Thyroid Fine Needle Aspiration:

Is Cytopathologist Review of Ultrasound Features Useful?

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Running title: Thyroid ultrasound for cytologists

Abstract

Cytopathologist review of thyroid US has been proposed to be useful in diagnosis and patient triage. This editorial explores the implications for practicing cytopathologists of integrating US review into thyroid FNA diagnosis. At present there is no agreed upon system for combining cytologic and ultrasound (US) features and communicating those results as a single report. If cytologists are performing tasks that require expertise in US interpretation, then they should know and be fully conversant with US interpretation. Whether cytologists performing aspirations require expertise in US interpretation is not clear. Regardless, cytologists should avoid using US results to alter their cytologic interpretations unless they clearly communicate that this is what they are doing. An evidence-based integrated reporting system that would allow cytologists to clearly explain to other physicians exactly how they reached their interpretation might provide value beyond current standard practice.

Keywords: Thyroid, cytology, fine needle aspiration, ultrasound

Condensed Abstract: Cytopathologist review of thyroid US has been proposed to be useful in diagnosis and patient triage. This editorial looks more closely at the implications of this for practicing cytologists.

Fine needle aspiration (FNA) biopsy of the thyroid is the single most useful

diagnostic tests to evaluate which patients with thyroid nodules should undergo surgery.

The results are reported as recommended by the Bethesda System[1] or other similar

terminologies e.g. Royal College of Pathologists (RCPath) 'Thy' or Italian TIR

terminologies[2]. The cytology report is then evaluated along with other clinical and

laboratory information, including, age, sex, physical examination, serum chemistry and

hormone levels, and imaging features. The imaging features, most commonly the

ultrasound (US) features, but also sometimes PET-CT, CT or MRI are used to select

patients who should undergo FNA, in some cases to target lesion(s) while performing

FNA, and in the selection of patients who may need repeat FNA or surgery.

The US features of a given lesion are therefore critical for managing patients with thyroid

nodules. US evaluation is typically performed by either clinicians or radiologists. At

present there are at least 5 internationally used systems for reporting US results: the

American Thyroid Association score[3,4], the ACR TIRADS[4], the European EU-TIRADS[5],

the South Korean K-Tirads[6], the Chilean TIRADS[7] and the British Thyroid Association

'U' classification[8,9]. These systems although quite similar are not identical. All aim to

give an indication of the clinical risk by evaluation of a wide variety of features,

including shape, margin, calcifications, hypo-echogenicity, solid vs. cystic features,

stiffness/elastographic features, and vascularity. Other features that have been suggested

to be of value in the US evaluation of thyroid nodules include the use of contrast

enhanced US[10-13], and Doppler imaging[14]. Depending on the US risk stratification score,

different size cut-offs for FNA are defined in each TIRADS system, in most cases only

for lesions greater than 1cm[3-5]. In addition, lesion size is strongly correlated with the

sensitivity of FNA[15]. However, whether the risk of malignancy for lesions greater than 1

cm can be correlated with size is less clear [16-18]. Because of these many features, the US

evaluation of thyroid nodules requires considerable training, skill and experience, and is

to some extent subjective. There is variation even among experienced clinicians about

how these criteria are interpreted and applied. Some have written that cytopathologist

review of thyroid US is extremely useful and can be helpful in triaging patients [19-22]. This

editorial looks more closely at the implications of this for practicing cytologists in three

different circumstances: participating in the management of thyroid nodules after FNA,

deciding which nodules should be submitted to FNA and how to perform an aspiration

biopsy, and evaluating the cytological diagnosis with respect to the US pattern.

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Most thyroid nodules are initially evaluated by clinicians and not by cytologists.

The decision to recommend follow-up, repeat aspiration, or surgery is also usually made

by clinicians rather than by cytologists. If a cytologist is part of a multidisciplinary team

(MDT) that discusses management of patients with thyroid nodules, then some

knowledge of thyroid nodule US features may be helpful to the participating cytologist.

