Differentiation of pseudonodules from the real nodules on ultrasonography using the guidance of elastography

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Purpose

Hashimoto thyroiditis or chronic lymphocytic thyroiditis is an autoimmune disease in which antibodies against thyroid peroxidase and/or thyroglobulin cause gradual destruction of follicles in the thyroid gland. Described by the Japanese specialist Hashimoto Hakaru in Germany in 1912, it was the first disease to be recognised as an autoimmune disease. Its incidence appears to be as high as 16-23% among elderly women and reveals diffuse parenchimal changes or nodules that can either be demarcated or undemarcated in the ultrasonography. Characterized by invasion of the thyroid tissue by leukocytes, mainly T-lymphocytes, it is also associated with non-Hodgkin lymphoma.

Asymmetrical involvement of the thyroid gland during the primary assessment may alert the attending physician and usually a surgical consultation is needed. As for the risk of lymphoma besides the other primary parenchimal neoplasms, differentiation of the nodules is of utmost importance and must be clearly stated.

Fine needle aspiration biopsy (FNAB) differentiates the true nodules from the pseudonodules, and differs the benign, inflammatory or malignant ones or diagnoses the lymphoma. Despite the accurate diagnostic value, FNAB is still a minimally invasive intervention. On the other hand, the sonoelastography is a non-invasive method that can differentiate the true nodules from the pseudonodules. Our aim is to diagnose the nodules and differentiate them by sonoelastography and prevent unnecessary surgical interventions or invasive approaches.
Methods and Materials

This is a multicenter study of a prospective dataset of patients. Institutional review board approval and informed consents of all the subjects were obtained for this study. 168 cases admitted with the diagnosis of HT between May 2009 and May 2010 were recruited. Gray scale and Doppler ultrasonography (US) of the thyroid glands (BG, BC) and the sonoelastographic evaluations (DY) were performed by different radiologists with the same system (Siemens, Acuson S2000 ultrasound unite). All patients received a detailed clinical examination, thyroid function tests and the thyroid auto-antibody titers were evaluated. 54 (3 male, 51 female, average age 42) of 168 cases were further evaluated and included in the study. The inclusion criteria were:

1. Parenchymal echo heterogenity (abnormal gland echo texture)

2. Elevated blood levels for antthyroidal antibodies (anti-TPO: thyroid peroxidase antibody, Anti-TG: thyroglobuline antibody)

3. Demarcated or nondemarcated nodular lesions with gray scale US images.

4. As for the standardization of the subjects, cases with the BMI between 18-30 kg/m², anteroposterior diameters of the thyroid glands between 8-30 mm and the largest diameters of the nodules between 8-20 mm were included in the study. Cases other than those standards were excluded.

Radiologic evaluation.

54 cases were divided into three groups according to their gray scale ultrasonographic results. Group I was consisted of nondemarcated hypoechogenic focal areas; group II of demarcated hyperechogenic focal areas and group III of demarcated hypoechogenic nodular lesions. Of these nodules, the most evident one was referred to as "focused lesion" and was stated as the dominant lesion.

If the dominant lesion was purely demarcated or vascularized differently, it was referred to as the real thyroid nodule, otherwise evaluated as pseudonodule. The dominant lesions were further studied by the sonoelastography and less or more elastical ones were categorized as the real nodules while isoelastical ones were categorized as pseudonodules. Eventually under ultrasonographic guidance FNAB were performed from the focused lesions. All of the specimens were evaluated by the same pathologist (AK) and stated as either true nodules or pseudonodules of the thyroid glands (Fig 1).

Pathologic evaluation.
All specimen were treated with May-Gruenwald-Giemsa stain. Adequacy of materials were evaluated according to Bethesda criteria as follows;

1. Materials were adequate if at least 5 groups of 10 cell clusters were present while values under those were claimed hypocellular.
2. Specimen with no cells were claimed acellular.
3. Specimen with lots of groups of cells were claimed hypercellular.

Neoplastic criteria were further evaluated also with Bethesda criteria and taken into consideration besides cellularity.

**Statistical Analysis**

All statistical analyses were performed using SPSS Version 15.0.1 (SPSS, Inc., Chicago, IL). Continuous data is displayed as mean ± standard deviation (SD). Statistical significance was accepted when \( P < .05 \). The Chi-Square test was used to compare the nonparametric data (gender, age, gland and nodular vascularity) of the patients and the nodules. Oneway-ANNOVA test was used to determine the statistically significant variances of the parametric data (BMI, the anteroposterior diameter of the lobe bearing the nodule) and the Kruskal-Wallis Test to compare the dimensions of the nodules (Table 1).

