INTRODUCTION

Papillary thyroid carcinoma (PTC) is the most common malignancy in the thyroid gland, which accounts for 90% of all thyroid cancers (1, 2). Several variants of PTC have been reported, and different histopathologic variants of PTC have varied clinical courses and prognosis (3). The columnar cell variant of papillary thyroid carcinoma (CCV-PTC) is a rare subtype, which accounts for 0.15–0.2% of all PTCs (4). The revised American Thyroid Association guidelines recently categorized the PTC variants according to their biological behavior as described in the literature, and CCV-PTC was classified as the aggressive type (5). Previous studies showed that CCV-PTC has a fast growth rate and a high incidence of recurrence, and this type of tumor is associated with local invasion and early lymph node (LN) metastasis (6-8). However, the prognosis of CCV-PTC remains controversial, because the encapsulated form has a more favorable outcome with indolent clinical process, which shows relatively slow growth and low incidence of recurrence or metastasis (9-11). To the best of our knowledge, there were few reports about the imaging
Columnar Cell Variant of PTC

Characteristics of CCV-PTC that can differ from other cell types in prognosis (12). Therefore, we evaluated the ultrasonography (US) features and clinical characteristics of CCV-PTC that can predict disease progression.

MATERIALS AND METHODS

Patients
From 1994 to 2016, six patients were diagnosed with CCV-PTC via surgical pathology analysis in our institution. Data on the clinical characteristics and cytopathological results were obtained from the electric medical record database at our institution and retrospectively reviewed. This study was approved by our Institutional Review Board, and obtaining a written informed consent was waived due to the retrospective design of this study.

Ultrasonography Analysis
All six patients underwent preoperative thyroid US examination. The thyroid glands were scanned by experienced radiologists with HDI 5000 or iU22 scanners (Philips Medical Systems, Bothell, WA, USA) equipped with a commercially available 7- to 12-MHz linear transducer. All six preoperative US images were retrospectively reviewed by two board-certified radiologists with 18 years and 6 years of thyroid imaging experience, respectively. According to the Revised Korean Society of Thyroid Radiology Consensus Statement and Recommendations, the US features of the nodules were categorized based on the following: size (the maximal diameter of the nodule was documented), internal content (solid [no obvious cystic content], predominantly solid [< 50% of the cystic portion], predominantly cystic [> 50% of the cystic portion], and cystic [no obvious solid content]), echogenicity (markedly hypoechoic [hypoechogenic relative to the anterior neck muscle], hypoechoic [hypoechogenic relative to the thyroid parenchyma], isoechoic [similar echogenicity as the thyroid parenchyma], or hyperechoic [more echogenic relative to the thyroid parenchyma]), shape (round, ovoid, and irregular), orientation (parallel [the anteroposterior diameter of the nodule is equal to or less than its transverse or longitudinal diameter] or nonparallel [when the anteroposterior diameter of the nodule is larger than its transverse or longitudinal diameter]), margin (smooth, spiculated/microlobulated, or ill-defined), calcifications (microcalcifications [< 1 mm, brighter echo than the surrounding thyroid tissue], macrocalcifications [echogenic foci that is greater than 1 mm in size with posterior shadowing], and rim calcifications [peripheral curvilinear or eggshell calcification at the nodule margin]). Nodular vascularity was not routinely evaluated via color Doppler imaging throughout the study period. The radiologists made the final diagnosis for each nodule as “no nodule,” “benign,” “low suspicion,” “intermediate suspicion,” and “high suspicion” based on the Korean Thyroid Imaging Reporting and Data System (K-TIRADS) (13).

Cytopathological Analysis
All six patients underwent preoperative US-guided fine needle aspiration (FNA) either in our institution (n = 3) or at other clinics (n = 3). The radiologists performed the preoperative US and US-guided FNA biopsy using a 23-gauge needle connected to a 2-mL disposable plastic syringe. FNA slides that were obtained from other clinics were reviewed by the pathology department of our institution. All six patients underwent total thyroidectomy. Prophylactic central compartment neck dissection for PTC surgery was performed in our institution before 2013. Modified lateral neck dissection was performed only when lateral neck LN metastasis was diagnosed at preoperative US and US-guided FNA. The final cytopathological diagnosis was evaluated by one of the seven pathologists, who was randomly selected based on their duty schedule. One specialized in thyroid pathology re-reviewed our cases to be CCV-PTC and agreed with their diagnosis.

