

Hyperechoic Nodules In Hashimoto's Thyroiditis: Correlation with Cytopathological Findings; Biopsy may not be Necessary at all!

Hashimoto Tiroiditinde Hiperekoik Nodüller: Sitopatolojik Bulgular ile Korelasyon; Biopsi Gerekmebilir!

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ABSTRACT

Background: We aim to elucidate the histopathologic findings and the necessity of biopsy of the hyperechoic nodules found in Hashimoto's thyroiditis cases in their follow up.

Material and Method: The study included those 11 patients who had admitted to the outpatient clinics with the diagnosis of thyroiditis whom with high anti-TPO and/or anti-thyroglobulin antibody levels and hyperechoic thyroid nodule at US examination. Patients scanned with 14 MHz frequency high resolution linear probe. Fine needle aspiration of the individual nodules were performed and the whole data collected to a special archive. After six months, the histopathologic findings of the nodules, laboratory and radiologically findings were cumulatively evaluated.

Results: The mean dimension of the nodules was 19 mm (8-32 mm). In 10 of the cases, the nodules were solitary with hyperechoic homogeneous nature, in the other case there were two nodules, one nodule with the same sonographic appearance as above and the other with minimally cystic degenerations. In neither of the cases, no malignancy was reported in the histopathology.

Conclusion: Owing to benign nature of the homogenous hyperechoic or minimally cystic degenerated hyperechoic nodules found in the Hashimoto's thyroiditis, for the first step, it is sufficient that these cases be evaluated and can be followed-up by clinically and sonographically. In the future studies which accomplished with broad series, the necessity of the biopsy in the evaluation of these depicted nodules in Hashimoto's thyroiditis may be eliminated.

Keywords: Hashimoto Thyroiditis, Thyroid Nodule

ÖZET

Amaç: Bu çalışma ile Hashimoto tiroiditli olgularda saptanan hiperekojen nodüllerin histopatolojik inceleme bulguları eşliğinde radyolojik evaluasyonunu ve bu nodüllerden biopsi gerekliliğini araştırmayı amaçladık.

Gereç ve Yöntem: Hastanemize poliklinik servisinden müracaat eden ve Anti-TPO ve/veya Anti-tiroglobulin antikör düzeyleri yüksek olup, tiroidit tanısı almış ve sonografide hiperekoik nodülü tespit edilmiş 11 olgu çalışmaya dahil edildi. Hastalar 14 mHz'lik yüksek frekanslı bir transduser ile tarandı. Her bir nodüle, ince iğne aspirasyon biopsisi yapıldı ve veriler arşivde toplandı. Toplam 6 ay sonra, klinik ve radyolojik olarak Hashimoto tiroiditi ile uyumlu bu olguların verileri toplanıp değerlendirildi.

Bulgular: Ortalama nodül boyutları 19 mm (8-32 mm) idi. Toplam 10 olguda homojen hiperekojen nodül soliter iken, bir olguda benzer natürde, ancak diğeri periferik mikrokistik dejenerasyon gösteren iki nodül izlenmekte idi. Herhangi bir olguda malignite bulgusu tespit edilmemişti.

Sonuç: Benign natürü nedeni ile, Hashimoto tiroiditli olgularda minimal derecede kistik dejenerasyon alanları içeren veya tamamen homojen tarzda hiperekoik natürde izlenen nodüllerde ilk aşama için klinik ve sonografik takip yeterli olacaktır. Daha geniş seriler ile yapılacak çalışmalar ile Hashimoto'lu olgulardaki bu tür nodüllerde biopsi gerekliliği ortadan kalkabilir.

Anahtar Kelimeler: Hashimoto Tiroiditi, Tiroid Nodülü

INTRODUCTION

Hashimoto's thyroiditis (HT) is an autoimmune disease that predominantly affects elderly woman (1). Patients usually present with diffuse swelling of the gland especially in acute phase. Sometimes, these patients develop asymmetric local lumps (nodules) for which unnecessary surgical intervention may be instituted due to the suspicion of a carcinoma (2). In the glands of the patients that have been diagnosed as HT, there may be nodules that are iso-, hypo- or hyperechoic in nature on ultrasound. Besides, pseudonodules due to inflammation that is not demarcated well may be observed on ultrasound (3).

In this study, we aimed to investigate the nature of the hyperechoic nodules frequently found in the patients with HT and so clarify the follow-up strategy whether to accomplish by imaging methods or invasively by fine needle aspiration biopsy.

