

# Sonographic Features of the Follicular Variant of Papillary Thyroid Carcinoma

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**Objective.** The purpose of this study was to evaluate the sonographic findings of the follicular variant of papillary thyroid carcinoma (FVPTC) and to assess the role of preoperative fine-needle aspiration biopsy (FNAB). **Methods.** The sonographic findings of 27 thyroid nodules in 26 patients (2 male and 24 female; mean age, 45 years) with surgically proven FVPTC were reviewed retrospectively. Findings were categorized according to the echogenicity, margin, shape, and presence of microcalcifications. Malignant findings included marked hypoechogenicity, irregular or microlobulated margins, a taller-than-wide shape, and microcalcifications. Thyroid nodules with a single malignant finding as described above were classified as malignant. All patients underwent sonographically guided FNAB, and the sensitivity of the cytologic results was calculated. **Results.** Lesion sizes varied from 3 to 34 mm (mean, 15.2 mm), and lesions were most commonly solid (23 [85.2%]), hypoechoic (14 [51.9%]), and oval (17 [63%]) with well-defined margins (14 [51.9%]) and no microcalcifications (23 [85.2%]). Eighteen lesions (66.7%) were correctly classified as malignant, whereas 9 (33.3%) were classified as benign on the basis of sonographic criteria. Twenty-four samples were adequate for cytologic examination, and 3 were inadequate. Twenty-one of 24 diagnostic cytologic results (87.5%) were suspicious for papillary carcinoma (5 of 21 [20.8%]) or malignant (16 of 21 [66.7%]), whereas 3 lesions (12.5%) had benign results. The sensitivity of FNAB was 77.8% (21 of 27). **Conclusions.** The follicular variant of papillary thyroid carcinoma tends to have relatively benign sonographic features, such as hypoechogenicity, well-defined margins, an oval shape, and no microcalcifications, but most lesions were correctly classified as malignant by both sonography and FNAB. The possibility of FVPTC should be considered when thyroid nodules with a relatively benign sonographic appearance have suspicious or malignant FNAB results. **Key words:** fine-needle aspiration biopsy; papillary thyroid carcinoma, follicular variant; sonography; thyroid.

## Abbreviations

FNAB, fine-needle aspiration biopsy; FTC, follicular thyroid carcinoma; FVPTC, follicular variant of papillary thyroid carcinoma; PTC, pure papillary thyroid carcinoma

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Papillary thyroid carcinoma is the most common malignancy in the thyroid gland, accounting for more than 70% of all thyroid tumors.<sup>1,2</sup> Numerous variants of papillary thyroid carcinoma have been reported, but pure papillary thyroid carcinoma (PTC) is the most frequent type, accounting for about 55% to 66% of all well-differentiated thyroid carcinomas. The follicular variant of papillary thyroid carcinoma (FVPTC) is the second most common variant, constituting 9% to 22.5% of all papillary thyroid carcinomas.<sup>2</sup> The follicular variant of papillary thyroid carcinoma is composed of cells with characteristic nuclear features of clear nuclei, nuclear grooves, and pseudoinclusions diagnostic for PTC.<sup>3</sup>

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However, these cells have a predominantly follicular growth pattern, consisting of more than 70% to 80% of the neoplasm, which mimics follicular thyroid adenoma or follicular thyroid carcinoma (FTC).

The follicular variant of papillary thyroid carcinoma is known to have a relatively benign appearance on sonography, more similar to a follicular neoplasm than PTC.<sup>4,5</sup> However, to our knowledge, there are no established sonographic characteristics of FVPTC. Thus, the purpose of this study was to evaluate the characteristic sonographic findings of FVPTC and the role of preoperative fine-needle aspiration biopsy (FNAB).

### Materials and Methods

This study was approved by the Institutional Review Board and did not require informed patient consent. The medical record database at our institution was searched for patients with a diagnosis of FVPTC between November 2002 and January 2006. During this period, 27 nodules in 26 patients (2 male and 24 female; age range, 21–67 years; mean age, 45 years) had a diagnosis of FVPTC by surgery. The sonographic findings of these thyroid nodules were retrospectively reviewed, and clinical information was obtained from the medical records.

