Fine Needle Aspiration of Thyroid Nodules: Experience in A Chinese Population

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Abstract

We present our experience of fine needle aspiration (FNA) of thyroid nodules at a single medical institution in China and discuss subclassification of the indeterminate FNA results with the correlated histological outcomes. Of a total of 1,703 FNA samples, 101 were classified as nondiagnostic (Thy1), 543 as negative for malignant cells (Thy2), 125 as indeterminate (Thy3), 95 as suspicious for malignancy (Thy4), and 839 as diagnostic of malignancy (Thy5). Histological results were available for 734 nodules, including 36.6% of the nodules with Thy1 reports, 8.5% with Thy2 reports, 41.6% with Thy3 reports, 73.7% with Thy4 reports, and 63.1% with Thy5 reports. The rates of surgically identified malignancy in those categories were 43.2%, 6.5%, 51.9%, 92.9%, and 99.4%, respectively. Indeterminate results were further subdivided into four groups based on the cytomorphology: Thy3-cannot exclude papillary thyroid carcinoma (Thy3-PTC), Thy3-follicular neoplasm (Thy3-FN), Thy3-Hürthle cell neoplasm (Thy3-HN), and Thy3-follicular lesion (Thy3-FL). A total of 125 cases were subclassified into Thy3-PTC (32), Thy3-FN (20), Thy3-HN (14), or Thy3-FL (59). Fifty-two of the 125 cases subsequently underwent surgical treatment. Malignant rates were 71.4% in Thy3-PTC, 46.2% in Thy3-FN, 42.9% in Thy3-HN, and 27.3% in Thy3-FL. In our practice, FNA performed by experienced clinicians and interpreted by dedicated cytopathologists has rarely false positive and false negative results. Subclassification of the indeterminate results contributes to stratify patients for the risk of malignancy.

Keywords: Thyroid, FNA, subclassification, indeterminate, China

Introduction

Nowadays fine needle aspiration (FNA) biopsy has been developed as the most accurate and cost-effective method for the preoperative diagnostic evaluation of patients with thyroid nodules (1-3). FNA cytology is a simple, rapid and minimally invasive procedure, which can define the extent of thyroid surgery in most patients with a diagnosis of malignant neoplasm or benign diseases (4). Nevertheless, except for some large comprehensive medical centers, this procedure has not been widely performed as a routine screening test in most areas of China, and the experience published for thyroid FNA practice by Chinese institutions is limited (5,6). Noninvasive methods such as serological tests, ultrasound or thyroid scan may aid clinicians in deciding the management of suspicious nodules. When the diagnosis cannot be confirmed by these tests, FNA biopsy has become the best choice. The objective of the current study was to present our experience with FNA cytology and to determine the risk of malignancy in each diagnostic category by using the modified 5-tiered system that is endorsed by the British Thyroid Association (BTA)-Royal College of Physicians (RCP) and the Italian Society for Anatomic Pathology and Cytopathology (SIAPEC)-International Academy of Pathology. This 5-tiered system includes the following categories: 1) nondiagnostic; 2) negative for malignant cells; 3) inconclusive/indeterminate; 4) suspicious for malignancy; and 5) diagnostic of malignancy (7, 8).

We report our institution’s experience with the 5-tiered system. FNA results were reviewed and correlated with the pathology of subsequent resection specimens.

Materials and Methods

A retrospective study was conducted for all patients with ultrasound-guided thyroid FNA (UG-FNA) between June 2012 and June 2014 in Jiangsu Institution of Nuclear Medicine. All patients had thyroid ultrasound records available. Incidental microcarcinomas detected in surgical specimens were excluded from statistical analysis.

FNA procedure

Prior to consideration of a thyroid nodule FNA, a history of relative contraindications and informed consent for the procedure were obtained from all patients. Immediate specimen adequacy evaluation was not provided.

Patients were placed supine with the chin slightly extended. The patient’s head was turned away from the side to allow easier access for the sonographer performing the biopsy. Before UG-FNA began, B-mode imaging was acquired in the transverse plane to determine the nodule location, as well as any lymphadenopathy or abnormalities of both thyroid lobes, isthmus, low central region and the lateral neck. Color Doppler imaging was used to observe and locate any large blood vessels in and around the nodule, so that vascular injury could be avoided during FNA.

