

RESEARCH ARTICLE

Diagnostic Value of Ultrasound-Guided Fine Needle Aspiration Biopsy in Malignant Thyroid Nodules: Utility for Micronodules

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Abstract

Background: The diagnostic approach to thyroid nodules involves ultrasound-guided fine needle aspiration biopsy (US-FNAB). We especially aimed to evaluate the contribution and the place of US-FNAB in preoperative evaluation of the malignant cases and draw attention to discordant cases diagnosed with papillary thyroid microcarcinoma (PTMC). **Materials and Methods:** A total of 276 cases were retrospectively reviewed who were subsequently diagnosed with a malignancy and who underwent US-FNAB. **Results:** Some 45 were found to have previously undergone the US-FNAB procedure. Of the patients in whom the surgical specimen was diagnosed with a malignancy, 21 (46.7%) were diagnosed as malignant or suspicious for malignancy, and 24 (53.3%) were concluded as benign or insufficient for diagnosis. Patients with the diagnosis of PTMC outnumbering the others was a striking finding (11 cases, 24%). **Conclusions:** We suggest performing repeat aspiration biopsy considering sampling errors in cases where inconsistency exists between clinical findings and cytological results in thyroid nodules smaller than 10 mm in diameter and with suspicious findings on ultrasonography.

Keywords: US-FNAB - thyroid - microcarcinoma - histopathology - correlation

Asian Pac J Cancer Prev, 15 (20), 8613-8616

Introduction

Papillary thyroid carcinoma is the most common malignancy of the thyroid gland. The tumor is characterized by painless, slow-growing nodules. The diagnostic approach to thyroid nodules involves ultrasound-guided fine needle aspiration biopsy (US-FNAB), which is a widely-used method offering a simple, minimally invasive and safe approach, and this method has become the first line in the diagnostic approach to evaluate the need for surgery and to determine the type of surgery. Apart from US-FNAB, the workup for thyroid nodules also includes sintigraphy, ultrasonography, and neck and soft tissue radiology. Although other diagnostic methods detect 20-60% of the malignancies, FNAB offers a sensitivity of 58-98% and a specificity of 72-100% (Silverman et al., 1986; Kiliturgay et al., 1992; Caraway et al., 1993; Geisinger et al., 1999). The American Thyroid Association (ATA) recommends the evaluation of large thyroid nodules with a diameter greater than 10 mm due to the potential risk of cancer, and recommends the evaluation of thyroid nodules with a diameter smaller than 10 mm in the presence of suspicious ultrasonographic findings (Gharib et al., 2006). A large number of studies have reported that the early diagnosis of thyroid cancer reduced recurrence and mortality (Mazzaferrri and Kloos, 2001). Early recognition of papillary thyroid micro-carcinomas (PTMC) measuring

less than 10 mm in diameter is particularly important due to high risk of lymph node metastasis and multicentricity (Xie et al., 2009). Currently, there is no any guideline for determining which thyroid nodules for biopsy, especially for micronodules (Cheng et al., 2013).

The present study retrospectively reviewed thyroidectomy materials diagnosed with malignancy by histopathological examination in patients who previously underwent US-FNAB. We especially aimed to evaluate the contribution and the place of US-FNAB in preoperative evaluation of the malignant cases and draw attention to discordant cases diagnosed with papillary thyroid microcarcinoma (PTMC).

Materials and Methods

The thyroidectomy materials of 276 cases that underwent surgical resection due to the detection of diffuse or nodular thyroid lesion on ultrasonographic and clinical evaluation at the Antalya Training and Research Hospital between 2009 and 2012 and who were subsequently diagnosed with a malignancy, were retrospectively reviewed. The patients, who underwent US-FNAB and of whom corresponding cytological slides were available, were included in the study. The results of the cytological and histological examinations, the consistency between the diagnoses, and major reasons underlying the

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Table 2. Correlation of Histopathological and Cytopathological Diagnosis of all Malignant Thyroid Nodules

| CUS-FNAB*/ Histopathology | Papillary microcarcinoma | Papillary carcinoma | Follicular carcinoma | Medullary carcinoma | Oncocytic carcinoma | Total |
|------------------------------|-----------------------------|------------------------|-------------------------|------------------------|------------------------|-------|
| Benign | 11 | 4 | 1 | 2 | 1 | 19 |
| Suspicious for malignancy | 5 | 13 | - | - | 1 | 19 |
| Malignant | 1 | 4 | - | - | - | 5 |
| Insufficient | 1 | 1 | - | - | - | 2 |
| Total | 18 | 22 | 1 | 2 | 2 | 45 |

Table 1. US-FNAB Diagnosis of Cases

| US-FNAB diagnosis | Number of cases |
|---------------------------|-----------------|
| Benign | 19 |
| Suspicious for malignancy | 19 |
| Malignant | 5 |
| Insufficient | 2 |
| Total | 45 |

inconsistencies were investigated.

