TİROİD NODÜLLERİNDE MALİGNİTE POTANSİYELİNİ DEĞERLENDİRMEDE ULTRASOUND VE SİNTİGRAFİNİN YERİ

The Value of Ultrasound and Scintigraphy in Evaluating Malignant Potential in Thyroid Nodules

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ÖZET

Amaç: Çalışmamızda tiroid biyopsisi yapılmış hastalarda ultrasonografi (USG), tiroid sintigrafisi bulguları, tiroid fonksiyon testleri (TFT) değerleri ve tiroid biyopsi sonuçları arasında ilişkiyi saptamayı amaçladık.

Gereç ve Yöntemler: Aralık 2013-Mayıs 2015 tarihleri arasında Sivas Numune Hastanesi Nükleer Tıp kliniğine başvuran ve USG eşliğinde tiroid ince iğne aspirasyon biyopsisi (TİİAB) yapılan nodüler guatr tanılı 101 hasta retrospektif olarak incelendi. Tiroid biyopsi patoloji sonucu diagnostik olanlar , USG ve tiroid sintigrafisi hastanemizde yapılan olgular çalışmaya dahil edildi. Tiroid nodülü olan hastalarda TFT değerleri, USG'deki ekojenite, kalsifikasyon, kenar düzensizliği ve sintigrafideki nodül karakteri nodülün malign benign potansiyelini değerlendirmede kullanıldı.

Bulgular: TİİAB yapılmış olgularda; TSH ile nodül boyutu, nodül ekojenitesi, kenar düzenliği, kalsifikasyon arasında; sintigrafideki nodül karakteri ile nodül boyutu, ekojenite, kenar düzenliği, kalsifikasyon arasında; patoloji sonucu ile nodül boyutu, ekojenite, sintigrafide nodül karakteri ve TSH arasında istatiksel olarak anlamlı bir ilişki bulunmadı (p>0,05). Mikrokalsifikasyon (p<0,001) ve kenar düzensizliği (p<0,001) ile malignite arasında istatistiksel olarak anlamlı ilişki saptandı. Mikrokalsifikasyon ve kenar düzensizliği birlikteliğinde malignite açısından istatistiksel anlamlılık mevcuttu (p<0,001). Mikrokalsifikasyon, kenar düzensizliği ve sintigrafide izlenen nodülün hipoaktifliği birlikteliğinde malignite açısından istatistiksel olarak anlamlılık mevcuttu (p=0,003).

Sonuç: Tiroid nodülünde USG de mikrokalsifikasyon, kenar düzensizliği ve tiroid sintigrafisinde hipoaktif nodül birlikteliğinde nodül büyüklüğüne bakılmaksızın TİİAB yapılmalıdır.

Anahtar Sözcükler: *Tiroid; USG; Sintigrafi; TİİAB.*

ABSTRACT

Objective: We aimed to determine the relationship between ultrasonography (USG), thyroid scintigraphy findings, found in thyroid function test values (TFT) and thyroid biopsy results in patients who had undergone thyroid biopsy.

Method: In the study, 101 patients with nodular goiter who were admitted to Sivas Numune Hospital, Nuclear Medicine Clinic between December 2013 and May 2015, and underwent thyroid fine needle aspiration biopsy (TIAB) under USG were retrospectively reviewed. Those with a diagnostic pathology report after thyroid biopsy and patients who underwent USG and thyroid scintigraphy in our hospital were included in the study. In patients with thyroid nodules, TFT values, echogenicity, calcification, irregular borders in USG and characteristics of the nodule in the scintigraphy examination were used in assessing malignant or benign potential of nodules.

Findings: In TIAB cases, no statistically significant correlation was found between TSH and the nodule size, nodule echogenicity, border regularity, calcification; between nodule size, echogenicity, border regularity, calcification in the scintigraphic nodule character; and between pathology results and nodule sizes, echogenicity, nodule characteristics in scintigraphy and TSH (p> 0,05). There was a statistically significant relation between microcalcifications (p <0,001) and irregular borders (p <0,001). There was a statistical significance in terms of malignancy when microcalcification and irregular borders coexisted (p <0.001). There was a statistical significance in terms of malignancy when microcalcification, irregular borders and hypoactivity of the nodule in scintigraphy coexisted (p = 0,003).

Conclusion: TIAB should be performed regardless of nodule size when microcalcification, irregular borders and hypoactive nodule in thyroid scintigraphy coexist in US examination of a thyroid nodule.