The neck was prepared in a sterile environment. Gel was applied to the transducer face, and the transducer was then enclosed in a sterile glove. Sterile gel then could be applied to the covered transducer face. Local anesthetic was not used. A 23-gauge needle was used with an attached 2.5-ML disposable syringe.

Basically, the perpendicular approach was adopted; the nodule was imaged and positioned in the mid portion of the screen. The operator, using a freehand biopsy technique, placed the needle just above the transducer, inserted adjacent to the side of the midpoint of the transducer, and angled the needle back toward the...
transducer. The angle varied depending on the depth of the nodule being biopsied. The needle was advanced toward the nodule under US guidance. Two techniques were employed for needle aspiration of cellular material based on the nodule texture. One was aspiration technique with the plunger being withdrawn for 2-3 cc of negative pressure to induce aspiration. When the aspiration pressure was released, the needle was withdrawn. When the nodule was honeycomb-like with a multilocular cyst and fluid or a hypervascular nodule was encountered, non-suction technique was applied and could work effectively. Non-aspiration technique utilized the capillary action uploading of cellular material into the needle. Once the needle was within the target region of the nodule, it was moved back and forth at about 2 to 3 oscillations per second while being rotated on its axis, to create an evenly distributed vacuum force. A dwell time of 2 to 5 seconds with continuous oscillations generally provided adequate cell yield without excessive blood contamination.

The operator obtained four smears by extracting two samples from each nodule, following the routine approach performed at our institute. The UG-FNA specimens were directly smeared on glass slides and fixed in 95% ethyl alcohol. Preparations were stained with hematoxylin and eosin (H&E). All cases were confirmed by three cytopathologists (Tiesheng Wang, Jun Dai, and Yun Zhu). The cytological morphology was subsequently matched to the clinical or ultrasound information and the final report was rendered.

Criteria for FNA

In general, the FNA criteria included enlarging nodule size, abnormal serological tests (such as high level of calcitonin or carcinoembryonic antigen), patient/clinician preference, or clinical suspicion concerning sonographic features. Microcalcification, an irregular microlobulated margin, marked hypoechogenicity, and a shape that was taller than it was wide, were the main factors of suspicious sonographic findings (9-11). Patients with one or more of these features were recommended for FNA biopsy and those with none of suspicious features were advised to be observed.

Criteria for surgical treatment

Thyroid surgery was recommended to all patients with Thy4 or Thy5 reports. Patients with at least one Thy3 report were recommended for repeat FNA or diagnostic partial thyroid lobectomy. Once malignant histological evidence was proved by frozen section, completion thyroidectomy was usually performed. Patients refusing surgical treatment or in a high surgical risk were recommended for clinical and ultrasonographic follow-up. Patients with benign FNA cytology diagnosis underwent surgery because of pressure symptoms, hyperfunctioning goiter or unwillingness to be carried out for follow-up. Patients with nondiagnostic reports were recommended for a repeat FNA or clinical and ultrasonographic follow-up. Sometimes patients with Thy1 reports were advised to undergo diagnostic surgery in the case of high-risk findings obtained from clinical data such as from ultrasound examination.

Results

As shown in Table 1, a total of 1,703 thyroid nodules from 1,565 patients classified by the 5-tiered system were included in this study. Of them, 359 (22.9%) were male and 1,206 (77.1%) were female, with a median age of 49 years, ranging 11-86 years.

Of a total of 1,703 FNA samples, 101 were classified as nondiagnostic (Thy1), 543 as negative for malignant cells (Thy2), 125 as indeterminate (Thy3), 95 as suspicious for malignancy (Thy4), and 839 as diagnostic of malignancy (Thy5) (Table 2).

The correlation between the FNA cytology and the histological diagnoses is shown in Table 3. Among the 734 samples, 37 (37/101, 36.6%) of the 101 nodules classified as Thy1 had final histological results and 16 of the 37 (43.2%) were found to be malignant. Thy2 reports were obtained for 543 nodules and 46 of them underwent surgical treatment. Among them, 43 had a
The British Association of Endocrine and Thyroid surgeons analyzed a total of 697 patients with Thy3 cytology, of whom 155 (22%) had a malignant nodule (15). A cohort of 711 patients with indeterminate results underwent surgical treatment and the rate of malignancy was 26% on the final histopathology in Italy during the 1998-2007 period (16). Radu et al. found a malignant rate of 25% for their indeterminate category (17). Nevertheless, the malignant rate of 51.9% (27 of the 52 specimens) in the present study was extremely higher compared to that in other reports for Thy3. The cause of variable malignancy rates may be related to the diagnostic criteria applied histologically and cytologically. Another important reason may be due to the subclassification of Thy3 in our practice.

