Ultrasonographic Findings of Papillary Thyroid Carcinoma with Hashimoto’s Thyroiditis

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Abstract

Objective Papillary thyroid carcinoma (PTC) sometimes occurs with Hashimoto’s thyroiditis (HT). It is often difficult to differentiate between benign and malignant nodules in HT because HT varies greatly on ultrasonography. We aimed to characterize the ultrasonographic features of PTC with HT.

Patients and Methods In this retrospective study, 2,167 patient records (1,897 women and 270 men) were examined for ultrasonographic features and thyroid autoantibodies between 1998 and 2002 at our university. Patients with Graves’ disease, positive TSH receptor autoantibody (TRAb) or thyroid-stimulating antibody (TSAb) were excluded. PTC was diagnosed by pathological examination.

Results Of the 1644 patients who were autoantibody negative (MCHA, TGHA, TgAb, TPOAb), 54 (3.3%) had PTC, while 29 (5.5%) of the 523 patients who were autoantibody positive had PTC. On ultrasonography, the frequency of dense calcification in patients with HT was significantly higher (P=0.0064) and frequency of psammoma bodies was less than PTC patients without HT (P<0.0001). On the other hand, PTC with HT had more irregular shapes and ill-defined edges of the borders with less hypoechogenecity and calcification than PTC without HT, but the difference was not significant.

Conclusion The frequency of psammoma bodies in PTC with HT was less, while dense calcifications were greater than in those of PTC without HT. Any type of ultrasonographic calcification features may represent a risk for PTC.

Key words: Hashimoto’s thyroiditis, papillary thyroid carcinoma, thyroid ultrasonography, calcification

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Introduction

Hashimoto’s thyroiditis (HT) is often associated with malignant lymphoma and occurs with papillary thyroid carcinoma (PTC). Since the first report by Daily et al in 1955 (1), the relation between HT and PTC has been frequently discussed (2-8). Patients with HT seem to have PTC more frequently than those without HT, but the assumption is not confirmed yet.

It is often difficult to differentiate between benign and malignant nodules in HT because HT varies greatly on ultrasonography. We aimed to characterize the ultrasonographic features of PTC with HT.

Patients and Methods

Study design and patients

In a retrospective study, 2,167 patient records (1,897 women and 270 men) were examined for ultrasonographic features and thyroid autoantibodies between 1998 and 2002 at our university, because of goiter, the nodule, cervical incompatibility and lymphadenopathy.

Patients with HT (n=523, mean age 54 ± 15; 50 men and 473 women) and patients without HT (n=1644, mean age 53 ± 17; 220 men and 1,424 women) were included. Patients with HT were those who were positive for antithyroglobulin hemagglutinin antibody (TGHA), or thyroglobulin antibody (TgAb) and antimicrosomal hemagglutinin antibody.
Table 1. Guidelines for the Diagnosis of Chronic Thyroiditis (Hashimoto’s thyroiditis)

<table>
<thead>
<tr>
<th>a) Clinical findings</th>
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<tr>
<td>Diffuse swelling of the thyroid gland without any other cause (such as Graves’ disease)</td>
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<th>b) Laboratory findings</th>
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<tr>
<td>1. Positive for anti-thyroid microsomal antibody or anti-thyroid peroxidase (TPO) antibody</td>
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<tr>
<td>2. Positive for anti-thyroglobulin antibody</td>
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<tr>
<td>3. Lymphocytic infiltration in the thyroid gland confirmed with cytological examination</td>
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</table>

A patient shall be said to have chronic thyroiditis if he/she has satisfied clinical criterion and any one laboratory criterion.

(MCHA), or thyroid peroxidase antibody (TPOAb), but patients with Graves’ disease or positive TSH receptor autoantibody (TRAb) or thyroid-stimulating antibody (TSAb) were excluded. HT was diagnosed by the diagnostic criteria of the Japan Thyroid Association (Table 1). A diagnosis of PTC was based on ultrasound-guided fine needle aspiration cytology and confirmed by pathological examination of surgically-resected neoplasms at our institution.

Ultrasonography and the classification of findings

Ultrasonography was performed using a 7.5 MHz linear probe (LOGIQ 500, GE Yokokawa Medical Co., Japan). On ultrasonography, thyroid nodules were evaluated by the criteria of the Japan Society of Ultrasonics in Medicine, 1999 (9). Nodules were described by their shapes (regular or irregular), borders (edge definition and character), echo levels (high, iso or low) and internal echoes (homogeneity and strong echoes), the presence or absence of a marginal hypoechoic zone, calcification (microcalcification or dense calcification), and the number of lesions (single or multiple). Echo levels in the solid parts of the nodules were compared with those of the surrounding healthy thyroid glands (10). Using color Doppler ultrasonography, we assessed blood flow within the tumor.