Keywords: *Thyroid; USG; Scintigraphy; TIAB.*

INTRODUCTION

Thyroid nodules are among the most common endocrinal disorders in the world. A nodule is seen in approximately 4-7% of the population without iodine deficiency, but this ratio is increased in regions where iodine deficiency is detected (1). There are no significant clinical findings in the majority of patients. The most valuable test that directly reflects thyroid functions is serum TSH. Thyroid hormone levels need to be determined in order to determine the degree of hyper and hypothyroidism detected by TSH. Thyroid nodules are evaluated using USG, thyroid scintigraphy and TIAB. USG is the first preferred imaging modality for the assessment of thyroid nodules (2).

Thyroid scintigraphy provides information about thyroid position, structure and function. Thyroid scintigraphy performed with a gamma camera and pinhole collimator can be used to visualize lesions between 4-6 mm in size. While Tc-99m pertechnetate can be used most commonly in thyroid scintigraphy, I-131 and I-123 can also be used. Technetium-99m has a half-life of 6 hours, and is low in energy, releasing a gamma radiation of 140 kilo electron volt (keV). Uptake is done by the thyroid but is not organified. Base activity is greater in this examination than iodinated scintigraphy. Thyroid scintigraphy is used to determine the thyroid/salivary gland ratio, characteristics of thyroid tissue and the nodules (hypoactive, normoactive, hyperactive) (3).

In thyroid nodules, it is very important to perform benign-malignant differentiation and to identify the patients who require surgical treatment. The gold standard method used for this is TIAB. It is a simple and safe procedure and sufficient material in experienced hands can be obtained in 90-97% of solid nodule aspirations (4). Sensitivity of TIAB is 88.2-97%, specificity is 47-98.2%, false negativity is 0.5-10%, and false positivity is 1-7% in detecting malignant nodules. TIAB is recommended for nodules with a thickness above 1 cm. However, in recent studies, it is suggested that when a limit of 1 cm is set for diameter for performing a TIAB, this may result in omitting many cancerous cases where there are nodules smaller than 1 cm. For this reason, thoroughly examining high risk nodules found in USG in terms of malignancy is highly recommended (2).

In our study, we aimed to determine the relationship between USG, thyroid scintigraphy findings, TFT values and thyroid biopsy results in patients with thyroid biopsy.

MATERIALS AND METHODS

In this study, 101 patients with nodular goiter who were admitted to Sivas Numune Hospital, Nuclear Medicine Clinic between December 2013 and May 2015 and underwent TIAB under USG guidance were retrospectively reviewed. Cases with a diagnostic pathology results from thyroid biopsy, and those who had USG and thyroid scintigraphy examinations at our hospital were included in the study.

FreeT3, freeT4 and TSH levels of patients were measured using electrochemiluminescence assay, and reference intervals for free T3 were reported as 0.67-7.02 pmol / L (2.0-4.4 pg / mL), for free T4 as 0.76-2, and for TSH as 0.01-12.56 (0.27-4.2 microIU / m L) (Roche Diagnostics GmbH D-68298 Mannheim, Germany). The USG examinations of the patients were performed by a radiologist using a Toshiba Aplio 500 device. Nodule size, echogenicity, calcification and irregular borders were retrospectively studied.

In thyroid scintigraphy, after intravenous 5 mCi Tc-99m pertechnetate injection, images were obtained in a period of 10-30 minutes using pinhole collimator with Siemens Symbia E device and images with 200.000 count rate using 20% window were taken so that submandibular glands and jugular notch would be in the imaging area. Characteristics of the thyroid gland and nodule were identified (hyperactive, hypoactive and isoactive).

Prior to TIAB, the patient's head was brought to a light hyperextension with supine position. Local anesthesia was not performed. The entry area was cleaned with 10% povidone solution. Aspiration was performed

using 22 G needle and 10 cc injector in the guidance of SonoScape A6V USG. During aspiration, the needle was seen in the nodule and it was advanced to various regions in the nodule and aspirated by back and forth vacuuming. Acquired materials were spread on the slides and fixed with 70% alcohol.

STATISTICAL DATA

SPSS-17.0 statistical package program (Statistical Package for Social Science) was utilized for the analysis of data and statistical methods. Student's t test was used for two independent groups in the normal distribution variables and Mann-Whitney U test was used for the abnormal distribution variables. The Chi-square (x2) test was used to assess the differences between the categorical variables. P <0.05 was considered statistically significant in analyses.