Ultrasound examinations were performed with an HDI 3000 or HDI 5000 system (Philips Medical Systems, Bothell, WA) or an Acuson Sequoia 512 system (Siemens Medical Solutions, Mountain View, CA). A 7- to 12-MHz linear array transducer was used in examining the entire thyroid gland and both sides of the neck. All 27 nodules underwent sonographically guided FNAB before surgery.

Each lesion was retrospectively described by 2 experienced radiologists using the sonographic features, including the internal component, echogenicity, margin, shape, and presence of microcalcifications. Color Doppler imaging was not routinely used. We classified the nodules on the basis of previous criteria suggested by Kim et al.<sup>6</sup> The internal component was defined as solid, mixed, or cystic. A mass with mixed components meant that the mass had both solid and cystic components; sonographic findings for masses with mixed components were evaluated

on the basis of the echogenicity of the internal solid component. The echogenicity of the mass was compared with that of adjacent thyroid parenchyma. Malignant sonographic features were defined as marked hypoechogenicity (echogenicity lower than that of the surrounding strap muscle), microlobulated or irregular margins, a taller-than-wide shape (greater in the anteroposterior dimension than the transverse dimension in any plane), and microcalcifications. Thyroid nodules were considered suspicious for malignancy if any 1 of the above findings was present on sonography. Fine-needle aspiration biopsy was performed in all of the thyroid lesions; 2 patients underwent FNAB at an outside hospital, and the remaining 24 underwent FNAB at our institution. Cytologic results were evaluated on the basis of the cytology reports; a result of papillary carcinoma or one suspicious for papillary carcinoma was considered a true-positive result, and we then calculated the sensitivity of FNAB.

### Results

Thyroid nodule sizes ranged from 3 to 34 mm (mean, 15.2 mm). Six nodules (22.2%) were palpable on physical examination, and 21 (77.8%) were incidentally detected during various imaging modalities such as sonography, computed tomography, and positron emission tomography. Twenty-three nodules (85.2%) were solid, and 4 (14.8%) were mixed. Common sonographic findings included hypoechogenicity (51.9%), well-defined margins (51.9%), an oval shape (63%), and no calcifications (85.2%). The sonographic findings are summarized in Table 1.

Eight cases (29.6%) had 1 suspicious sonographic finding; 8 (29.6%) had 2 suspicious findings; and 2 (7.5%) had 3 suspicious findings. In the 18 nodules with suspicious sonographic features, the most common sonographic finding was microlobulated margins (11). Eighteen lesions (66.7%) were classified as malignant nodules according to the sonographic criteria described above (Figures 1 and 2), and 9 (33.3%) were classified as benign (Figure 3).

In terms of the cytologic results from sonographically guided FNAB, there were 24 diagnostic and 3 nondiagnostic results. Of the 24

**Table 1.** Sonographic Findings of FVPTC

Characteristic	n	%
Internal components		
Solid	23	85.2
Mixed	4	14.8
Cystic	0	0
Echogenicity		
Hypoechoic	14	51.9
Isoechoic	10	37
Markedly hypoechoic	3	11.1
Margin		
Well-defined	14	51.9
Microlobulated	11	40.7
Irregular	2	7.4
Shape		
Oval	17	63
Taller than wide	10	37
Microcalcifications		
No microcalcifications	23	85.2
Internal microcalcifications	4	14.8

diagnostic results, 3 cases (12.5%) were diagnosed as benign (1 case of a follicular neoplasm and 2 cases of adenomatous hyperplasia); 5 (20.8%) were diagnosed as suspicious for papillary carcinoma; and 16 (66.7%) were diagnosed as papillary carcinoma. Among the 16 cases diagnosed as papillary carcinoma on FNAB, 1 (3.7%) was accurately diagnosed as FVPTC. When considering papillary carcinoma or a suspicious finding for papillary carcinoma on FNAB as positive results, the sensitivity of diagnosing papillary carcinoma on FNAB was 77.8% (21 of 27). Three cases (11.1%) were diagnosed as benign nodules, and 3 (11.1%) were nondiagnostic samples on FNAB, which were surgically excised for either suspicious sonographic findings (5) or the patient's desire (1).

Of the 9 nodules classified as benign lesions on sonography, 7 (77.8%) were diagnosed as papillary carcinoma (5) or suspicious for papillary carcinoma (2) on FNAB.