The literature reported that cytological subclassification of the indeterminate results could stratify risks of patients for malignancy and reduce unnecessary surgery in favor benign category (18-21). Based on the data in the present study, the Thy3 cases were subdivided into four groups, including 32 cases of Thy3-PTC, 20 cases of Thy3-FN, 14 cases of Thy3-FL, and 59 cases of Thy3-FL. The surgical resection rate of each sub-category was 65.7% (21/32) for Thy3-PTC, 65.0% (13/20) for Thy3-FN, 50.0% (7/14) for Thy3-FL, and 18.6% (11/59) for Thy3-FL. Actually, diagnostic partial thyroidectomy and frozen section analysis that were recommended to patients with a Thy3 report except for those with Thy3-FL results have been currently advised for clinical and ultrasound follow-up. Groups with Thy3-PTC and Thy3-FN carried a significantly high risk of malignancy at 71.4% and 46.2%, respectively, while the group with Thy3-FL brought a relatively low risk of malignancy at 27.3%. The consequences indicate that cytological subclassification of the Thy3 contributes to help determine a more accurate risk of malignancy and better selection of patients for surgery or follow-up.

The most common FNA diagnosis rendered in our practice was Thy5, which was quite different from Bethesda expected incidence (22) and other literature using the similar 5-tier system reporting a range from 2.9% to 18.6% (16, 20, 23-25). During June 2012 to June 2014, a total of 74,599 patients were found to carry single or multiple thyroid nodules in our out-patient department. Of these nodules, 5,394 were suspected of malignant tumors by ultrasound. Though the criteria for FNA biopsy was strictly based on those of American Thyroid Association and Korean guideline (9, 10), it was impossible to perform FNA biopsy for all suspected nodules. As at that time, there was just one skilled clinician who could perform the ultrasound-guided FNA procedure in our hospital. Hence only 1,565 patients with 1,703 nodules finally underwent FNA biopsy and furthermore, nearly one-third of them were in-patient. That may be the main reason for our high rate of Thy5 and for the relatively low rate of Thy2. This limitation should be taken into consideration as a potential source of bias when explaining our data. The other limitation of this study was the low ratio of FNA repetition. Among 1,703 nodules underwent initial biopsies, 35 (21 in Thy1, 3 in Thy2, 7 in Thy3, and 4 in Thy4) accepted a repeat FNA. This low proportion was mainly due to the work overload and staff shortage. Patients who were required FNA repetition moved to or managed in other hospitals and thus lost to be followed-up. Since 2015, four well-trained clinicians have joined us and the data would be changed in the next few years.

Strickland et al. reported that the rate of malignancy for FNA diagnostic categories would be decreased significantly, particularly in the category of suspicious of malignancy if non-invasive follicular variant of papillary thyroid carcinoma (NFVPTC) was not considered as carcinoma (26). However, the reproducibility in the diagnosis of NFVPTC is very low (27, 28), the outcome of this
type of tumor is practically benign, and there is no recurrence or metastasis after surgery, even with lobectomy resection alone (29, 30). Non-invasive thyroid follicular neoplasm with papillary-like features (NIFT) was not included in the malignancy category and they were classified as benign in this study. It may be because Chinese pathologists apply stricter criteria to non-invasive follicular pattern tumors with questionable PTC type nuclei (well-differentiated tumor of uncertain malignant potential: WDT-UMP). The lesions with equivocal or incomplete PTC nuclear features were classified as benign in our preceding study.

In conclusion, FNA biopsy is a reliable initial test for patients with thyroid nodules. FNA performed by experienced clinicians and interpreted by dedicated cytopathologists has rarely false positive and false negative results. Further subclassifications of Thy3 may contribute to identify the patients who have a significantly higher risk of malignancy and therefore require more aggressive surgical management.

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Conflicts of Interest: None

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