RESULTS

Clinical Findings
The main clinical features and pathological results of the six patients with CCV-PTC are shown in detail in Table 1. The six patients aged 27–70 years (median age, 34 years; mean, 41.7 years) included in this study consisted of one male and five female patients. Clinical follow-up ranging from 1–17 years was (mean: 9 years) conducted for all six patients. Four cases were clinically indolent (cases 1–4), while two were aggressive (cases 5 and 6). Recurrence or distant metastasis (case 5 for brain metastasis, three years after diagnosis and case 6 for lung metastasis at the diagnosis) was observed in two patients during the follow-up period; these patients demonstrated recurrence immediately after surgery and died 4 years after diagnosis of thyroid cancer. During follow-up period, no metastasis and recurrence was detected in the other four patients (case 1–4). The median
Age was 32 years (range: 27–34 years) for the indolent group, and 66 years (55 years and 70 years) for the aggressive group. The mean tumor size was 1.2 cm (range: 0.4–2.0 cm) for the indolent group, and 3.9 cm (1.8 cm and 6.0 cm) for the aggressive group, respectively. Three out of the six patients underwent \textit{BRAFV600E} mutation analysis (cases 2, 3, and 6). \textit{BRAFV600E} mutation was observed in each patient from the indolent and aggressive groups; whereas one patient in the indolent group was negative for \textit{BRAFV600E} mutation.

### Cytopathological Features

All six patients underwent preoperative US-guided FNA either in our institution (n = 3) or other clinics (n = 3). A specific variant could only be diagnosed in one out of six patients.

Four patients had CCV-PTCs in the right lobe, while two had CCV-PTCs in the left lobe. The median size of the nodule was 1.2 cm (range: 0.4–6.0 cm). Five patients underwent total thyroidectomy and central compartment neck dissection. One of the six patients underwent modified lateral neck dissection because lateral nodal metastasis was observed on preoperative US and FNA. Extrathyroidal extension to the muscle layer was observed in two patients (cases 5 and 6) and no microscopic extrathyroidal extension was reported in the other patients (cases 1–4).

Microscopically, CCV-PTC demonstrated microfollicles or elongated follicles of columnar cells with palisading oval nuclei and eosinophilic cytoplasm, and minimal papillary nuclear features. Hematoxylin & eosin (x 400). CCV-PTC = columnar cell variant of papillary thyroid carcinoma, US = ultrasonography

### Ultrasonographic Features

The US features of the six nodules are summarized in Table 2. The common US features of CCV-PTC were solid composition (n = 5, 83.3%), hypoechogenicity (n = 6, 100% [hypoecholic, n = 4], [markedly hypoecholic, n = 2]), and associated calcifications (n = 4, 66.7%, microcalcifications). The final diagnosis of the six nodules was intermediate suspicion (n = 2) or high suspicion (n = 4) based on K-TIRADS. Among the four patients in the indolent group, one (25%) had a nodule with a microlobulated margin, while 3 (75%) demonstrated smooth margins (Fig. 1); whereas both patients (100%) in aggressive group presented nodules with microlobulated margins (Fig. 2).
Two nodules had parallel orientation, and two had a non-parallel orientation in the indolent group. On the other hand, all two patients presented with nodules that had parallel orientation in the aggressive group. Two patients from the indolent group had nodules with an irregular shape and two other nodules with an oval shape in indolent group. On the other hand, two patients in the aggressive group presented with nodules that are irregular in shape. In addition, the two nodules in the aggressive group showed infiltrative anterior margin abutting to anterior strap muscle which was suspicious for extrathyroidal extension. Finally, gross extrathyroidal extension on pathology and surgical report was present. He was included in aggressive group and died from disease 4 years after diagnosis.

**DISCUSSION**

Columnar cell variant of papillary thyroid carcinoma is a rare tumor that accounts for 0.15–0.2% of all PTCs, which was originally described as a hostile tumor by Evans in 1986 (4, 7). The concept of CCV-PTC being a clinically aggressive tumor with a poor prognosis, was later challenged by several studies who reported more favorable outcomes in patients diagnosed with the encapsulated form of CCV-PTC (9, 10, 14). However, these studies did not show the image features of CCV-PTC, which is clinically indolent. In the present study, only half of the patients in the indolent group had a tumor with the typical suspicious malignant feature (K-TIRADS 5), where the tumor size was relatively small and confined to the thyroid parenchyma.

