were female. The median follow-up duration was 85 months (985 days; range, 3–3,250 days). The largest tumor, evaluated in postsurgical specimens, was 0.7 ± 0.7 cm. This is smaller than the "1 cm" value used to classify papillary microcarcinoma. Nevertheless, 80% of those in the pyramidal lobe-dominant PTC group had extrathyroidal extension and an advanced tumor stage (T3 or T4). Five patients (50%) had cervical lymph node metastasis: 3 in the central lymph nodes and 2 in the lateral lymph nodes. Overall, 70% of the patients showed advanced AJCC stage disease (stage III or IV). The prevalence of the somatic $BRAF^{V600E}$ mutation was 70%. Five patients (50%) had multifocal PTC in other thyroid lobes.

Eight patients underwent total thyroidectomy, and 2 underwent complete thyroidectomy after previous thyroid lobectomy. Three patients underwent central lymph node dissection (CLND). Modified radical neck dissection (MRND) was performed in 2 patients, although the tumors were smaller than 1 cm (0.7 cm and 0.2 cm). Postoperative pathologic node status was confirmed as N1b. No recurrence was observed during the follow-up period. A representative image showing the surgical field is shown in the Fig. 1A; a resected specimen is shown in Fig. 1B.

Table 1 also compares patients with pyramidal lobe PTC and those with nonpyramidal lobe PTC. The age of patients with pyramidal lobe PTC was significantly higher than that of those with nonpyramidal lobe PTC ($P = 0.004$). The tumors in those with pyramidal lobe PTC were smaller than in those with nonpyramidal lobe PTC; however, the difference was not significant ($P = 0.065$).

Lymphatic invasion was frequently observed in the pyramidal lobe PTC group ($P = 0.031$). Tumor stage was also significantly different between the 2 groups ($P = 0.034$). In the pyramidal lobe PTC group, 80% of patients had advanced stage T3 or T4 disease. There was also a significant difference between the groups in terms of AJCC stage ($P = 0.022$): the majority of patients in the nonpyramidal group were AJCC stage I/II (67.7%), whereas 70% of patients in the pyramidal group were AJCC stage III/IV.

Among the 1,097 surgically resected pyramidal lobes, incidental papillary carcinoma was identified in 39 cases

Table 1. Clinical and pathologic characteristics of patients with nonpyramidal lobe PTC (n = 1,058) or pyramidal lobe-dominant PTC (n = 10)

Variable	Nonpyramidal lobe PTC (n = 1,058)	Pyramidal lobe PTC (n = 10)	P-value[a]
Age (yr)	43.0 ± 11.8	58.0 ± 12.5	0.004
Sex, male:female	168:890	2:8	0.665
Size (cm)			0.065
Mean ± SD (range)	0.9 ± 0.6 (0.1–6.5)	0.7 ± 0.7 (0.2–2.4)	
Extrathyroidal extension	639 (60.4)	8 (80)	0.331
Lymphatic invasion	75 (7.1)	3 (30)	0.031
Microvascular invasion	18 (1.7)	0 (0)	>0.999
Surgical margin involvement	81 (7.7)	1 (10)	0.552
Presence of thyroiditis	394 (37.2)	2 (20)	0.338
BRAF^{V600E} mutation	829 (78.4)	7 (70)	0.460
T stage			0.034
T1	403 (38.1)	2 (20)	
T2	11 (1.0)	0 (0)	
T3	641 (60.6)	7 (70)	
T4	3 (0.3)	1 (10)	
N stage			0.531
N0	638 (60.3)	5 (50)	
N1a	320 (30.2)	3 (30)	
N1b	100 (9.5)	2 (20)	
AJCC stage			0.022
I	714 (67.5)	3 (30)	
II	2 (0.2)	0 (0)	
III	302 (28.5)	5 (50)	
IV	40 (3.8)	2 (20)	

Values are presented as mean ± standard deviation (SD) or number (%) unless otherwise indicated.
PTC, papillary thyroid carcinoma; AJCC, American Joint Comitee on Cancer.
[a]Fisher exact test was used for cross table analysis.