MATERIALS AND METHODS

From February 2006 to July 2007, 27 patients diagnosed as HT based on clinical and biochemical findings (anti-TPO = microsomal and/or anti-TG = thyroglobulin antibodies), underwent ultrasound examination of their thyroid glands at our institution. The patients scanned with 12-14 MHz frequency high resolution linear transducer (GE Logic 7 Ultrasound Imager-Milwaukee, WI).

The nodules embedded in the gland were evaluated for their features of size, echogenicity (iso-, hypo- or hyperechoic), composition (cystic, solid, or mixed, presence or absence of coarse or fine calcifications), margin (having a halo or an irregular border) and internal blood flow. Of the 27 patients evaluated, 11 (nine female, two male, mean age = 37 years) were included into the study with a total of 12 hyperechoic nodules. Vascularisation of these hyperechoic nodules were also

determined with low pulse repetition frequency settings on colour Doppler examination. After the US imaging, sonography guided fine needle aspiration (FNA) was performed with a 22-gauge needle. Each slice were fixed with alcohol and than stained by the May-Grunwald Giemsa method. All slices were evaluated at our pathology unit by two experienced pathologists.

Biochemical data including serum levels of free T3, free T4, thyroid stimulating hormone (TSH), auto-antibodies, all of which had been tested by means of radioimmunoassay on the day closest to the day of the US imaging study were also evaluated.

Sonographic findings, FNA cytology findings of the individual nodules and the biochemical values of the patients were collected.

RESULTS

The biochemical laboratory data of the patients are displayed in **Table 1**. On sonography, all glands were diffusely enlarged and of inhomogeneous echogenicity, with a generally increased vascularity (**Figure 1a**). Echogenicity of the thyroid gland was less than that of the strap muscles in all the patients. The mean dimension (in the transverse greatest diameter) of the nodules was 19 mm (8-32 mm, in the right lobe n = 6, in the isthmus n = 1, in the left lobe n = 5). While eleven of the nodules were homogenous hyperechoic in nature (**Figure 1b**), the other one was having peripheral micro-cystic degenerations (**Figure 1c**). Except one nodule which showed minimally increased low resistance (RI:0.52) internal vascularity, all of the other nodules demonstrated only mild peripheral and also low resistance (RI:0.50-0.54) vascularity (**Figure 2a**). No malignity was reported in the histopathology of these nodules (**Figure 1d, 2b**).

Histologic diagnosis were obtained for all nodules. Of the 12 nodules, follicular adenoma was found in three, pseudotumor in two and adenomatous hyperplasia in the remaining seven.

DISCUSSION

Of the inflammatory diseases of the thyroid, HT is the most common. It is also the most common cause of hypothyroidism. It is an autoimmune disease where antibodies develop against both thyroglobulin (Tg) and the thyroid peroxidase (TPO) enzyme (4, 5). The diagnosis of HT is usually confirmed by serological tests, including anti-Tg and anti-TPO antibodies, rather than FNA (3, 4, 5). Microscopically, there is diffuse infiltration of the thyroid parenchyma by lymphoplasmacytic infiltrates, which form lymphoid follicles, and varying amounts of fibrosis, which account for the sonographic nodular and hyperechoic band features (4). Besides these laboratory findings, the sonographic appearance of HT is often typical. Grossly, the gland is symmetrically enlarged, depleted of its fine granular echogenicity with visible discrete nodules separated with echogenic fibrous bands.

Generally speaking, microcalcifications, local invasion, metastasis to lymph nodes, greater dimension, markedly reduced echogenicity are helpful features in differentiating malignant from benign thyroid nodules although there can be some overlap between the US appearances (6). Other features such as absence of halo, ill-defined margins, solid composition, vascularity are less specific but may be used helpful signs (6).

We think that the nodule determined on US is perceived hyperechoic relatively due to the hypoechoic background of the actual thyroid gland in which an inflammatory process pursues. Besides, the vascularity of the gland and the nodule itself may differ according to the phase of the inflammatory response and disease process. This may cause faulty

results on Doppler US examination of these nodules.

There are some reports of palpation-guided FNA of nodules associated with HT (7, 8). In these studies it is reported that, in contrast to hyperechoic nodules which were mentioned to be usually benign, hypoechoic nodules involve carcinomas and lymphomas. However, to our knowledge, only one study includes the follow-up and cytology reports of the nodules of the patients with HT (2).