FINDINGS

Of the 101 patients who underwent TIAB, 93 were females (92.1%) and 8 were males (7.9%). The mean age of all patients was 50 ± 14 (20-82), of females 49 ± 14 and males 62 ± 12 years. In 90 of these patients, pathologic end result was benign (89.1%), and it was malignant in 11 cases (10.9%). All of the 11 patients with malignancy were females. The size of nodules in USG were as follows: below 1 cm: 9 (8,9%), 1-3 cm: 71 (70,3%), 3 cm and above: 21 (20,8%). Nodule size was less than 1 cm in one (11.2%) of the 11 patients with malignancy, between 1 and 3 cm in 8 patients (11.3%) and it was larger than 3 cm in 2 patients (9.6%). These nodules were hypoechoic (45.5%) in 46 patients in USG and 5 of these hypoechoic nodules were malignant. Twenty-nine patients had hyperechoic (28.7%) and 5 of them were maligned, 12 patients had isoechoic (11.9%) and one of them was malignant, 14 patients had a nodule mixed in character (13.9%) and no malignancy was detected in these nodules. In USG, 6 patients had irregular borders (5.9%) in nodule and irregular borders were not defined in 95 (94.1%) patients. Malignancy was detected in 5 (83.3%) of the 6 patients with irregular borders and in 6 of 95 patients without irregular borders. There was no calcification in 83 (82.2%) patients' nodules, macrocalcification was present in 11 (10.9%) and microcalcification was seen in 7 (6.9%) patients. Malignancy was found in 1 (9,1%) of the 11 patients with macrocalcified nodules, and in 4 (57,1%) of the 7 patients with microcalcification nodules, and in 6 (7.2%) of the 83 patients with non-calcified nodules. The TSH, fT3, fT4 values of 98 patients were evaluated. The TSH value of 8 patients was below 0.27 microIU/ml, 2 of which were malignant (25%), and in 90 patients it was above 0.27 microIU/ml and 8 of them were malignant (6.8%). Thyroid scintigraphy was present in 41 of 101 patients with TIAB. There were 8 hyperactive nodules (19,5%), 30 hypoactive nodules (73,2%) and 3 isoactive nodules (7,3%) in these patients. Malignancy was not detected in 3 patients with isoactive nodule. Malignancy was found in 6 of 30 patients with hypoactive nodule (20%) and in 1 of 8 (12.5%) patients with hyperactive nodule. Scintigraphy findings of 4 patients with malignancy could not be found in our retrospective study. Malignancy was detected in four of 5 patients (80%) with microcalcification along with irregular borders. Three (75%) of 4 patients with microcalcification, irregular borders and hypoactive nodule on thyroid scintigraphy had malignancy.

In TIAB cases, no statistically significant correlation was found between TSH and nodule size, nodule echogenicity, border regularity, calcification; between nodule size, echogenicity, border regularity, calcification in the scintigraphic nodule character; and between pathology result and nodule size, echogenicity, nodule characteristics in scintigraphy and TSH (p> 0,05). There was a statistically significant relation between microcalcifications (p <0,001) and irregular borders (p <0,001). There was a statistically significance in terms of malignancy when microcalcification and irregular borders coexisted (p <0.001). There was a statistical significance in terms of malignancy when microcalcification, irregular borders and hypoactivity of the nodule in scintigraphy coexisted (p = 0,003). (Table 1).

	Nodules (number(%))	Benign nodule(number(%))	Malign nodule(number(%))	P
Nodul Size				
0-1 cm	9 (8,9)	8 (88,8)	1 (11,2)	0,579
1-3 cm	71 (70,3)	63 (88,7)	8 (11,3)	
>3 cm	21(20,8)	19 (90,4)	2 (9,6)	
Nodul echogenicity				
Hyperechoic	29 (28,7)	24 (82,8)	5 (17,2)	0,272
Hypoechoic	46 (45,5)	41 (89,1)	5 (10,9)	
İsoechoic	12 (11,9)	11 (91,7)	1 (8,3)	
Mixed	14 (13,9)	14 (100)	0	
Irreguler borders				
Irreguler	6 (5,9)	1 (16,7)	5 (83,3)	<0,001
Reguler	95 (94,1)	89 (93,7)	6 (6,3)	
Calsification				
Non-calsification	83 (82,2)	77 (92,8)	6 (7,2)	<0,001
Microcalsification	7 (6,9)	3 (42,9)	4 (57,1)	
Macrocalsifikation	11 (10,9)	10 (90,9)	1 (9,1)	
TSH values				
TSH<0,27	8 (8,2)	6 (75)	2 (25)	0,181
TSH<0,27	90 (91,8)	82 (93,2)	8 (6,8)	
Scintigraphy findings				
Hypoactive	30 (73,2)	24 (80)	6 (20)	0,166
Hyperactive	8 (19,5)	7 (87,5)	1 (12,5)	
İsoactive	3 (7,3)	3 (100)	0	
Associations				
USG Microcalcification+ border disorder	5(100)	1 (20)	4(80)	0,001
USG Microcalcification+ border disorder+				
Scintigraphic hypoactivite	4(100)	1(25)	3(75)	0,003

DISCUSSION

Thyroid nodules are among the most common endocrinal disorders in the world. Nodule is seen in approximately 4-7% of the population without iodine deficiency, but this ratio is increased in regions where iodine deficiency is detected (1). Thyroid cancers are the most common endocrinal cancers in the world however they constitute only 1% of all cancers. The incidence of annual thyroid cancer in males in the USA is about 1,2-2,6 in100.000; in females it is about 2-3000 in 100.000 (1).