## Discussion

The follicular variant of papillary thyroid carcinoma is the second most common variant,<sup>7,8</sup> accounting for approximately 9% to 22.5% of papillary thyroid carcinomas.<sup>9</sup> It was first described by Crile and Hazard<sup>10</sup> in 1953 as a neoplasm with the nuclear features of PTC and a predominantly follicular growth pattern.<sup>1</sup> Histologically, the pres-

ence of characteristic features such as clear nuclei, nuclear grooves, and pseudoinclusions is diagnostic for PTC.<sup>3</sup> The follicular variant of papillary thyroid carcinoma is composed of follicles lined by cells, which have nuclear features of papillary carcinoma and consist of more than 70% to 80% of the neoplasm.<sup>9</sup>

Recent studies suggest that FVPTC presents with a larger tumor and in younger patients.<sup>11</sup> Some reports showed that FVPTC mimics pathologic and clinical features of a follicular neoplasm, with well-encapsulated tumors featuring metastasis in distant organs without lymph node metastasis. Higher incidences of angiovascular or capsular invasion and distant metastases compared with PTC have also been reported. On histologic examination, FVPTC is more often encapsulated, with a considerably lower incidence of lymph node metastasis and less frequent extrathyroidal extension compared with conventional PTC. In general, FVPTC is considered to have more favorable clinicopathologic features and a better tumor risk profile but results in a long-term outcome similar to that of conventional PTC.<sup>11</sup>

Pure papillary thyroid carcinoma is often multifocal and nonencapsulated and shows spread through the lymph nodes. Conversely, FTC is more unifocal and encapsulated and shows frequent metastasis to distant organs with low rates of regional nodal metastasis.<sup>9</sup> The follicular variant of papillary thyroid carcinoma shares features of FTC, sometimes misleading physicians to a benign diagnosis, which can have an adverse effect on treatment of the patient. Differentiation of a benign from malignant follicular neoplasm is not possible by sonography even cytologically.<sup>12</sup> To the best of our knowledge, no previous literature exists comparing and contrasting FVPTC and follicular neoplasms sonographically or by FNAB results. In our cases, most of the masses had well-defined (51.9%) or microlobulated (40.7%) margins, which is pathologically compatible with relatively well-encapsulated tumors.

In our study, the common sonographic findings of FVPTC were hypoechogenicity (51.9%), well-defined margins (51.9%), an oval shape (63%), and no microcalcifications (85.2%). These findings appear relatively benign on sonogra-

