Echographic Findings and Histological Feature of the Thyroid:  
A Reverse Relationship Between the Level of Echo-Amplitude and Lymphocytic Infiltration

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Abstract

In 43 patients with Graves' disease, 5 patients with painless thyroiditis and 30 patients with Hashimoto-thyroiditis ultrasonographical observations and histological examinations by needle biopsy of the thyroid were carried out simultaneously. In all cases the level of echo-amplitude was well correlated with the rate of lymphocytic infiltrations and fibrosis. In cases which exhibited marked lymphocytic infiltrations in the thyroidal biopsy specimen, no apparent echoes or very low amplitude echoes were observed in the whole thyroid and in cases in which replacement with lymphocytic infiltration was observed in almost a half part of the thyroid, several sonolucent regions were observed in the thyroid and in cases in which lymphocytic infiltration or fibrosis was observed sporadically, low-amplitude and ununiform echoes were observed in the whole or several regions of the thyroid. In cases with no lymphocytic infiltration in the histological specimen, diffuse high-amplitude and uniform echoes were observed throughout the whole lobe of the thyroid. In patients with painless thyroiditis, the amplitude of echo was low when the level of lymphocytic infiltration was high and the echo-amplitude showed a tendency to increase along with the decrease in the rate of lymphocytic infiltration. From these observations it is concluded that echo-amplitude is well correlated with lymphocytic infiltration and fibrosis in patients with Hashimoto-thyroiditis, Hashitoxicosis and painless thyroiditis.

Recently echography has been applied to diagnose the nodular lesion in the thyroid (Asano et al., 1963, Blum et al., 1971, Croker et al., 1974, Kobayashi et al., 1976, Oka et al., 1963). Correlation between the patterns of echography and histological findings of the nodular lesions has been reported. But we are not aware of any reports concerning the application of this method to diffuse goiters. Sheible et al., reported that Hashimoto-thyroiditis was characterized by enlargement of the gland accompanied with a decrease in echo-amplitude (Sheible et al., 1979), and Blum et al., mentioned that in patients with Graves' disease uniform echoes of low amplitude were frequently observed.
in the A-mode, and in the B-mode very fine stipplings were generally exhibited (Blum et al., 1972). However these authors did not examine the relationship between the echographic patterns and histological findings. The patients with Graves' disease whose glands exhibit marked lymphocytic infiltration are designated as having Hashitoxicosis (Buchanan et al., 1961, Means, 1963), and the echographic pattern of these patients is quite different from those with Graves' disease, possibly due to the high rate of lymphocytic infiltration. In the present study, echography and needle biopsy of the thyroid were performed in 73 patients with Hashimoto-thyroiditis or Graves' disease and the results were compared to reveal any correlations between these physical and histological observations in the hope of using echography for diagnosis of diffuse goiters.

Materials and Methods

Studies were performed on 30 patients with untreated Hashimoto-thyroiditis, 4 patients with painless thyroiditis and 43 patients with Graves' disease. They were diagnosed by ultrasonic and histological evaluation of the gland. The patients with Graves' disease were examined two weeks after the administration of Methimazole, because of the high risks of complication due to needle biopsy in the period of hyperthyroidism. The ultrasonic apparatus used was Aloka Model EU 3014B and Model ASU-13, water immersion scanner. A polyethylene vinyl water bag filled with degassed water was positioned in contact with the overlying skin of the thyroid. Conductivity Gel was used to complete acoustic coupling between the transducer and the skin. A grayscale equipment consisted of a 5 MHz transducer 10 mm in diameter, focused at the water approximately 5 cm from the skin surface was used to take an echogram. The transducer was housed in a water bag and was mechanically driven in arc scanning fashion. The echo gain and the sensitivity time control (time-gain compensation) settings were kept constant at 70 dB and 5 dB/cm, respectively. As echo amplitude expressed on the bistable Polaroid image varies according to the echo gain, the time of exposure and time of development of the film, these were performed in the same conditions. A Silverman biopsy needle was used for percutaneous needle biopsy of the gland. Specimens obtained were fixed in 10% solution of formaldehyde, and stained with hematoxylin and eosin. Statistical evaluation was performed using Pearson's product-moment correlation coefficient.

Results

Patients with Graves' disease and Hashimoto-thyroiditis were classified in 4 grades according to echographic findings. Grade 1: no apparent echoes or very low-amplitude echoes throughout the whole thyroid, Grade 2: several sonolucent regions in the thyroid, Grade 3: low-amplitude and ununiform echoes in the whole or several regions of the thyroid, Grade 4: diffuse high-amplitude echoes throughout the whole lobe of the thyroid (Fig. 1 a, b, c, d). The patients were also classified in the following 4 groups based on the histological findings. Grade 1: replacement with lymphocytic infiltration and fibrosis in almost all thyroidal structure, Grade 2: replacement with lymphocytic infiltration or fibrosis in almost half the thyroidal structure, Grade 3: lymphocytic infiltration is observed sporadically, Grade 4: almost no apparent lymphocytic infiltration or fibrosis in the gland (Fig. 2 a, b, c, d).

There was observed a good correlation between echo grade and histological grade; almost all patients who were classified as echo grade 1 were also histological classification grade 1, and this was also the case in grade 2, 3 and 4 patients echographically, they were all classified in the corresponding histology grade (Tables 1 and 2). These results indicate that lymphocytic infiltration and fibrosis resulted in a decrease in the amplitude of the echo.

To confirm the relationship between the amplitude of the echo and the rate of lymphocytic infiltration, we followed changes
Table 1. Relation between echo grade and histological grade in patients with Graves’ disease.