Opponents of this view would argue that detailed knowledge of US features is not

required by cytologists since MDTs comprise clinicians and radiologists whose role it is

to provide expertise in US interpretation. However, in the experience of some of the

authors (DP, GR) many FNA cases, particularly in the lower risk of malignancy US or

FNA categories (The Bethesda System for Reporting Thyroid Cytopathology [TBSRTC] categories- III-IV, equivalent to UK RCPath Thy 3a-Th 3f) are not listed for MDT discussion because of time and resource constraints[23]. The UK Royal College of Pathologists Guidance only recommends mandatory MDT discussion of higher risk Thy 4 and Thy 5 aspirates, equivalent to TBSRTC categories V and VI[24]. In such cases, a cytologist might attempt to select a subset of patients from the lower risk group who might benefit from further discussion at MDT conference. In this situation a cytologist would then be performing a task that clinicians most often do, so an understanding of the US characteristics to the same extent as a clinician would appear appropriate. In the opinion of some of the authors (DP, GR), the most important US feature of a thyroid nodule is whether it is solid, purely cystic, or partially cystic/solid. Specifically, if there is a solid component, a borderline or non-diagnostic aspirate is unlikely to be representative and re-aspiration may then be helpful[19,25]. A description of how one author (DNP) routinely integrates US into his daily practice is shown in Table 1.

Alternatively, it is not uncommon for cytopathologists to perform US guided FNA[21,26-29], and a course on the subject is offered by the College of American Pathologists[30]. Cytopathologist guided US thyroid FNA has very low rates of non-diagnostic aspirates, typically 3-7%[27]. If a cytologist is selecting nodules to aspirate, then adequate knowledge to evaluate the US results at the same level as radiologists and clinicians is important. If the cytologist is simply using the US to identify the nodule and guide the needle to the appropriate area of a nodule that is selected for biopsy by someone else, then knowledge of the US technique and results that are relevant for this

task would be appropriate. Any supporting documentation for the procedure should clearly indicate which of these 2 scenarios applied in the acquisition of the sample.

The setting in which the use of US features is more controversial is in the actual evaluation of the cytologic diagnosis of the nodule. This scenario most commonly arises in evaluating the adequacy of an aspirate or in refining classification of an indeterminate aspirate. In settings where there may be an issue with adequacy, rapid on site evaluation (ROSE) can be of value in increasing the adequacy rate [31]. However, the benefit of ROSE in settings with experienced practitioners who already have a high adequacy rate is limited [32]. Certainly ROSE allows one to immediately assess adequacy and do more passes to obtain additional material to achieve adequacy. In a cystic lesion, the needle may be directed into a more solid area to increase the yield of cellular material. However, some cystic lesions will remain non-diagnostic due to an absence of epithelial cells or colloid. While the TIRADS systems have a defined method to manage these patients, a cytologist with knowledge of US evaluation might be tempted to seek to combine the cytologic and US evaluation into a single report that they might regard as "adequate" based on primarily imaging criteria rather than cellularity. Indeed, it is the experience of one of the authors (AR) that some cytologists do diagnose an aspirate without any epithelial cells as 'adequate' if the US characteristics are those of a simple cyst. If the report does not clearly indicate that assessment of adequacy is based on the imaging characteristics there is a risk that the follow-up recommendation (i.e. repeat aspiration or no further follow-up) may be determined based on the impression that

adequacy was based on cytologic criteria rather than the imaging characteristics, and the follow-up or clinical management may be different. Cytopathologists undertaking US guided thyroid FNA therefore should adhere to the strict cellular adequacy criteria as detailed by either the relevant reporting terminology system, evidence-based criteria[33-35], or clearly state how their evaluation of adequacy was determined. In contrast, some authors have suggested that cystic lesions deserve their own separate diagnostic category [36,37], which would at least make the way the diagnosis of adequacy was made clearer.