The technique for ultrasound-guided fine needle aspiration biopsy,

Ultrasound-guided fine needle aspiration biopsy was performed for each thyroid nodule. The patients were selected according to ATA criteria, and the procedure was performed under local anesthesia. A

2-gauge needle attached to a 10 ml plastic syringe was employed to collect 1-3 aspirates from each patient. One to ten slides were prepared for each biopsy specimen, and the samples were fixed in 95% ethanol.

Cytopathological Evaluation

The cytological findings were classified as follows, insufficient for histopathological diagnosis, benign, suspicious for malignancy, and malignant.

Benign lesions included normal thyroid tissue, thyroiditis, nodular hyperplasia, or other benign lesions.

The lesion was considered suspicious for malignancy in the presence of atypical follicular cell clusters with nuclear grooves.

The lesion was considered malignant in the presence of intranuclear pseudoinclusions and atypical follicular cell clusters with marked nuclear grooves.

The presence of at least 5 groups of thyroid follicular epithelial cells each comprising 10 cells in artifact-free areas was established as sufficiency criterion for insufficient material.

Alcohol-fixed smears of fine-needle aspirates were stained with H&E and all slides were microscopically evaluated and classified according to the abovementioned four headings.

Results

A total of 276 thyroidectomy materials with an established diagnosis of malignancy were evaluated in the present study. In retrospective review of these cases, 45 were found to have previously undergone the US-FNAB procedure. Smears of FNAB aspirates were microscopically re-examined. Microscopic re-examination revealed malignancy in 5 cases (11.1%),

Histopathological diagnosis of benign cases in US-FNAB

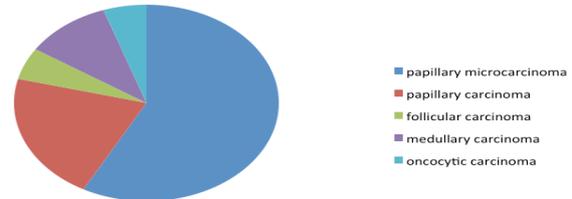


Figure 1. Histopathological Diagnosis of Cases who were Diagnosed “Benign” in US-FNAB

benign lesions in 19 cases (42.2%), suspicious lesions for malignancy in 19 cases (42.2%), and insufficient material for histopathological diagnosis in 2 cases (4.5%).

The histopathological re-examination of 19 cases who were diagnosed with benign lesion in FNAB revealed PTMC in 11 patients, papillary carcinoma in 4 patients, follicular carcinoma in 1 patient, medullary carcinoma in 2 patient, and oncocytic carcinoma in 1 patient. Of two cases, in whom the FNAB specimen was considered insufficient for diagnosis, one was diagnosed with PTMC and the other was diagnosed with PC in the histopathological examination. In addition, among the cases with a suspicious lesion for malignancy in FNAB, five were diagnosed with PTMC, 13 were diagnosed with PC, and one was diagnosed with oncocytic carcinoma. Among the patients with a malignant lesion, one patient was diagnosed with PTMC and four patients were diagnosed with PC. Of the patients in whom the surgical specimen was diagnosed with a malignancy, 21 patients (46.7%) were diagnosed as malignant or suspicious for malignancy, and 24 patients (53.3%) were concluded as benign or insufficient for histopathological diagnosis. The rate of false negative results was 42.2% with the exception of two cases with insufficient material.

Histopathological diagnoses in surgical specimens for each FNAB group are shown in the table (Table 1, 2 and Figure 1).