<table>
<thead>
<tr>
<th>Histological Grade</th>
<th>Total No. of Patients</th>
<th>Echo Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>1 9 4 2</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>1 5 1</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>0 1 2 12</td>
</tr>
</tbody>
</table>

\[(r=0.8931 \ p<0.001)\]

Table 2. Relation between echo grade and histological grade in patients with Hashimoto-thyroiditis.

<table>
<thead>
<tr>
<th>Histological Grade</th>
<th>Total No. of Patients</th>
<th>Echo Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>1 2 3 4</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>0 6 2 0</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>0 0 3 1</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>0 0 1 4</td>
</tr>
</tbody>
</table>

\[(r=0.9684 \ p<0.001)\]

in the echography and histological findings in the four patients with painless thyroiditis throughout the hyperthyroidal and recovery periods. Fig. 3a, b shows one example of the echography and histological features during the hyperthyroidal state of the patients; marked lymphocytic infiltration was accompanied with almost no echo in the thyroidal area and fig. 4a, b shows the histological and echographic observations of the same patients during recovery from the disease; decreased lymphocytic infiltration and diffuse uniform echoes of high-amplitude can be seen. Similar changes in histology and echography were also observed in the other 3 patients examined.

Discussion

It seems important to investigate the level of lymphocytic infiltration to diagnose Hashimoto-thyroiditis. Hashimoto-thyroiditis is classified into two types, diffuse and focal thyroiditis, according to their histological features (Woolner et al., 1959). The rate of the lymphocytic infiltration is different in both types of Hashimoto-thyroiditis. The patients who show a marked lymphocytic infiltration tend to be in the hypothyroid state and hormonal therapy is required. In the present study we did not discriminate between the two types of Hashimoto-thyroiditis mentioned above, since we considered that degeneration of the follicle could not be identified on the echography. Therefore we used the percentage of the area which is occupied by the lymphocytic infiltration in the biopsy specimen as the parameter by which classify the grade of the disease.

It is also important to estimate the level of lymphocytic infiltration in patients with Graves’ disease, since patients with Hashimoto-toxicosis show a high frequency of development of hypothyroidism if 131I-therapy or subtotal thyroidectomy is applied.

Recently diagnosis of these disease has been based on the histological observations of needle biopsy specimens, but this method is always accompanied by the risk of complications. From the present observations it is considered that thyroid echography seems to be one of a useful method to use in estimating the level of lymphocytic infiltration in the thyroid, since the level of echo-amplitude is closely correlated with the level of lymphocytic infiltration. In the cases which show marked lymphocytic infiltrations, very low-amplitude echoes or completely sonolucent areas are observed on the echographies. A reverse relationship between the level of echo-amplitude and of lymphocytic infiltration is evident and when high-amplitude echoes were observed, almost none of the cases exhibited apparent lymphocytic infiltrations.

The above observations were further confirmed in the examination of patients
Fig. 1a, b, c, d  Classification of echo grade.

**Fig. 1a**

Grade 1: No apparent echoes or very low-amplitude echoes throughout the whole thyroid.

**Fig. 1b**

Grade 2: Several sonolucent regions in low-amplitude and ununiform echo.
Grade 3: Low-amplitude and ununiform echoes in the whole or several regions of thyroid.

Grade 4: Diffuse high-amplitude echoes in the whole lobe of the thyroid.
Fig. 2a, b, c, d Classification of histological findings.

**Fig. 2a**

Grade 1: Replacement with lymphocytic infiltration and fibrosis in almost the entire thyroidal structure.

**Fig. 2b**

Grade 2: Replacement with lymphocytic infiltration or fibrosis in almost half the thyroid.
Fig. 2c

Grade 3: Lymphocytic infiltration is observed sporadically.

Fig. 2d

Grade 4: Almost no apparent lymphocytic infiltration or fibrosis in the gland.
Fig. 3a, b  Echography and histological features during the hyperthyroidal state of patients with painless thyroiditis.

Fig. 3a

Echography (a) and histological feature (b) during the hyperthyroid state of the patients: marked lymphocytic cell infiltration was accompanied with almost no echo in the thyroidal areas.
Fig. 4 a, b  Echography and histological feature during the recovery period of the patients with painless thyroiditis.

Fig. 4 a

Echography (a) and histological feature (b) during the recovery period: decreased lymphocytic infiltration and uniform echoes of high-amplitude can be seen.
with painless thyroiditis. This disease is characterized by transient thyrotoxicosis and an increase in lymphocytic infiltration (Gorman et al., 1978, Inada et al., 1979, Inada et al., 1980). In the state of hyperthyroidism of these patients, the level of echo-amplitude was quite low, while in the recovery period of the same patients, the level of echo-amplitude was elevated along with the decrease in the rate of lymphocytic infiltrations.

It was reported that in subacute thyroiditis, in which all the thyroidal structure is replaced by inflammatory cells and granulomas (Crill, 1948, Green, 1971), the amplitude of echoes was low or almost no internal echo was observed (Blum et al., 1977). The lymphnode shows no internal echo. Therefore, it is quite possible that occupation with uniform cells in tissues reflects the low amplitude or no echo on the echography.

On the other hand, the coexistence of lymphocytic infiltration and fibrosis is commonly observed in the thyroid of patients with Hashimoto-thyroiditis and Hashitoxicosis. Fibrosis of the thyroid also influences the echo-amplitude. We performed echography of on a patient with idiopathic thyroid fibrosis. His thyroid gland was entirely occupied with fibrosis and no lymphocytic infiltration was observed, and the echographic finding showed a very low-amplitude echo. It is therefore considered that fibrosis of the thyroid also reflects the low amplitude on the echography. From these observations it is concluded that echography is a useful method to use in estimating the level of lymphocytic infiltration and fibrosis in the thyroid of patients with Hashimoto-thyroiditis, Graves' disease and painless thyroiditis.

Reference