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Research Article

The evaluation of fine needle aspiration biopsy results in differentiating between benign and malignant thyroid nodules

Tiroit nodüllerinde benign-malign ayrımında ince iğne aspirasyon biyopsi sonuçlarının değerlendirilmesi

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Abstract

Introduction: Thyroid fine-needle aspiration biopsy (FNAB) has begun playing an important role in the evaluation of thyroid nodules, in addition to physical examination and imaging techniques. The purpose of this study was to evaluate the results of patients who underwent thyroid FNAB together with their demographic data, imaging findings, and follow-up compliance.

Methods: Patients who underwent thyroid FNAB procedures in our hospital's interventional radiology unit between January 2022 and May 2024 were evaluated retrospectively. Data were retrieved from patient records. Cytological results were classified as malignant, atypia of undetermined significance, benign, and non-diagnostic material.

Results: Two hundred twelve solid nodules were detected in the patients who underwent biopsy, and 59 mixed nodules with a cystic component. Non-diagnostic material was reported in 51 cases at cytological examination, benign cytology in 150, atypia of undetermined significance in 53, and malignant material in 17. The incidence of non-diagnostic results was significantly higher in hypoechoic nodules and low-volume nodules.

Conclusions: Thyroid FNAB is a valuable diagnostic tool due to its ease of application and provision of useful information in benign-malignant differentiation. Once it becomes capable of application by primary physicians and local state hospitals in Türkiye it will reduce delayed diagnoses, unnecessary surgical procedures, and economic burdens on social security institutions.

Keywords: Thyroid Nodule, Fine-Needle Biopsy, Ultrasonography

Öz

Giriş: Tiroit ince iğne aspirasyon biyopsisi (İİAB), fizik muayene ve görüntüleme tekniklerine ek olarak tiroit nodüllerinin değerlendirilmesinde önemli bir rol oynamaya başlamıştır. Bu çalışmanın amacı, tiroit İİAB uygulanan hastaların demografik verileri, görüntüleme bulguları ve takip uyumları ile sonuçlarını değerlendirmektir.

Yöntem: Ocak 2022 ile Mayıs 2024 tarihleri arasında hastanemizin girişimsel radyoloji ünitesinde tiroit İİAB uygulanan hastalar retrospektif olarak değerlendirildi. Veriler hasta kayıtlarından elde edildi. Sitolojik sonuçlar malign, önemi belirsiz atipi, benign ve tanısal olmayan materyal olarak sınıflandırıldı.

Bulgular: Biyopsi uygulanan hastalarda 212 solid nodül ve kistik bileşenli 59 mikst nodül tespit edildi. Sitolojik incelemede 51 olguda tanısal olmayan materyal, 150 olguda iyi huylu sitoloji, 53 olguda önemi belirsiz atipi ve 17 olguda kötü huylu materyal rapor edildi. Tanısal olmayan sonuçların görülme sıklığı hipoekoik nodüllerde ve düşük hacimli nodüllerde anlamlı olarak daha yüksekti.

Sonuç: Tiroit İİAB, uygulama kolaylığı ve iyi huylu-kötü huylu ayrımında yararlı bilgi sağlaması nedeniyle değerli bir tanı aracıdır. Türkiye'deki birincil hekimler ve yerel devlet hastaneleri tarafından uygulanabilir hale geldiğinde gecikmiş tanıları, gereksiz cerrahi prosedürleri ve sosyal güvenlik kurumlarındaki ekonomik yükleri azaltacaktır.

Anahtar kelimeler: Tiroit Nodülü, İnce İğne Biyopsisi, Ultrasonografi

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Key Points

1. Malignancy is more common in nodules with microcalcification.
2. Non-diagnostic results are more common in low-volume nodules.
3. The incidence of atypia of undetermined significance increases in hypoechoic nodules.