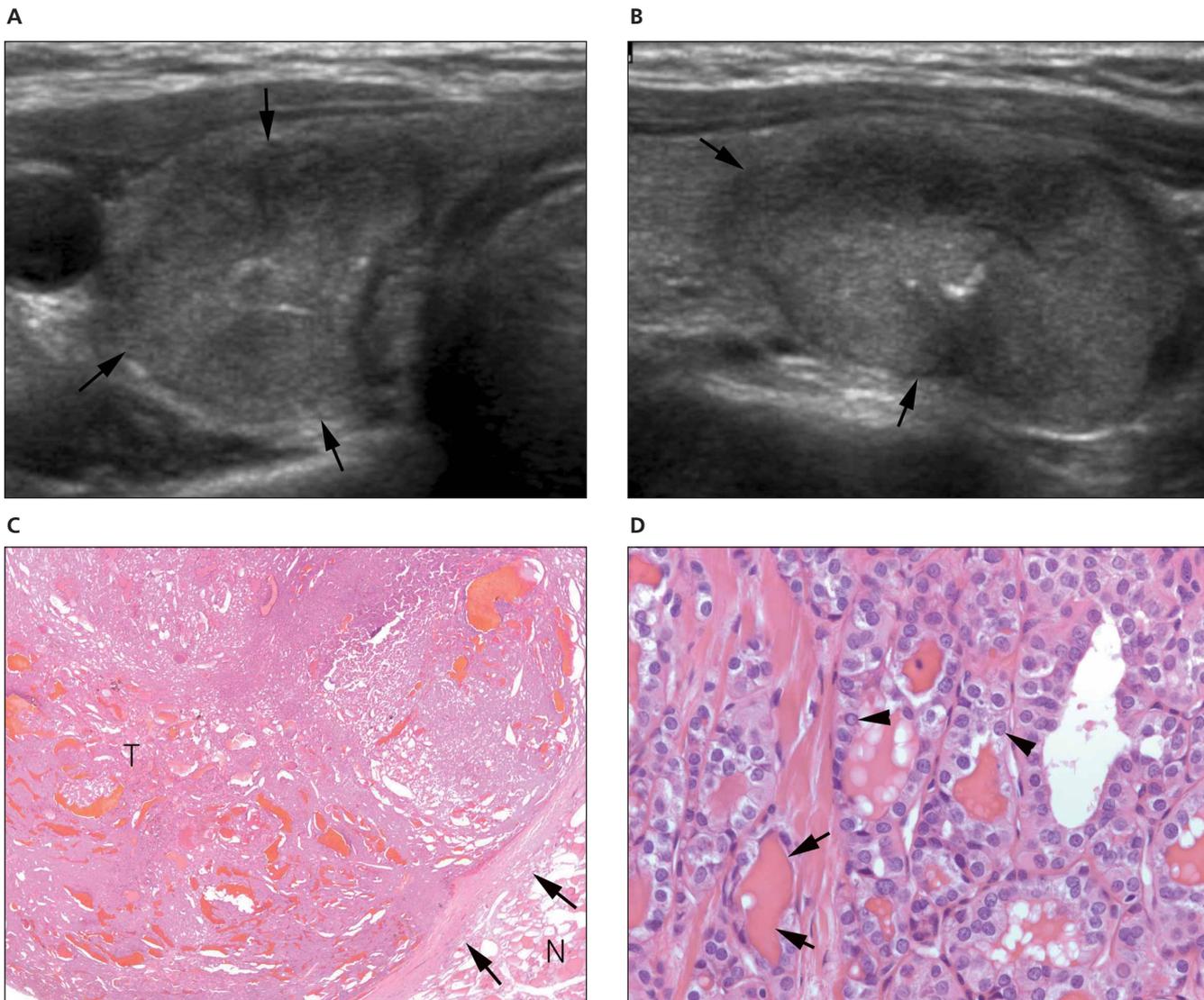
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phy; however, 18 cases (66.7%) had at least 1 suspicious sonographic finding, which classified the nodules as malignant. On average, 1.94 suspicious sonographic findings were seen in the malignant or suspicious nodules, and the single most common suspicious sonographic finding was microlobulated margins.

Diagnosis of FVPTC by FNAB is known to be difficult and unreliable. Most cases of FVPTC can be diagnosed only on permanent sections of sur-

gically resected lesions.<sup>8</sup> Recent studies reported very low sensitivity for FNAB in identification of FVPTC; the sensitivity of FNAB for diagnosis of FVPTC varied from 25% to 37%, whereas the sensitivity of PTC was reported to be greater than 60% to 90%.<sup>13,14</sup> Cytologic diagnosis of FVPTC is more difficult than PTC for 2 reasons: (1) its cytomorphic features overlap with those of benign and neoplastic follicular lesions because of the abundant thin colloid and monolayer

**Figure 1.** Thyroid nodule found incidentally on sonography in 27-year-old female patient who had anterior neck discomfort. Transverse (A) and longitudinal (B) scans show a 15-mm irregularly shaped hypoechoic nodule with calcifications in the right thyroid (arrows). The sonographic findings were classified as suspicious for malignancy. The cytologic diagnosis from sonographically guided FNAB was papillary carcinoma. A low-power field pathologic specimen (C) shows a tumor (T) with a capsule (arrows) and adjacent non-neoplastic tissue (N) (hematoxylin-eosin, original magnification  $\times 12$ ). A high-power view (D) shows a predominantly follicular pattern with abundant follicular structures and abundant pink-staining colloid (arrows), neoplastic nuclei with nuclear grooves, and nuclear inclusions (arrowheads) (original magnification  $\times 400$ ).