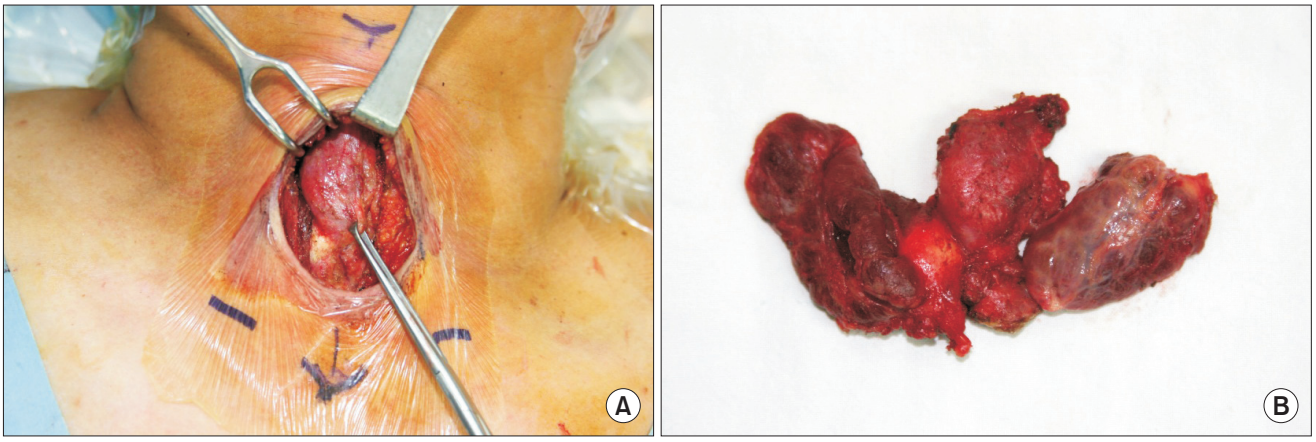

Fig. 1. (A) Pyramidal lobe papillary thyroid carcinoma identified during surgery. (B) Gross specimen of pyramidal lobe thyroid carcinoma.

(3.56%). Overall, 31 patients underwent total thyroidectomy, 2 underwent lobectomy with pyramidal lobe resection, and 1 underwent complete thyroidectomy. CLND was performed in 28 cases, and MRND in 11 cases. Table 2 shows the clinical and pathologic characteristics of the 39 patients with incidental pyramidal lobe PTC. The pathologic descriptions and staging shown in Table 2 refer to the main tumor. The mean age of the patients was 52.2 years, and 33 were female. The greatest tumor diameter in the pyramidal lobes was 0.37 ± 0.24 cm (range, 0.1–1.1 cm), whereas that of the main tumors was 1.35 ± 1.20

Table 2. Clinical and pathologic characteristics of patients with incidental pyramidal lobe PTC (n = 39)[a]

Variable	Value
Age (yr)	52.2 ± 11.6
Sex, male:female	6:33
Pyramidal lobe tumor size (cm)	
Mean ± SD (range)	0.37 ± 0.24 (0.1–1.1)
Main tumor size (cm)	
Mean ± SD (range)	1.35 ± 1.20 (0.2–5.8)
Main tumor location	
Right	21 (53.8)
Left	15 (38.5)
Isthmus	3 (7.7)
Extrathyroidal extension	30 (76.9)
Lymphatic invasion	5 (12.8)
Microvascular invasion	1 (2.6)
Surgical margin involvement	3 (7.7)
Presence of thyroiditis	13 (33.3)
BRAF^{V600E} mutation	22 (56.4)
T stage	
T1	7 (17.9)
T2	1 (2.6)
T3	31 (79.5)
T4	0 (0)
N stage	
Nx	1 (2.6)
N0	16 (41.0)
N1a	12 (30.8)
N1b	10 (25.6)
AJCC Stage	
I	13 (33.3)
II	0 (0)
III	11 (28.2)
IV	15 (38.5)

Values are presented as mean ± standard deviation (SD) or number (%) unless otherwise indicated.
PTC, papillary thyroid carcinoma; AJCC, American Joint Comitee on Cancer.
[a]Pathologic findings were based on the main tumor.

cm (range, 0.2–5.8 cm). Extrathyroidal extension was noted in 76.9%, and 79.5% had T3/T4 disease. Neck node metastasis was found in 22 patients: 12 in the central and 10 in the lateral compartment. Finally, 66.7% of patients were advanced stage (III and IV). The *BRAF*^{V600E} mutation was identified in 22 main tumors.

DISCUSSION

During embryonic development, the thyroid gland originates from the midline endodermal invagination of the foregut and then descends to the anterior neck. The thyroglossal duct is a canal that allows thyroid migration before disappearing at the 9th–10th weeks of embryonic development. The pyramidal lobe of the thyroid gland is thought to be a remnant of the inferior part of the thyroglossal duct, which comprises normal thyroid tissue [9,10]. The length of the pyramidal lobe ranges from 8 to 40 mm [2,3,10]. Previous studies report that the pyramidal lobe is present in 40%–60% of South Koreans [11-13].