Introduction

The thyroid is the body's largest endocrine gland, abnormal growth being known as goiter. This growth can be diffuse or else derived from one or more nodules. Thyroid nodule diseases are the most widespread thyroid lesions encountered in regions with low iodine intake [1]. Detection rates have improved with the widespread use of ultrasonography (USG) of the neck and technological advances in USG equipment. A prevalence in the community of 4-7% has been reported with physical examination, compared to 13%-67% with USG [2]. It has been reported in approximately 40% of the population in the autopsy series, the malignancy rate in these nodules being approximately 5% [3]. Although the malignancy rate is low, nodules nevertheless represent an important problem in terms of public health and costs due to their prevalence in the community.

Since thyroid nodules can exhibit a gradual course and be asymptomatic, early diagnosis can be problematic. Imaging methods are not sufficient for differentiating between benign and malignant nodules, and this may result in unnecessary surgery or delayed diagnosis [1]. Thyroid fine-needle aspiration biopsy (FNAB) evaluation of all nodules regarded as suspicious at USG is recommended. Thyroid FNAB currently plays an important role in differentiating between neoplastic and non-neoplastic lesions and in determining the need for surgery. Accurate diagnosis can be achieved by combining USG and scintigraphy in suspected cases.

The purpose of this study was to perform a retrospective evaluation of thyroid FNAB results performed following USG in the Çanakkale Onsekiz Mart University Medical Faculty interventional radiology clinic, Türkiye.

Methods

The study population consisted of 291 patients presenting to our hospital between January 2022 and May 2024, with thyroid nodules detected at USG, and undergoing thyroid FNAB. Twenty patients younger than 18 were excluded. Two hundred seventy-one patients were thus finally enrolled.

Nodule evaluation was performed using a routine protocol during USG examination, including size, internal structure, contour structure, echogenicity pattern, the presence of microcalcification, and vascularization. Only age and sex information in the patient files were included on the data form. Indications for biopsy were determined by the physician requesting thyroid FNAB.

Ultrasonographic examinations were conducted using a Samsung RS 80 device and a 3-12 MHz linear transducer probe. Biopsy procedures in our hospital are carried out using a routine protocol. Accordingly, an informed consent form is obtained from all patients prior to the procedure. The thyroid biopsy procedures were all performed by the same physician. The patient was placed in a supine position with the head in hyperextension. The procedure site was first cleansed with povidone iodine, and the USG probe was covered with a sterile sheath. The nodule was entered with USG guidance, and the needle tip was moved inside the nodule in the same plane. In the case of nodules with a large cystic component, the thyroid FNAB procedure was performed once that component had been emptied. A 21 gauge needle was employed in all cases, and the procedure was repeated twice. After the procedure had been carried out under negative pressure with a 10 ml injector, the negative pressure was terminated, and the needle was withdrawn. The patients were re-evaluated in terms of hematoma under USG guidance approximately 30 min after thyroid FNAB. The thyroid FNAB results were classified as insufficient sample, benign, atypia of undetermined significance (AUS), and malignant. No local anesthetic substance was employed during the procedure.

Statistical Analysis

Data analyses were performed on SPSS software (SPSS Inc., Chicago, IL, USA). Mean, standard deviation, range minimum, maximum, and percentage values were given for descriptive analysis. Differences between the groups were evaluated using Student's t test and the chi-square test. p values smaller than 0.05 were considered statistically significant.

Ethical approval was obtained from the Çanakkale Onsekiz Mart University Rectorate Graduate Education Institute Ethics Committee Scientific Research and Publication Ethics Commission with the decision numbered 11/14 dated 25.07.2024.

Results

Two hundred seventy-one patients, 222 women and 49 men, were included in the study. The total mean age was 53.66 ±14.17 years. Mean ages were 53.13±13.36 years for women and 56.10±17.32 for men. There was no significant age difference between the sexes. One hundred thirty-nine thyroid nodules subjected to biopsy were in the right lobe, 127 in the left lobe, and five in the isthmus. In terms of morphology, 212 nodules were solid, and 59 were mixed with a cystic component. The second biopsy results among the 12 of the 51 patients with non-diagnostic material reported after biopsy who subsequently re-presented were reported as AUS in three cases, adenomatoid nodule in three, and non-diagnostic material in six. Non-diagnostic material was finally reported in 51 cases, benign cytology in 150, AUS in 53, and malignancy in 17 (Table 1).