In 2011, Chen et al. (15) reviewed several previous studies and presented 48 patients of CCV-PTC, of which 20 were clinically indolent (18 women and 2 men; mean age, 44.9 years), and 23 cases where the tumors were considered as aggressive (10 women and 13 men; mean age, 55.6 years). The size of the indolent tumors ranged from 0.9–8.0 cm.
individuals (range: 27−34 years). Recurrence was not confined to the thyroid gland, and present in younger study were small (mean size: 1.2 cm), encapsulated, to the previous studies, the four indolent tumors in our extension, accounting for 67−100% (11, 15, 16). Similarly of clinically aggressive CCV-PTC showed extrathyroidal clinically indolent CCV-PTC were not reported while most after diagnosis. Also, the extrathyroidal extension of tumors, 13 died from disease approximately 7−126 months years after diagnosis. Of the 20 patients with aggressive tumors, 13 died from disease approximately 7−126 months after diagnosis. Of the 20 patients with aggressive tumors, 13 died from disease approximately 7−126 months after diagnosis. A previous report insisted that CCV-PTC is a unique histologic subtype but not a unique clinical type of tumor and treatment of patients with these tumors should be based on the clinical stage and not on the histomorphologic appearance (11). The results of our study suggest that the CCV-PTC has two distinct clinical types, one of which is more fatal than the similar stage of conventional PTC. Because the case number of our series was too small to draw a conclusion, further investigation including US features is necessary to distinguish aggressive CCV-PTC from indolent CCV-PTC and conventional PTC for risk stratification. In conclusion, favorable prognosis in CCV-PTC is observed in young patients with T1 staging and demonstrates a smooth margin at US. These US findings might help exclude the same treatment as in the aggressive type in the indolent type of CCV-PTC.

REFERENCES

1. Hundahl SA, Fleming ID, Fremgen AM, Menck HR. A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the U.S., 1985-1995 [see comment]. Cancer 1998;83:2638-2648
2. Papp S, Asa SL. When thyroid carcinoma goes bad: a morphological and molecular analysis. Head Neck Pathol 2015;9:16-23
3. Lee JH, Shin JH, Lee HW, Oh YL, Hahn SY, Ko EY. Sonographic and cytopathologic correlation of papillary thyroid carcinoma variants. J Ultrasound Med 2015;34:1-15
4. Sywak M, Pasieka JL, Ogilvie T. A review of thyroid cancer with intermediate differentiation. J Surg Oncol 2004;86:44-54
5. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel
Columnar Cell Variant of PTC

SJ, Nikiforov YE, et al. 2015 American Thyroid Association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer: the American Thyroid Association guidelines task force on thyroid nodules and differentiated thyroid cancer. *Thyroid* 2016;26:1-133

6. Berends D, Mouthaan PJ. Columnar-cell carcinoma of the thyroid. *Histopathology* 1992;20:360-362

7. Evans HL. Columnar-cell carcinoma of the thyroid. A report of two cases of an aggressive variant of thyroid carcinoma. *Am J Clin Pathol* 1986;85:77-80

8. Gaertner EM, Davidson M, Wenig BM. The columnar cell variant of thyroid papillary carcinoma. Case report and discussion of an unusually aggressive thyroid papillary carcinoma. *Am J Surg Pathol* 1995;19:940-947

9. Evans HL. Encapsulated columnar-cell neoplasms of the thyroid. A report of four cases suggesting a favorable prognosis. *Am J Surg Pathol* 1996;20:1205-1211

10. Ferreiro JA, Hay ID, Lloyd RV. Columnar cell carcinoma of the thyroid: report of three additional cases. *Hum Pathol* 1996;27:1156-1160

11. Wenig BM, Thompson LD, Adair CF, Shmookler B, Heffess CS. Thyroid papillary carcinoma of columnar cell type: a clinicopathologic study of 16 cases. *Cancer* 1998;82:740-753

12. Shin JH. Ultrasonographic imaging of papillary thyroid carcinoma variants. *Ultrasound* 2017;36:103-110

13. Shin JH, Baek JH, Chung J, Ha EJ, Kim JH, Lee YH, et al. Ultrasonography diagnosis and imaging-based management of thyroid nodules: revised Korean Society of Thyroid Radiology consensus statement and recommendations. *Korean J Radiol* 2016;17:370-395

14. Huang WT, Yang SF, Wang SL, Chan HM, Chai CY. Encapsulated columnar-cell carcinoma of the thyroid: a case report. *Kaohsiung J Med Sci* 2005;21:241-244

15. Chen JH, Faquin WC, Lloyd RV, Nosé V. Clinicopathological and molecular characterization of nine cases of columnar cell variant of papillary thyroid carcinoma. *Mod Pathol* 2011;24:739-749

16. Sujay V, Pinto A, Nosé V. Columnar cell variant of papillary thyroid carcinoma: a study of 10 cases with emphasis on CDX2 expression. *Thyroid* 2013;23:714-719

17. Verma R, Paul P. Columnar cell variant of papillary thyroid carcinoma: a diagnostic dilemma in fine-needle aspiration cytology. *Diagn Cytopathol* 2016;44:816-819

18. Ylagan LR, Dehner LP, Huettner PC, Lu D. Columnar cell variant of papillary thyroid carcinoma. Report of a case with cytologic findings. *Acta Cytol* 2004;48:73-77

19. Bongiovanni M, Mermod M, Canberk S, Saglietti C, Sykiotis GP, Pusztaszeri M, et al. Columnar cell variant of papillary thyroid carcinoma: cytomorphic characteristics of 11 cases with histological correlation and literature review. *Cancer* 2017;125:389-397