Collapsing Benign Cystic Nodules of the Thyroid Gland: Sonographic Differentiation from Papillary Thyroid Carcinoma

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BACKGROUND AND PURPOSE: The US features of benign and malignant nodules overlap, and benign thyroid lesions can mimic thyroid malignancy on US. Benign cystic nodules after spontaneous collapse or needle aspiration, can mimic malignant thyroid nodules. Our aim was to evaluate the US features of CBCNs of the thyroid that distinguish such nodules from malignant thyroid nodules.

MATERIALS AND METHODS: US and clinical findings in 13 patients, each with a single CBCN, were evaluated to determine if they showed >50% cystic content on initial US or CT and >30% decrease in maximum diameter on follow-up US. We compared these findings with those of 26 patients, each with a single surgically confirmed PTMC. US scans were analyzed for internal content, shape, margin, echogenicity, presence of echogenic dots suggesting micro- and macrocalcification, inner isoechoic rim, and low-echoic halo.

RESULTS: Six of the 13 (46%) CBCNs were classified as malignant on US due to their marked hypoechoogenicity, microcalcification, or spiculated margins. US features that differed between CBCNs and PTMCs were shape (ovoid-to-round versus taller-than-wide, \( P = .016 \)); margins (ill-defined versus spiculated, \( P < .000 \)); low-echoic halo \( (P < .000) \); inner isoechoic rim \( (P < .000) \) with high negative predictive values (100%, 91%, 91%, and 89%, respectively); and clinically acceptable diagnostic accuracy (59%, 80%, 82%, and 85%, respectively).

CONCLUSIONS: US features helpful for differential diagnosis of CBCNs from PTMCs include shape, margin, and the presence of an inner isoechoic rim and a low-echoic halo. Familiarity with US features suggesting CBCNs may be helpful in reducing unnecessary repeated FNABs.

Materials and Methods

Patient Selection

This retrospective study was approved by our institutional review board, and informed-consent documents were waived. We reviewed the computerized medical records and US images of the 2529 patients who underwent thyroid US in our institution from January to June 2007. CBCN was diagnosed when nodules showed >50% cystic content on initial US or CT and there was a >30% decrease in the long diameter of the initial nodule on follow-up US. We identified 13 patients, each with a single CBCN. During a mean follow-up period of 13 months (range, 3–34 months), 4 of the 13 CBCNs showed >50% decreases in the long diameter without pathologic confirmation. The 9 other CBCNs were histologically diagnosed as benign follicular cell lesions \( (n = 4) \), cystic change with macrophages \( (n = 4) \), and colloid cyst \( (n = 1) \) (Table 1). Mean patient age was 54 years, with a range of 39–68 years, and the mean diameters of the CBCNs on initial and follow-up images were 1.4 cm (range, 0.7–5.0 cm) and 0.5 cm (range, 0–0.9 cm), respectively.

For each patient with a CBCN, we also enrolled patients who underwent US and surgery during the same period for PTMC of similar nodule size range. Of the 427 patients who had surgically confirmed PTMCs, we recruited 26 consecutive patients, each with a single PTMC. The mean age of these patients was 42 years (range, 22–63 years), and the mean diameter of the PTMCs was 0.7 cm (range, 0.3–1.0 cm).

Analysis of US Findings and Statistics

US examinations were performed with an HDI 5000 scanner (Philips-Advanced Technology Laboratories, Bothell, Washington) by using...
Results

Demographic data, including age and sex, did not differ significantly between the CBCN and PTMC groups ($P > .05$). The contents of all 13 CBCNs showed a solid appearance on US, and all 13 had an ovoid-to-round shape and were hypo- or markedly hypoechogenic. In addition, 11 CBCNs had ill-defined margins and inner isoechoic rims, while 6 had echogenic dots suggesting microcalcification and 10 had low-echoic haloes (Fig 2).

In comparison, the contents of all 26 PTMCs had a solid appearance on US. All were hypo- or marked hypoechogenic, and 20 had spiculated margins. Microcalcification was observed in 15 patients, and macrocalcification, in 23. Five PTMCs had an inner isoechoic rim, and 3 had low-echoic haloes (Fig 3). Although their incidence rates were low, taller-than-wide shape and macrocalcification were observed only in PTMCs.

Among the US features, shape, margin, inner isoechoic rim, and low-echoic halo differed significantly between CBCNs and PTMCs (Table 2). The overall diagnostic accuracies of ovoid-to-round shape, ill-defined margins, inner isoechoic rim, and low-echoic halo in differentiating CBCNs from PTMCs were 59%, 80%, 82%, and 85%, respectively (Table 3).

Discussion

Several studies have assessed the natural history of thyroid nodules, with reporting that the most common outcome of benign thyroid nodules, untreated for an average of 15 years after the first examination, was a decrease in nodule size, including disappearance (52.9%), with a decrease in size being more prominent in cystic nodules. In contrast, others have reported that 39% of benign thyroid nodules increase in size during follow-up, with cystic nodules being more likely to maintain or decrease in size than solid nodules.