Primary PTC arising from the pyramidal lobe is rare [4-7]. Santrac et al. [7] reported three cases of pyramidal lobe PTC over 10 years. A recent study by Zizic et al. [8] evaluated pyramidal lobe cancer as a subcategory, which they termed UPTC because it arose around the upper neck area near the thyroglossal duct tract. They identified eight cases of pyramidal lobe PTC; again, the incidence was very low. UPTC comprises TGDC cancer, pyramidal lobe thyroid cancer, Delphian node metastasis, and indeterminate group. Preoperative diagnoses were mostly TGDC cancer; however, after reviewing the pathologic data, the diagnoses in 53% of cases were changed to pyramidal lobe cancer or Delphian node metastasis. Accordingly, the authors suggested that previous diagnoses of TGDC cancer, which is frequently associated with a high rate (20%–62%) of concurrent thyroid cancer, were not actually TCGC cancer in some cases [14-19]. Santrac et al. [7] suggested that a final diagnosis of TGDC cancer does not have to involve a simultaneous thyroid lesion, although they only identified four cases. However, pyramidal lobe cancer and Delphian node metastasis are associated with a high rate of concurrent thyroid cancer. Thus, the authors recommended new therapeutic algorithms for UPTC patients, which were modified from the Pribitkin and Friedman recommendations [20]. If patients are initially diagnosed with UPTC, clinicians should use CT or ultrasound scans to identify nodal metastasis or concurrent thyroid lesions. After surgery, clinicians should check the pathology carefully. If the final diagnosis is indeed TGDC cancer, with no abnormal findings on ultrasonography (US), then orthostatic thyroid surgery is not necessary. Orthotopic thyroid surgery is recommended for pyramidal lobe PTC or Delphian node metastasis because these are associated with a high rate of thyroid gland cancer (24%–80%) [21-24].

Here, we examined ten cases of pyramidal lobe-dominant PTC. This is the largest number of primary pyramidal lobe cancer cases at a single institution. Although the size of the pyramidal lobe tumors was small (0.7 ± 0.7 cm), their presence was associated with poor prognostic factors such as extrathyroidal extension, advanced T-stage, cervical lymph node metastasis, advanced AJCC stage (III, IV), and *BRAF*^{V600E} mutation (Table 1). Furthermore, lateral neck node metastasis was found in 2 patients, even though their tumors were smaller than 1 cm. We found that 50% of patients had multifocal PTC (i.e., tumors in other thyroid lobes). Accordingly, we need a more thorough surgical strategy for pyramidal lobe PTC patients. It is natural to assume that total thyroidectomy is necessary in these cases because many reports suggest the

presence of multifocal thyroid cancer. However, we suggest that preoperative neck node evaluation be performed (using CT scans or US) to determine the surgical extent in these patients.

However, pyramidal lobe excision during total thyroidectomy is important because half of the residual uptake of radioactive iodine is observed in the pyramidal lobe [25,26]. From an oncologic perspective, we found that residual pyramidal lobe tissue can harbor cancer cells. Although a single report mentions recurrence of thyroid cancer in residual pyramidal lobe tissue in a South Korean patient [5], the actual prevalence of occult malignancy in the pyramidal lobe is unclear. The present study is the first to analyze the prevalence of occult malignancy in surgically resected pyramidal lobe tissue (prevalence, 3.56%). Proper preoperative evaluation and surgical removal of the pyramidal lobe during thyroid surgery may be important if we are to prevent residual cancer tissue. A recent radiologic study shows that neck ultrasound and CT are effective ways of evaluating the status of the pyramidal lobe [11].

The present study has some limitations. First, it was a retrospective case series with no control group. Second, the number of cases was small, even though this is the largest number examined to date. Prospective data collection is necessary to establish treatment guidelines for primary pyramidal lobe cancer and to identify the actual prevalence of occult malignancy in the pyramidal lobe.

In summary, pyramidal lobe-dominant PTC is rare; however, it is related to the presence of poor prognostic factors. Proper thyroid resection with regional lymph node excision should be performed according to the preoperative diagnosis. In addition, pyramidal lobe excision is helpful not only for radioiodine therapy but also in the context of removing occult cancer during thyroid cancer surgery.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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