Statistical analysis

All data were expressed as means ± standard deviation. Statistical analysis was performed using the chi-square test or Student’s non-paired t-test for comparison between two groups. The differences were considered significant at P<0.05.

Results

Characteristics and comparison of PTC

Table 2 shows the characteristics of PTC with or without HT. In this study, there was no significant difference in age between men and women in the two groups, although there were more women than men. The mass in the thyroid gland of one patient was not discovered, but she was diagnosed with PTC by the aspiration biopsy cytology (ABC) from the lymph node. Gender, age, tumor size of PTC, number of microcarcinoma (<1 cm), and other complications of the thyroid did not differ between the two groups. PTC was more complicated in the patients with HT than in those without HT (5.5% vs. 3.3%, p<0.05), the same result was found in only the women group (p<0.05).

Ultrasonographic features of PTC

We compared the ultrasonographic features of the two groups (Fig. 1). In both groups, most of the patients demonstrated typical PTC findings such as irregular shape, ill-defined edge of the border, heterogeneous and hypoechoic echogeneity, calcification, and color Doppler in the thyroid gland. The frequency of dense calcification in patients with HT was significantly higher (P=0.00064) and the frequency of psammoma body was less than PTC patients without HT (P<0.0001). Fig. 2 shows calcification of PTC with or without HT on ultrasonography. On the other hand, PTC with HT had more irregular shapes and ill-defined edges of the borders with less hypoechoegenecy and calcification than PTC without HT, but the difference was not significant. There were no significant differences in marginal hypoechoic zone defect, absence of calcification, and color Doppler in the thyroid between the two groups, either.
Figure 1. Comparison of ultrasonographic findings of papillary thyroid carcinoma (PTC) between patients with or without Hashimoto's thyroiditis (HT). Shaded columns represent patients without HT. Closed columns represent patients with HT. $P<0.05$.

Figure 2. Ultrasonographic findings of PTC showed psammoma body (arrows) in the patient without HT (A) and dense calcification (arrows) in the patient with HT (B).

Discussion

A close association of HT with PTC has been reported (1, 8). Daily et al reported 37 carcinomas in 302 HT autopsy specimens (12%) (1). The present study showed that PTC with HT had a prevalence of 5.5%, higher than PTC without HT. Recently, the prevalence of HT coexistence is reported to associate with a favorable prognostic factor of PTC, and the expression of the RET/PTC fusion gene is a marker of PTC in HT (11). Moreover, the Fas/Fas ligand has been expressed in HT, and it is known to be an inducer of apoptosis in PTC (12).

Accurate screening or diagnosing PTC with HT accurately is necessary but whether or not PTC associated with HT is detectable by ultrasonography is disputable, because PTC and HT are very similar. Ultrasonographic features of HT include fibrous, enlarged, and lobulated glands with ill-defined hypoechoic heterogeneous areas, focal or diffuse, and hypoechoic areas separated by echogenic fibrous septa. Numerous micronodulations varying from 1.5 to 3 mm in size are observed (13). PTC shows a predominantly ill-defined, irregular margin, hypoechoic (79-90%) (14, 15), mostly solid (70%), multifocal (10-20%), and specific mi-
These findings make it difficult to differentiate PTC from HT. In the present study, the ultrasonographic findings of PTC both with or without HT were typical. Especially, the irregular shape and ill-defined edges of the border, heterogeneous echogenicity, hypoechoic echogenicity, and calcifications were frequently seen between the two groups. As for calcification, the presence of calcifications within a thyroid nodule should raise suspicion for malignancy (17, 18). Histopathologically, thyroid calcification is divided into “psammoma body” and “dystrophic calcifications”. In particular, psammoma body on ultrasonography is generally accepted as the most reliable indicator for malignancy (19). Dense calcification is seen in 10% of all thyroid nodules (20) and these findings are associated with multinodular goiter (21). Other previous studies, however, have also indicated that dense calcification has no diagnostic value or it can even serve as an indicator for benign lesions (22). Taki et al reported that 52% of intranodular coarse calcification is malignant (23), but they did not investigate the thyroid antibody. The tendency for large-sized calcification may be associated with the presence of lymphocytic infiltration, as Nakamoto et al has reported (24). In the present study, there were fewer psammoma body calcifications, but there were more dense calcifications in PTC with HT. The ultrasonographic findings of fewer psammoma body calcification and/or much more dense calcifications could not deny PTC in patients with HT of proclaimed great interest. Further studies are necessary to examine the efficacy of these ultrasonographic findings.

In summary, the prevalence of PTC was estimated to be 5.5% in patients with HT at our institution. On ultrasonography, not only psammoma body but also dense calcification in the PTC patients with HT suggested the presence of PTC. Therefore, it is important to make a careful examination in the PTC with HT because HT represents various findings on ultrasonography.

References


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