The revised guidelines of the American Thyroid Association in 2009 recommended that FNAB is warranted for subcentimeter nodules with suspicious findings or in patients at high risk, including patients exposed to radiation or those with a family history of papillary thyroid carcinoma. Mazzaferr and Sipos have recommended, however, that nodules <5 mm should not be biopsied because of high rates of false-positive results on US and of inadequate cytology. Recently, Moon et al reported that US features have been found to depend on the size of thyroid cancers, with subcentimeter tumors having a lower frequency of microcalcification but higher frequencies...
of marked hypoechogenicity, taller-than-wide shape, and spiculated margin. Because these characteristics are also more frequent in smaller benign nodules, the false-positive rate of malignancy may be higher for smaller nodules.

Cytologically diagnosed benign thyroid nodules after aspiration may have US features similar to those of malignant thyroid nodules, including marked hypoechogenicity due to solid-appearing internal content. Of the 13 CBCNs that were examined in this study, 6 (46%) were classified as malignant by US criteria. These US features may be due to collapse of the cystic cavity, infarction of the solid component, and other destructive processes such as hemorrhage, followed by replacement by fibrous tissue. These pathologic alterations may appear on US as marked hypoechogenicity of a nodule with ill-defined margins.

Other than marked hypoechogenicity of solid-appearing internal content, we found that the US features of CBCNs that differed significantly from PTMCs were ovoid-to-round shape, ill-defined margins, microcalcification, inner isoechoic rim, and low-echoic halo. Of these US features, inner isoechoic rim and low-echoic halo showed the highest diagnostic accuracies with acceptable negative predictive values.

Our study had several limitations, including its retrospective design and the small number of patients, which may have introduced a selection bias. However, because the purpose of this study was not to assess the general US features of CBCNs but to determine the specific US features that distinguish CBCNs from PTMCs, this bias may not have had a large im-

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**Table 2: US features of collapsing benign cystic nodules and papillary thyroid microcarcinomas**

| Characteristic                  | CBCN (n = 13) | PTMC (n = 26) | P Value |
|--------------------------------|---------------|---------------|---------|
| Internal content               |               |               |         |
| Solid                          | 13 (100)      | 26 (100)      | .016    |
| Shape                          |               |               |         |
| Ovoid-to-round                  | 13 (100)      | 16 (62)       | .016    |
| Taller-than-wide               | 10 (39)       |               |         |
| Margin                         |               |               | <.000   |
| Spiculated                     | 2 (15)        | 20 (76)       | <.000   |
| Ill-defined                    | 11 (85)       | 6 (23)        | <.000   |
| Echogenicity                   |               |               | <.000   |
| Marked hypoechogenicity        | 6 (46)        | 7 (28.9)      | <.000   |
| Hypoechogenicity               | 7 (54)        | 19 (73)       | <.000   |
| Microcalcification             | 6 (46)        | 15 (58)       | .734    |
| Macrocalcification             | 0 (0)         | 23 (89)       | .538    |
| Inner isoechoic rim            | 11 (85)       | 5 (19)        | <.000   |
| Low-echoic halo                | 10 (77)       | 3 (1)         | <.000   |

**Table 3: Diagnostic sensitivity, specificity, PPV, NPV, and accuracy of the individual US features suggesting CBCNs**

| Characteristics             | No. (%) | Sensitivity | Specificity | PPV | NPV | Accuracy |
|-----------------------------|---------|-------------|-------------|-----|-----|----------|
| Ovoid-to-round              | 13 (100)| 100         | 39          | 45  | 100 | 59       |
| Ill-defined margin          | 11 (85) | 85          | 77          | 65  | 91  | 80       |
| Inner isoechoic rim         | 11 (85) | 85          | 81          | 69  | 91  | 82       |
| Low-echoic halo             | 10 (77) | 77          | 89          | 77  | 89  | 85       |

Note: PPV indicates positive predictive value; NPV, negative predictive value. Data are percentages.
impact on our results. Our results, however, suggest the need for larger scale prospective studies.

Conclusions

We found that 46% of CBCNs could be misclassified as malignant on US because they showed marked hypoechogenicity, microcalcification, and/or spiculated margins. Among the US features that can be used to distinguish CBCNs and PTMCs are the presence of an inner isoechoic rim and low-echoic halo, nodule shape, and margin. Therefore, although US features suggesting CBCNs may not completely abrogate the need for FNAB, familiarity with the US findings of CBCNs may reduce the incidence of unnecessary repeated FNABs. Furthermore, rather than performing immediate FNAB, nodules with US features suggesting CBCN can be followed-up, especially in patients without a high likelihood of malignancy.

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