THYROID FINE NEEDLE ASPIRATION BIOPSY: WHICH METHOD SHOULD BE PREFERRED IN AN ENDEMIC GOITER REGION?

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ABSTRACT

To prospectively compare the results of palpation-guided fine needle aspiration biopsy (PG-FNAB) and ultrasound-guided fine needle aspiration biopsy (USG-FNAB) of thyroid nodules in an area of endemic goiter. Patients with solitary or multinodular goiter were included in this study. These patients underwent either PG-FNAB or USG-FNAB. The demographic and clinical characteristics and ultrasound findings of all patients were recorded. Each nodule was classified as mixed, cystic and solid. Patients with nodules smaller than 1 cm and larger than 4 cm were excluded. Regardless of whether the needle was guided by palpation or ultrasound, basic technique of thyroid FNAB was essentially the same for all procedures. All biopsy procedures were performed by a single physician and evaluated by the same cytopathologist. The results of both biopsy methods were statistically compared. Totally, 222 FNABs were obtained from 158 (133 females, 25 males) patients. There was no significant difference between the groups sampled with PG-FNAB (88) and USG-FNAB (134) for age, sex, hormonal status, TSH levels and ultrasound characteristics of nodules. The rate of diagnostic cytology was significantly higher in the USG-FNAB, whereas the number of nondiagnostic cytology was significantly higher in the PG-FNAB group (p=0.001). However, there was no significant difference between two groups for malignant cytology and suspicious malignant lesions. Routine USG-FNAB is superior than PG-FNAB for diagnostic yield and reducing unnecessary interventions, particularly for patients with multinodular goiter in an endemic goiter region findings. It is especially important that in endemic areas clinicians and family physicians should be informed of the epidemiological, clinical and laboratory features of brucellosis in order to prevent delayed diagnosis and complications. Furthermore, considering that the most important way of infection is still the use of unpasteurized milk products and animal farming, we believe that it is necessary to work on preventive measures.

Key words: Thyroid gland, Goiter, endemic, Ultrasonography, Aspiration Biopsy.

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Introduction

Goiter, as indicated by the presence of single or multiple nodules within the thyroid, remains a common clinical problem, especially in iodine-deficient areas. In iodine-sufficient areas, any thyroid nodule has to be regarded as potentially malignant, whereas in endemic goiter regions thyroid nodules are common and vast majority can be regarded as benign due to iodine-deficiency. These nodules may require further investigation, including tissue diagnosis. Fine-needle aspiration biopsy (FNAB) has become the screening method for the triage of patients with thyroid nodules into operative and nonoperative candidates. FNABs of the thyroid are especially important in goiter endemic regions. However, universally accepted recommendations are lacking, and data from the literature on endemic goiter are still controversial on the preferred method for thyroid FNAB sampling. FNAB can be performed by either palpation-guided (PG-FNAB) or ultrasound-guided (USG-FNAB) methods. Optimized results can be obtained when USG-FNAB is performed by experienced clinicians/radiologists and evaluated by cytopathologists. The use of ultrasound guidance for FNAB of thyroid
nODULES INVOLVES ADDITIONAL COST. OFFICE THYROID ULTRASONOGRAPHY IS NOT WIDELY AVAILABLE AND PERFORMING FNAB IN A BUSY RADIOLOGY DEPARTMENT IS INCONVENIENT. THEREFORE, PG-FNAB IS PREFERRED IN AREAS OF THE WORLD WHERE HEALTHCARE RESOURCES ARE LIMITED.

IN THE TERRITORY OF TURKEY, THERE ARE MANY REGIONS OF ENDEMIC GOITER OF A MODERATE TO SEVERE DEGREE AND A MANDATORY IODINE SUPPLEMENTATION HAS BEEN GOING ON ROUTINELY IN OUR COUNTRY FOR LAST 15 YEARS. OUR INSTITUTION IS LOCATED IN AN ENDEMIC GOITER AREA DUE TO IODINE DEFICIENCY, WHICH HAS BEEN KNOWN FOR 75 YEARS AND RATE OF TOTAL IODIZED SALT CONSUMPTION WAS NOT AT A SATISFACTORY LEVEL. THUS, GOITER PREVALENCE REMAINS A SERIOUS PROBLEM, ESPECIALLY IN THE ELDERLY POPULATION WITH A LONG-TERM IODINE DEFICIENCY, EVEN AFTER MANDATORY SUPPLEMENTAL IODIZATION.

GIVEN THE OBSERVED CHARACTERISTICS OF FNAB METHODS, AND THE KNOWN FEATURES OF ENDEMIC GOITER, WE DESIGNED A PROSPECTIVE STUDY TO DETERMINE WHICH METHOD SHOULD BE USED IN AN ENDEMIC GOITER REGION. WE COMPARED THE RESULTS OF BIOPSY SPECIMENS OBTAINED BY USG-FNAB AND PG-FNAB.