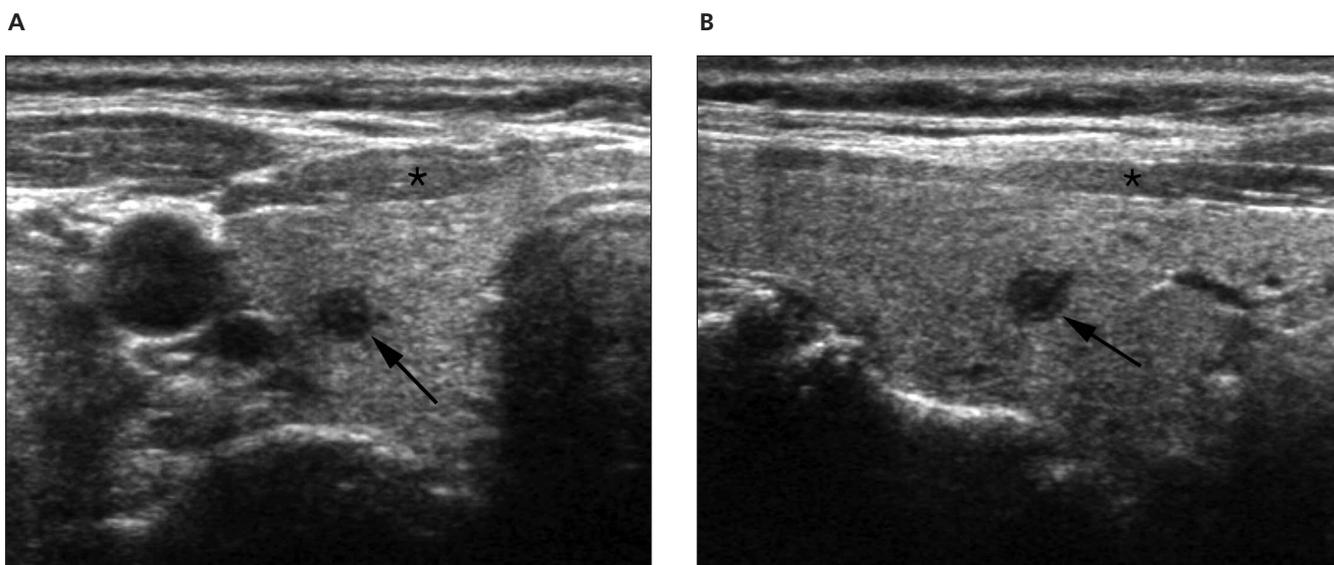
sheets of follicular cells; and (2) FVPTC contains only focal areas of the nuclear characteristics of papillary carcinoma.<sup>7,8,14</sup> These factors have a critical effect, leading to false-negative results and misdiagnosis of FVPTC as a benign lesion. The diagnostic rate of FVPTC (3.7%) was also low in the cytologic studies at our institution, but the diagnostic rate of cytologic studies for malignancy or lesions suspicious for malignancy was relatively high. Twenty-one cases (78%) were diagnosed as definite or suspicious for papillary carcinoma, and 7 (77.8%) of the 9 cases classified as benign lesions on sonography were diagnosed as definite or suspicious for papillary carcinoma on FNAB. This result shows that the possibility of FVPTC should be considered when thyroid nodules with relatively benign sonographic appearances have a suspicious or malignant FNAB result.

Our study had several limitations. First, this retrospective analysis was limited by the small sample size. A larger study would be helpful in characterizing the sonographic findings of this disease. Second, vascularity was not included in

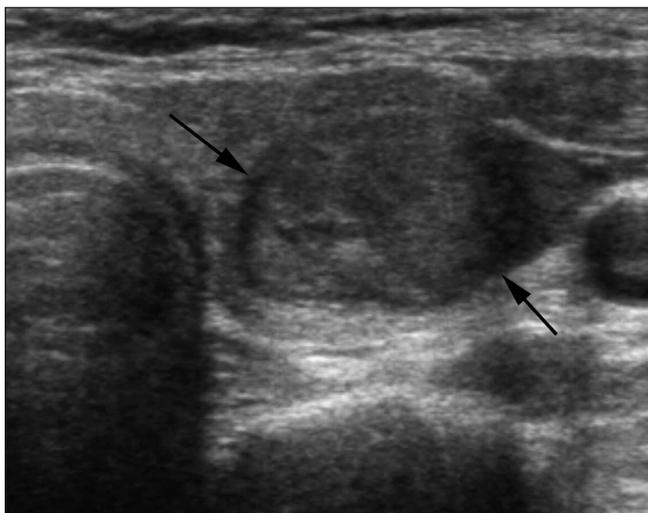
the sonographic findings in our study. The most commonly known pattern of vascularity in thyroid malignancy is marked intrinsic hypervascularity, which shows increased flow in the central portion of the tumor compared with the surrounding thyroid parenchyma. This is not a specific sign of thyroid malignancy but has sensitivity of up to 69% to 74%.<sup>15</sup> Combining the pattern of vascularity with gray scale sonographic findings may have an effect on the sonographic classifications of thyroid nodules and may aid in diagnosis of FVPTC.