**Table I.** Cases, demographics and nodule features with statistical analyses.

<table>
<thead>
<tr>
<th>Data</th>
<th>Group I (Non-demarcated nodules)</th>
<th>Group II (Hyperechogenic nodules)</th>
<th>Group III (Hypochochogenic nodules)</th>
<th>Statistical Analyses</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>33</td>
<td>12</td>
<td>9</td>
<td>( p=0.0001&lt;0.01, ) Chi-Square test</td>
</tr>
<tr>
<td>Male/female: (51/4)</td>
<td>f=31, m=2</td>
<td>f=11, m=1</td>
<td>f=8, m=1</td>
<td>( p=0.575, ) Chi-Square test</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>41.12±6.78</td>
<td>42.33±9.74</td>
<td>44.22±10.09</td>
<td>( p=0.585&gt;0.05, ) Oneway-ANNOVA</td>
</tr>
<tr>
<td>BMI (unit)</td>
<td>23.85±3.69</td>
<td>24.17±3.04</td>
<td>23.17±4.34</td>
<td>( p=0.823&gt;0.05, ) Oneway-ANNOVA</td>
</tr>
<tr>
<td>Nodule localization</td>
<td>18</td>
<td>5</td>
<td>4</td>
<td>( p=0.992, ) Chi-Square test</td>
</tr>
<tr>
<td>Right lobe</td>
<td>12</td>
<td>6</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>#sthmus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Vascularity | Increased | Normal | Decreased |
| | 28 | 11 | 9 |
| | 4 | 1 | 0 |
| | 1 | 0 | 0 |

For parenchymas: p=0.952, For nodules: p=0.211, Chi-Square test

| Nodule dimensions | 11.64±2.93 | 11.52±2.66 | 11.49±2.63 |
| | | | p=0.992>0.05, Kruskal-Wallis Test |

| Related thyroid lobe anetroposterior dimension | 17.24±4.71 | 16.70±5.45 | 19.49±4.96 |
| | | | p=0.397>0.05, One way ANNOVA |

All data were interpreted and the sensitivity (sens), specificity (spec), positive predictive value (ppv), negative predictive value (npv), accuracy (acc) values for both the individual groups were calculated. ROC curves were prepared by the spec ve sens values. Both methods (conventional US and the sonoelastography) success rates and kappa analyses were determined.
Fig. 0

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Results

All three groups had different nodule-pseudonodule numbers as compared to the FNAB (Gold standard) (Table 2).

Group I had 33 cases with at least one nondemarcated but suspicious nodule on a heterogenous ground on US. FNAB results revealed only two cases as true nodules and the rest were pseudonodules supporting the thyroiditis. The sonoelastographic assessment stated one case with demarcated strain while the only true nodule or the other 32 pseudonodullary zones were isoelastical supporting pseudonodullary development.

Group II had 12 cases with hyperechogenic nodules. FNAB results revealed 9 cases as true nodules (benign colloidal nodules) and 3 cases as pseudonodules. Nine cases with true nodules had aliasing on the sonoelastography images. Three pseudonodules were demarcated in the gray scale US imaging but the sonoelastographic assessment revealed identical color aliasing which supported the isoelasticity of the nodulary area in concordance with background parenchyma also affected by HT.

Group III had nine cases with demarcated hypoechogenic nodules. FNAB results revealed three cases as true nodules (benign colloidal nodules) and six were pseudonodules. Three true nodules that were assessed with the sonoelastography and concordant with the cytopathological results were demarcated in the strain images while two of them were falsely reported as true nodules. Four other cases of this group were reported as pseudonodules with sonoelastography.

No malignancy was reported in the FNAB reports.

In differentiation of pseudonodules, while gray scale US has sens (85.7%), spec (77.5%), ppv (57.1%), npv (93.9%) ve acc (79.6%) values; rates for sonoelastography were; sens (92.9%), spec (95.0%), ppv (86.7%), npv (97.4%) and acc (94.4%) respectively.

The ROC curves with respect to the sens ve spec values, area under the curve (success rate) for US was calculated as 0.816 where it was 0.939 for the sonoelastography (p=0.0001<0.01) (Fig 2). US-FNAB were correlated by 54.4% and the sonoelastography-FNAB were correlated by 85.9% (Kappa analysis). Both methods were statistically significant as correlated with the FNAB (p=0.0001<0.01, McNemar Test).
Conclusion

In the HT, the true thyroid nodules misdiagnosed by conventional US are significantly recognized by sonoelastography and the sensitivity increases from 85.7% to 92.9%, specificity from 77.5% to 95.0% and the accuracy from 79.6% to 94.4%. Thus, in order to eliminate the needless surgical interventions, nodular lesions must be examined by sonoelastography, also.
References

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