The literature shows that the risk of malignancy increases below 16 years of age and over 45 years of age. Thyroid nodules are 5-11 times more common in females than males. In a study by Sclabas GM et al. conducted on 240 cases, nodule prevalence was 3 times higher in females than in males, while Yang J et al. reported that females had 5.4 times higher nodule prevalence than males in 4703 cases (5-8). The average age of patients in our study was over 50 years. We had no patients under 16. Ninety-three of 101 patients were females, 8 were males. Number of the female patients was higher, in accordance with the literature. All of the cases with malignancy in our study group were females.

Ultrasonography, the most preferred diagnostic modality for thyroid diseases, is a reliable and rapid method for assessing thyroid nodules (9). There are many advantages of using the USG in imaging the thyroid gland. These include characterizing the nodule (solid or cystic), ability to reveal the presence of other nodules, usability in follow up of the detected nodules, ability to give an idea about the presence of thyroiditis, ability to recognize the accompanying pathological cervical lymph nodes and ability to guide the biopsy. However, no ultrasound scan alone features high sensitivity and specificity.

Studies conducted to evaluate the role of USG in thyroid nodules reported a 3-times increase in the risk of cancer in presence of microcalcifications and 2-fold increase in presence of macro-coarse calcifications. The sensitivity of sonographic microcalcifications for nodular malignancy was 76%, specificity 44-95%, and positive predictive value 77.9% (9,10). In a study conducted by Kwak et al., malignancy was detected in 92 (86%) of 107 patients who had irregular borders in the nodule in USG examination and in 111 (68.5%) of 162 patients who had microcalcification (11). In our study, 4 of 7 cases with microcalcification in the nodule had malignancy (57.1%) and 1 of 11 cases with macrocalcification nodule had malignancy (9.1%). Malignancy was detected in 5 of 6 patients with irregular border in the thyroid nodule (83.3%). Moreover, coexistence of microcalcifications in the nodule with irregular borders are statistically significant in terms of malignancy.

Thyroid malignancies tend to be more common as hypoechoic nodules in in USG examination. In the literature, microcalsification as an ultrasonographic image is interpreted in favor of hypoechoic malignancy (12). In our study, there was no statistically significant relationship between hypoechogenicity and malignancy, which may be due to scarce number of patients.

Thyroid scintigraphy is used to determine the characteristics of the nodules (hypoactive, normoactive, hyperactive) (3). Malignancy has been reported in 10-25% of hypoactive nodules in scintigraphy (13). In some studies this rate reaches up to 35% (14). In our study, when the cases with scintigraphy were analyzed, malignancy was found in 6 of 30 cases with hypoactive nodule (20%) and it is in accordance with the literature. The risk of thyroid cancer in hyperfunctional nodules was 6.5% according to the literature, while in a study by Lee et al., rate thyroid cancer was 11% in hyperfunctional nodules. In our study, malignancy was detected in 1 of 8 patients with hyperactive nodule in scintigraphy (12.5%) (15). Some of the hyperactive nodules that were reported as hyperactive with Tc99m pertechnetate would have been considered as hypoactive if they had been evaluated by iodine scintigraphy. Tc-99m pertechnetate scintigraphy can result in false positive results since lesions can be detected before organification (15,16).

While USG and thyroid scintigraphy findings can be suggestive of malignancy, in terms of diagnosis, ultrasound-guided TIAB should be the next procedure. The sensitivity and specificity of TIAB varies between 80 up to 100% in most studies (7). TIAB is generally recommended for nodules larger than 1 cm and; those with a risk factor in ultrasound (hypoechogenicity, microcalcification, irregular borders) and measuring less than 1 cm (4,5).

As a result, we suggest that TIAB should be performed regardless of nodule size when microcalcification and irregular borders are found in ultrasound along with hypoactive nodule detected in thyroid scintigraphy.
Limitations of the study: Our study is a single centered and retrospective study. In addition to the low number of patients, the lack of a single radiologist and nuclear medicine physician performing ultrasound and scintigraphy in patients and absence of both 'interobserver' and 'intraobserver' analyzes constitute the limitations of the study.

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