Discussion

Ultrasound-guided fine needle aspiration biopsy (US-FNAB) is one of the first line diagnostic methods used in the diagnosis of the thyroid lesions, and this method determines the need for surgery and the type of surgery to be performed. Thyroid nodules are common findings on USG examinations, and in autopsy series, 25-40% of the thyroid glands are reported to contain thyroid nodules. FNAB is a widely-accepted, effective, simple, and safe procedure in the evaluation of head and neck lesions, particularly in thyroid lesions. According

to the classification of the World Health Organization (WHO), papillary thyroid carcinomas measuring smaller than 10 mm in diameter are called “papillary thyroid micro-carcinoma” (PTMC) (Lantsov DS, 2006). The American Thyroid Association (ATA) and the Society of Radiologists in Ultrasound Consensus Statement suggests that thyroid nodules larger than 10 mm should be evaluated for the potential risk of cancer (Gharib et al., 2006). However, lesions smaller than 10 mm in diameter should be evaluated for malignancy only in the presence of suspicious ultrasonographic findings and medical history suggestive of thyroid cancer (Cooper et al., 2009). Recently, widespread use of US-FNAB has facilitated the diagnosis of PTMC (Zhou et al., 2012).

In the present study, the ultrasonographic examination showed lesions smaller than 10 mm in 21 patients, who subsequently underwent FNAB due to the presence of suspicious ultrasonographic findings. The remaining 24 cases had lesions larger than 10 mm in diameter, and these patients underwent FNAB based on ATA criteria. The histopathological re-examination of 19 cases who were diagnosed with benign lesion in FNAB revealed PTMC in 11 patients, papillary carcinoma in four patients, follicular carcinoma in one patient, medullary carcinoma in one patient, and oncocytic carcinoma in one patient. Of two cases, in whom microscopic examination was considered insufficient for diagnosis, one was diagnosed with PTMC and the other was diagnosed with PC. Considering the inconsistencies between histopathological diagnoses and the diagnoses in FNAB, patients with the diagnosis of PTMC outnumbering the others was a striking finding (11 cases, 24%).

Ylagan et al. examined the cytological and histopathological correlation in 255 cases, and reported that the inconsistencies mostly resulted from patients with insufficient data to render a diagnosis. They suggested that false negative results in 4% of their cases were caused by the presence of microscopic papillary thyroid carcinoma (Ylagan et al., 2004).

Nam Goong examined the utility of US-FNAB in 25 small thyroid nodules (less than 5 mm), and reported a concordance rate of 64% (Nam-Goong et al., 2004). In the present study, the ultrasonographic examination showed lesions smaller than 10 mm in 21 patients, who subsequently underwent aspiration biopsy due to suspicion for malignancy, and 11 patients were diagnosed with PTMC. The concordance rate in the current study was 52.4%, considering thyroid nodules smaller than 10 mm in diameter.

Kim et al. compared the diagnoses in US-FNAB and in thyroidectomy specimens among 65 patients with small thyroid nodules (less than 5 mm), and reported true positivity rate of 55%, false positivity rate of 0%, true negativity rate of 37%, and false negativity rate of 8%. They suggested that US-FNAB was an effective diagnostic procedure in thyroid nodules smaller than 5 mm in diameter (Kim et al., 2009).

It is well-known that PTMC may show multicentricity in 15-44% of the cases, and regional lymph node metastasis may be found in 14-64% of the cases (Hay et al., 1992; Lin et al., 1997; Rodriguez et al., 1997; Rassal

et al., 1998; Sugitani and Fujimoto, 1999; Chow et al., 2003; Falvo et al., 2003). These are two important clinical features, and the nodules are non-palpable, therefore difficult to detect on physical examination. The studies in autopsy series report a 0.5-5.2% occurrence rate for latent PTMC measuring between 3 mm and 9.9 mm in diameter (Fukunaga et al., 1975; Harach et al., 1985; Samson RJ, 1977). Ultrasonographic examination and FNAB become more important in such circumstances.

The studies to date have highlighted several features of the FNAB procedure. These include specimen quality, sampling technique, the experience of the operator performing the aspiration biopsy, the experience of the cytopathologist examining the aspirates, and the presence of cytological features that show similarities in differentiating benign from malignant follicular lesions (Peli et al., 2012).

FNAB is a simple, affordable, and minimally invasive method used in preoperative assessment; however, inconsistencies may exist between cytological and histological examination of small thyroid nodules. PTMC is particularly important for its potential to show multicentricity and lymph node metastasis. The researchers therefore suggest performing repeat aspiration biopsy considering sampling errors in cases where inconsistency exists between clinical findings and cytological results in thyroid nodules smaller than 10 mm in diameter and with suspicious findings on ultrasonography. The repeat of FNAB procedure may provide diagnostic sampling and prevent the patient from losing the opportunity for surgery in the early stages.

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