In conclusion, FVPTC tends to have relatively benign sonographic features such as hypoechogenicity, an oval shape, and no microcalcifications; however, in this study, 66.7% were classified as malignant based on the published sonographic criteria. Considering the high sensitivity of FNAB for diagnosing malignancy in FVPTC, a diagnosis of FVPTC should be considered when thyroid nodules with a relatively benign appearance have suspicious or malignant FNAB results.

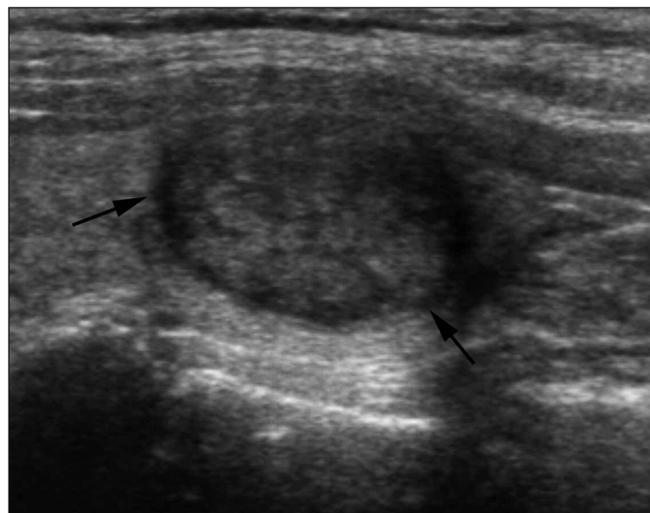
**Figure 2.** Follicular variant of papillary thyroid carcinoma in a 58-year-old female patient. A thyroid nodule was incidentally found during a carotid Doppler examination. Transverse (**A**) and longitudinal (**B**) scans show a 4-mm taller-than-wide markedly hypoechoic (lower echogenicity than that of the surrounding strap muscle [asterisks]) nodule (arrows), which was suspicious for malignancy.



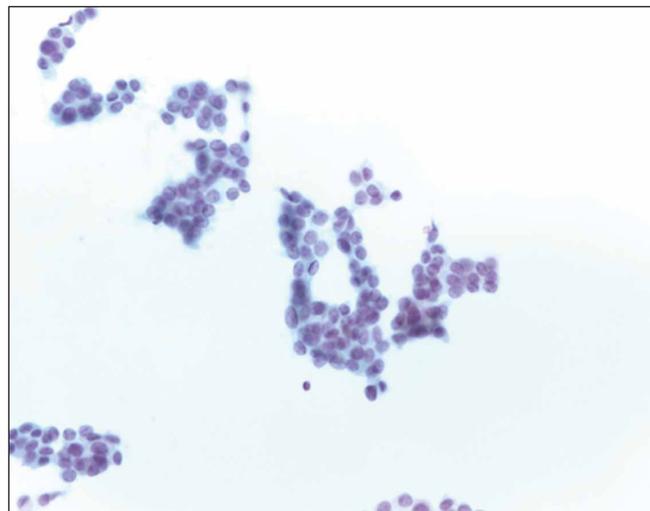
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A



B



C

**Figure 3.** Palpable anterior neck mass in a 48-year-old female patient. Transverse (A) and longitudinal (B) scans show a 16-mm hypoechoic nodule (arrows) with well-defined margins in the left thyroid, classified as a probably benign nodule because of lack of any suspicious features. The cytologic findings (C) are compatible with papillary carcinoma, showing nuclear grooves, clearing, and inclusions (Papanicolaou, original magnification  $\times 400$ ). The patient underwent surgical resection, which resulted in a diagnosis of FVPTC.

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