There was no difference in terms of non-diagnostic results between the solid and mixed type nodules (p=0.346). However, the nodule volume was significantly lower in the patients with non-diagnostic nodules than those with diagnostic nodules (p<0.001).

Malignant results were reported in 17 patients, papillary carcinoma being determined in 10, follicular carcinoma in five, and medullary carcinoma in two.

Table 1. Distribution of thyroid FNAB cytology results

Thyroid FNAB diagnosis	Case number	percentage (%)
Non-diagnostic material	51	18.83
Benign cytology	150	55.35
Atypia of undetermined significance	53	19.55
Malignant cytology	17	6.27

Evaluation of nodule echogenicity characteristics in patients with AUS revealed a significantly greater incidence of AUS in hypoechoic nodules (p=0.047, Table 2). Similarly, the incidence of AUS was higher in patients with a single nodule (p=0.009), although no association was determined with nodule contours (p=0.574). In contrast, irregular borders were significantly more common in malignant lesions (p=0.006). No relationship was observed between malignancy and gender or nodule numbers. Microcalcification was present in 21 of the nodules subjected to biopsy and macrocalcification in 33, malignancy rates being significantly higher in nodules with microcalcification (p<0.001).

Table 2. The relationship between atypia of undetermined significance and nodule echogenicity

Echogenicity	AUS (-)	AUS (+)	Total	p
Hypoechoic	146	43	189	0.047
Isoechoic/Hyperechoic	72	10	82	
Total	218	53	271	

Student's t test, AUS: Undetermined significance

Discussion

Thyroid nodules are usually round or oval-shaped lesions of different sizes that develop in the thyroid gland. These ubiquitous entities are more prevalent in regions with low iodine intake levels. The method used to detect nodules also affects these results. The prevalence in the community determined by means of palpation is 4-7%, while figures of approximately 13-67% are reported with USG [1]. The prevalence is higher in women and rises with age [4]. Women also outnumbered men in the present study. However, our study was intended for the cytological examination of existing nodules, rather than for the detection of new ones. The gender difference may be due to nodules being observed more frequently in women, or to women attaching greater importance to cosmetic problems and being more sensitive on the subject of health.

Patients may be present with cosmetic problems or pressure symptoms deriving from swelling in the neck or may be identified incidentally. Additionally, they may be identified at USG tests performed in cases of thyroid dysfunctions emerging for various reasons. Nodules detected incidentally are frequently smaller than 15 mm. Due to the retrospective nature of the present study, it was unclear how the nodules were first detected.

Pinchot et al. reported an age-related increase in the incidence of malignancy [5], although Şahin et al. observed no association with age [6]. No association was also observed either by Raparia et al. or in the present study [7].

Thyroid nodules can be single or numerous. Some studies have reported that palpable thyroid masses generally consist of more than one nodule at USG examination [8]. Morphological characteristics can be evaluated in addition to the presence of nodules using USG. An irregular contour, the absence of a distinct border, hypoechogenicity, and intranodular bleeding can predict malignancy at USG, although the positive predictive value of these findings is low [9].

Scintigraphy and thyroid FNAB can be used in addition to clinical findings and USG in the diagnosis of thyroid lesions. Thyroid FNAB is currently one of the main diagnostic methods employed in almost all centers. The first cytological diagnosis in this area was made by Martin and Ellis in the 1930s, and it began being widely employed in Europe and Scandinavian countries from the 1950s onward [10,11].