MATERIALS AND METHODS

THE STUDY WAS CONDUCTED IN AN ENDOCRINOLOGY OUTPATIENT CLINIC OF A UNIVERSITY HOSPITAL. PATIENTS WITH SOLITARY OR MULTINODULAR GOITER WERE INCLUDED IN THIS STUDY.

AT THE BEGINNING OF THE STUDY PATIENTS WERE RANDOMIZED FOR PG-FNAB GROUP AND USG-FNAB GROUP RANDOMLY. USG GUIDED BIOPSY USED IN PATIENTS WHENEVER A FIRST PALPATION-GUIDED BIOPSY IS NOT DIAGNOSTIC. WE REPEATED BIOPSY UNDER USG GUIDANCE IN PATIENTS WHO HAD NON DIAGNOSTIC PALPATION-GUIDED BIOPSY. THE STATISTICAL ANALYSIS OF THIS GROUP IS NOT CALCULATED AND NOT INCLUDED TO THE STUDY FOR THE REASON OF THE RISK OF THE BIAS. THE STUDY WAS APPROVED BY THE LOCAL ETHICS COMMITTEE, AND WRITTEN INFORMED CONSENT WAS OBTAINED FROM ALL PATIENTS.

THE DEMOGRAPHIC AND CLINICAL CHARACTERISTICS (AGE, SEX, HORMONAL STATUS, TSH LEVELS, DIAGNOSIS, AND CYTOLOGY RESULTS OF THE PATIENTS) AND ULTRASOUND FINDINGS OF ALL PATIENTS WERE RECORDED. AFTER CLINICAL EXAMINATION AND PALPATION ULTRASOUND EVALUATION OF THYROID GLAND WAS PERFORMED BY THE SAME CLINICIAN USING A 7.5 MHz TRANSDUCER WITH A REAL-TIME B-MODE ULTRASONOGRAPHY (SHIMADZU 2200). THYROID NODULES WERE CLASSIFIED BY THEIR SONOGRAPHIC PROPERTIES IN TERMS OF THEIR NODULE SIZE, ECHOGENICITY, ECOSTRUCTURE (MIXED, CYSTIC AND SOLID NODULES) AND BOUNDARIES. PATIENTS WITH NODULES SMALLER THAN 1 CM AND LARGER THAN 4 CM WERE EXCLUDED. ALL BIOPSY PROCEDURES WERE PERFORMED BY A SINGLE EXPERIENCED PHYSICIAN.

HOWEVER, REGARDLESS OF WHETHER THE NEEDLE WAS GUIDED BY PALPATION OR ULTRASOUND, BASIC TECHNIQUE OF THYROID FNAB WAS ESSENTIALLY THE SAME FOR ALL THE PROCEDURES AND HAS BEEN DESCRIBED IN DETAIL ELSEWHERE. USG-FNAB WAS PERFORMED BY FREE-HAND TECHNIQUE. ASPIRATION OF THE NODULES IN BOTH METHODS WERE PERFORMED USING A 22-GUAGE (0.7 MM) NEEDLE ATTACHED TO A 10 ML PLASTIC SYRINGE. NO LOCAL ANESSTHETIC WAS USED DURING THE PROCEDURE, AND 2-3 PASSES WERE MADE INTO EACH NODULE. AIR-DRYED SMEARS WERE PREPARED FROM ALL ASPIRATES. SMEARS WERE STAINED WITH MAY-GRUNwald-Giemsa STAINS AND ALL WERE EXAMINED BY THE SAME EXPERIENCED CYTOPATHOLOGIST, WHO WAS BLINDED TO ULTRASOUND FEATURES AND THE TECHNIQUE OF FNAB.

THE RESULTS OF BOTH BIOPSY METHODS WERE COMPARED STATISTIcALLY. FOR STATISTICAL ANALYSES, CHI-SQUARE TEST WAS USED TO COMPARE CATEGORICAL DATA OF THE PATIENTS. MANN-WHITNEY U TEST AND STUDENT’S T TEST WERE USED TO COMPARE CONTINUOUS VARIABLES. TWO-TAILED P VALUE OF LESS THAN 0.05 WAS CONSIDERED SIGNIFICANT.

RESULTS

A HUNDRED AND THIRTY THREE FEMALES (84.17%) AND 25 MALES (15.82%) PATIENTS WERE INCLUDED IN THE STUDY. TOTALLY, 222 FNABs WERE OBTAINED FROM 158 PATIENTS. WHILE PG-FNAB WAS PERFORMED IN 72 PATIENTS (45.56%), 86 PATIENTS (54.43%) WERE SAMPLED BY USG-FNAB. OF THE PATIENTS BIOPSIED, 98 (62.02%) WERE EUTHYROID, 47 (29.74%) WERE SUBCLINICAL HYPERTHYROID, 12 (7.59%) WERE HYPERTHYROID AND ONE WERE HYPOTHYROID (0.6%).

DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE PATIENTS, INCLUDING AGE, SEX, TSH LEVELS AND DIAGNOSIS ARE SHOWN IN TABLE 1. THERE WAS NO SIGNIFICANT DIFFERENCE BETWEEN THE GROUPS SAMPLED WITH PG-FNAB AND USG-FNAB FOR AGE, TSH LEVELS, SEX, DIAGNOSIS, AND HORMONAL STATUS (P>0.05) (TABLE 1).

OF THE 222 NODULES, 88 (39.6%) WERE SAMPLED UNDER PALPATION GUIDANCE, WHEREAS ULTRASOUND GUIDANCE WAS USED FOR OTHER 134 (60.4%) NODULES. TABLE 2 DEMONSTRATED THE ULTRASOUND EVALUATION, INCLUDING SIZE, ECHOGENICITY AND ECOSTRUCTURE OF NODULES. WE
found no significant difference between the two groups in respect of size, echogenicity and echostructure of nodules (p>0.05) (Table 2).

Histocytologic examination yielded benign cytology in 161 (72.52%), nondiagnostic cytology (NDC) in 52 (23.42%), malignant cytology in 5 (2.25%), suspicious malignant cytology in 1 (0.45%), and Hurthle cell cytology in 3 (1.35%) cases (Table 3). The rate of benign cytology was significantly higher in the USG-FNAB group compared to the PG-FNAB cases (p=0.003). On the other hand, the number of NDC lesions was significantly higher in the PG-FNAB group (p=0.001). However, no significant difference detected between the two groups for malignant cytology, suspicious malignant lesions and Hurthle cell lesions (Table 3).

**Histopathological findings**

### Discussion

We prospectively studied the results of biopsy specimens obtained by USG-FNAB and PG-FNAB from solitary nodular or multinodular goiter patients living in an endemic goiter region. FNAB should be considered the most sensitive diagnostic technique in the assessment of thyroid nodules. FNAB is often performed with palpation guidance. Mostly it is performed with use of ultrasonographic guidance when a first aspiration with palpation guidance results in a nondiagnostic specimen or when certain other risk factors are present. However routine use of FNAB for the examination of thyroid nodules have led to a decrease in the number of patients referred to surgery as well as an increase in the number of malignancies detected.

The rate of malignancy for palpable thyroid nodules is reported to be 3% to 6% in the literature. Eventually in our study, surgical interventions for thyroid nodules were limited to 10 cases (6.3%). Of 10 cases referred to surgery, 6 (60%) were considered as malignant or suspicious by preoperative FNAB and after surgery 4 (40%) of those 6 cases were diagnosed as malignant. This finding is also in favor of the success of FNAB in avoiding unnecessary operations. In various series in the literature, malignancy rates for patients referred to surgery vary between 11% and 84%.

The rates of inadequate material reported for PG-FNAB vary between 2% and 62%. Substantial differences were also observed in the rates of inadequate material reported for USG-FNAB, ranging between 0% and 45%.

We strongly recommend that, FNAB must be done under US guidance in endemic goiter regions, reasons for this statement are summarized as following:
The diagnostic accuracy of USG-FNAB is higher and the rate of nondiagnostic cytologic specimens is lower in comparison with PG-FNAB. Gharib even reported a 95% accuracy of USG-FNAB after a review of several studies.

FNABs of the thyroid are especially important in endemic goitre regions, where there are many patients (up to 60% of the population) with an enlarged nodular thyroid gland. PG-FNAB is not feasible in nonpalpable nodules and not accurate in multinodular goiter.

The thyroid nodules that were not detected by palpation had a maximal diameter of 15 mm. Generally it is expected that, even nodules larger than 20 mm may be missed on palpation if they are located in a posterior or suprasternal position or if the patient has a short or thick neck. PG-FNAB may not be accurate in a nodule located posteriorly in the gland. A study reported that 15.9% of all carcinomas with extrathyroidal invasion are smaller than 1 cm. Biopsy of such small nodules can only be performed with ultrasonographic guidance.

US guidance can decrease the number of unnecessary biopsies by demonstrating definitely benign nodules (i.e., thin regular walled wholly cystic, eggshell or totally calcified). US guidance can also point the most suspicious nodule (i.e., solid, tall, hypoechoic nodule, with microcalcifications or vascular halo, with irregular margins) in a multinodular goitre patient.

We also want to emphasize the importance of ultrasound follow-up of the nodules in endemic goitre region since the follow-up can show a newly formed nodule or the nodule increasing in size. So the thyroidologist can easily choose the nodule to be biopsied.

In this study, although the number of patients are relatively enough, some subgroups have small sample size. This may be one limitation for our study, thus, larger prospective studies are needed to reach more accurate conclusions about the best method for routine thyroid FNAB in patients with thyroid nodules in an endemic goiter region.

Conclusion

In conclusion, we consider USG-FNAB to be superior to PG-FNAB with respect to obtaining adequate material as well as reducing unnecessary interventions, such as repeated biopsy or surgery. In view of our results, we recommend universal use of ultrasound guidance for thyroid fine-needle aspiration biopsy, especially in endemic goiter areas.

References