The authors in this study have examined all of the nodules found in the glands of patients with HT and hyperechoic nodules have not been emphasized particularly. Contrary to previous studies, we only included the hyperechoic nodules into our study which were found to be all benign histologically. Hyperechogeneity of a nodule in HT may be called as "don't touch lesion" when observed on US examinations on follow-up of these patients.

The small number of the hyperechoic nodules investigated is one limitation of the study. Our study is the first investigating particularly the hyperechoic nodules and their nature. Future studies needed to clarify this relationship.

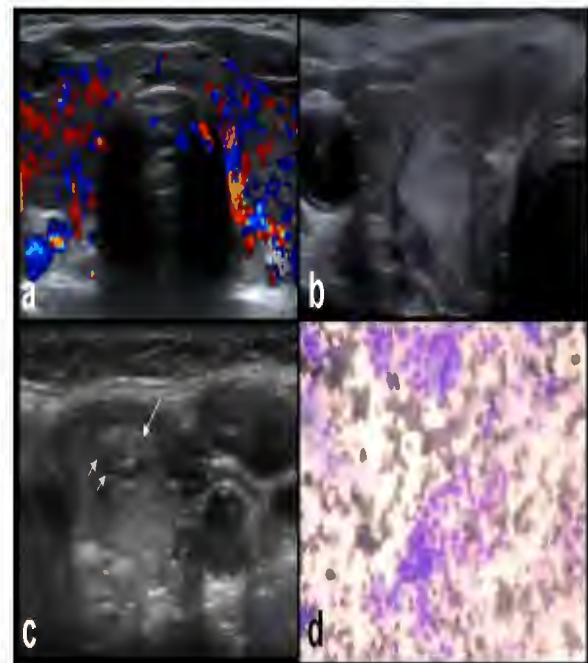


Figure 1. Images from different patients **a)** Diffusely enlarged thyroid gland and a general increased vascularity on color Doppler US window image. **b)** Hyperechoic nodule which has peripheral regular hypoechoic halo. **c)** Heterogenous hyperechoic nodule with microcystic degenerations (arrows). **d)** Microscopy of the fixed specimen (from the nodule at c) with alcohol and then stained with May- Grunwald Giemsa method. No malignancy reported but only hypercellular normal thyrocytes, inflammatory macrophages and lymphocytic infiltrations were noted.

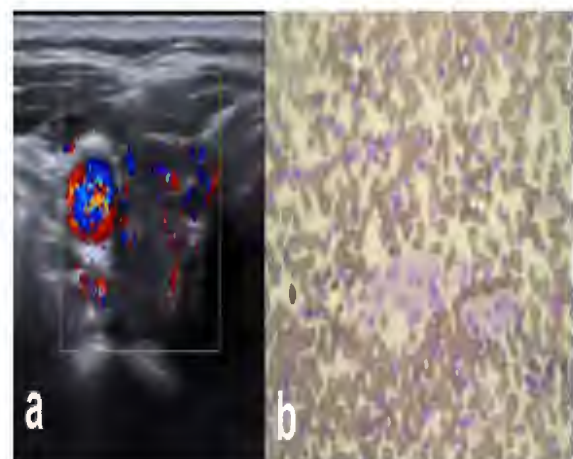


Figure 2. **a)** Doppler US shows the increased vascularity of lateral pole of the echogen nodule in the right lobe. **b)** FNAB findings (May-Grünwald-Giemsa) concordant with hyperplastic nodule that consist normal size thyrocytes and scattered lymphocytes that support HT.

Table 1. Serological laboratory test results.

Patients (number)	TSH* (mean±SD)	ft3*, ft4*
10(subclinical hypothyroid)	6.9±1.8	ft3 normal (n=10), ft4 normal (n=8), ft4 subnormal (n=2)
1(hyperthyroid-acute phase)	0.25	ft3 high (4.28 pg/ml), ft4 high (4.5 ng/dl)
All patients had high Anti-TG and Anti-TPO levels (170±31 IU/ml and 430±142 IU/ml respectively).		

*: Abbreviations and reference values; (TSH: Thyroid stimulating hormone (0.35-4.94 microIU), ft3: free triiodothyronine (1.71-3.71 pg/ml), ft4: free tetraiodotreonin (0.70-1.48 ng/dl), Anti-TPO: thyroid peroxidase antibody (0-5.61 IU/ml), Anti-TG: thyroglobuline antibody (0 IU/ml).

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