In addition to being effective in discriminating between benign and malignant thyroid nodules, FNAB is also inexpensive, simple, and minimally invasive. However, one important problem involves non-diagnostic results. The non-diagnostic material problem has been reported at rates of 8-24% in the literature [12]. This limitation is affected by the experience of the pathologist and radiologist, and by the nodule size. Hall et al. reported that non-diagnostic material was detected at a rate of 6.4% by hospital physicians and of 32% by physicians working in the field [14]. This result indicates the importance of the experience of the physician performing the biopsy. The non-diagnostic material rate in the present study was 21%, with a negative correlation being observed between non-diagnostic results and the nodule volume. We think that the presence of 4-5 mm and deeply seated nodules in our patients may partly explain this high figure. One interesting association in this research was the statistically significantly higher incidence of non-diagnostic material in hypoechoic nodules. Lili et al. reported a similar finding. This may be associated with greater fibrosis and a hemorrhagic structure in hypoechoic nodules.

The frequency of non-diagnostic results rises as the cystic component in the nodule increases or as the nodule size decreases [12]. This was consistent with the present study. Performing a biopsy after the cyst has been drained may be effective in lesions with large cystic components. In their study of 2234 patients, Jack et al. reported non-diagnostic biopsy results in 8% of repeat biopsies, even in patients with thyroid cancer. Another conclusion discussed in that study was that the procedure should be repeated in the case of non-diagnostic results, but that surgery or close follow-up are required in the event of repeated non-diagnostic results [4]. Inan G et al. evaluated FNAB results and surgical outcomes and reported non-diagnostic specimens in 31.3% of patients, with malignancy being reported in four of these after surgery [15]. The American Thyroid Association recommends the repetition of non-diagnostic FNAB together with cytopathological evaluation in the biopsy site if possible [16]. Follicular lesions represent another important problem. Follicular edema/follicular carcinoma, the differential diagnosis of which can be established by means of capsule and vascular invasion in tissue, also create a diagnostic difficulty for FNAB [13].

Another important problem for FNAB is AUS. Various studies have reported AUS rates of between 2% and 18% [17]. İyidir et al. reported an incidence of 7%. They also reported a malignancy rate of 25% in cases with AUS [18]. The risk of malignancy in these patients is significant, and clinicians must take due care when planning of repeat FNAB or surgery. Age, sex, radiological findings, detailed history, and physical examination findings must all be evaluated as an integral whole [6]. Renshaw et al. reported a false negative rate for FNAB of 2.7%. Those authors noted that interpretation, sampling errors, or newly developed lesions may all affect false negativity [19]. A number of recent papers have shown that malignancies may develop gradually in some patients with benign pathologies.

Another controversial issue is the size of the needle to be employed. Some studies maintain that 21 gauge needles can yield greater cellular material than 25 and 27 gauge needles [20]. However, Lili et al. reported no difference in specimens collected using needles of different sizes [21].

Various factors can be considered in terms of surgical treatment in non-diagnostic cases or those in which no definite diagnosis is possible, such as AUS. These factors include suspicion of malignancy at USG, a marked increase in size, exposure to radiation, cosmetic problems, and compression effects [4,22].

Limitations

The principal limitations of this study involve its retrospective character and the fact that the patients could not be primarily followed by our clinic. Cases undergoing biopsy are referred to us for diagnosis from the general surgery, ear nose and throat, and internal diseases clinics. This reduces our effectiveness in terms of patients' follow-up compliance. Another limitation is the low number of patients undergoing surgery.

Conclusions

Thyroid FNAB reduces nodule diagnosis costs. It also offers advantages of high sensitivity and specificity rates, reducing the numbers of operations and unnecessary surgical procedures, and the absence of severe complications. However, due to false positives and negativity, evaluation in combination with clinical findings and imaging methods will be advantageous for both the patient and the physician. Once the procedure can be applied by primary physicians it will provide further advantages, such as early diagnosis and a reduction of the labor and cost burden on regional hospitals.

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Author Contributions	Author Initials
SCD (Study Conception and Design)	GCU, NT
AD (Acquisition of Data)	GCU, NT
AID (Analysis and Interpretation of Data)	GCU, NT
DM (Drafting of Manuscript)	GCU
CR (Critical Revision)	GCU, NT

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