Similarly, even though clinicians appropriately review the US findings when trying to determine how to manage patients with an indeterminate aspirate, some studies[38-43] but not all[43-46] suggest that this information is of limited value. In general, it is difficult to construct reproducible criteria that would allow one to consistently reclassify an indeterminate aspirate as benign based on US features alone. However, specific US features may be more useful in specific settings to reliably reclassify a subset of indeterminate cases as benign. If a cytologist with extensive US knowledge undertakes and reports an US guided FNA and the cytologist has some diagnostic uncertainty as to the cytologic diagnosis, it is possible that the cytologist may, possibly unconsciously, be influenced by cognitive bias, and use the combination of the US characteristics and the cytological findings to further "refine" the cytologic diagnosis into a more determinate result. For example, it is well documented that the diagnosis of atypical/suspicious follicular lesions (i.e. a sample with microfollicles) is associated with a very low risk of malignancy if the nodule is less than 1 cm in size[47]. As a result, a cytologist may be tempted to incorporate knowledge of the size of a lesion into the

cytology report and report the lesion in a lower malignancy risk category, TBSRTC category II or III, UK RCPath Thy 2 or Thy 3a. However, the same nodule may grow larger than 1 cm and if re-aspirated will still show the same microfollicular pattern. Because of the larger lesion size the cytologist may report the lesion in a higher risk category[48]; TBSRTC Category IV, UK RCPath Thy 3f. As a result, the clinician might assume that the lesion not only had grown in size but had also changed its cytologic features over time which would not be true and also might result in a different management strategy. Similarly, some US features have been noted to be inconsistent with a diagnosis of Non invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP)[49]. Most clinicians would assume that if a cytologist chooses to make a definitive diagnosis of papillary carcinoma it is based on cytologic criteria, not US features, and if their assessment of those US features were different than the cytologist's assessment management may be affected. Another example worth considering is when a diagnosis of Hashimoto's thyroiditis is contemplated and is potentially used for calling an aspirate benign vs AUS vs suspicious for a Hurthle cell neoplasm. If the evidence for thyroiditis on the slide is weak, some pathologists may be influenced about the presence of a description of a diffusely heterogeneous gland on US.

Finally, the level of experience cytologists have with US interpretation may vary considerably, even though they may be "fully conversant" with the TIRADS criteria. If a cytologist alters their cytologic interpretation based on their interpretation of the US features, this may create a problem if a clinician with more experience does not agree

with that US interpretation.   Alternatively, some cytologists with enormous US

experience[20] may use that experience to alter their cytologic interpretation of the case in

ways that are difficult to defend based on evidence based criteria alone.   After all, some

studies[38-43] but not all[43-46] suggest that this information is of limited value. Different

clinicians may appreciate a cytologist taking this approach more or less depending on a

variety of factors.   At best, the knowledge that is included in that experience is lost to

the cytologist's colleagues and future generations of cytologists if it is not published. At

worst, the conclusions that the cytologist reaches based on their experience in the absence

of any confirmatory data may simply be wrong.   Indeed, one of the strengths of the Paris

criteria for urine cytology[50] was to finally put to rest some "diagnostic criteria" that past

leaders in the field had promoted based on their experience alone and which were never

able to be confirmed.

As a result, when a cytologist interprets US results either for performing

aspirations or in evaluating patients for management, there is a need to clearly define

exactly what information is being obtained from the US and which information is being

obtained from the aspirate. One of the strongest arguments for standardized

terminologies such as the TBSRTC and the TIRADS systems is that use of a standardized

terminology facilitates communication between physicians. At present there is no agreed

system for combining cytologic and US features and communicating those results as a

single report. Such a system might have some advantages over the two separate systems

that are currently used. When authors say that it useful for cytologists to know the detail

of the US interpretation, it is important to clarify what exactly they mean. If a cytologist

is only rendering cytologic interpretations and is not reviewing the US, then interpreting the specimen along the lines defined in TBSRTC and having no particular knowledge of the US features is perfectly reasonable. If cytologists are performing tasks that require expertise in US interpretation, then the answer is yes of course they should know and be fully conversant with US interpretation. Whether cytologists performing aspirations require expertise in US interpretation is not clear. However, cytologists should avoid using US results to alter their cytologic interpretations unless they clearly communicate that this is what they are doing. An evidence-based reporting system that would allow cytologists to clearly explain to other physicians exactly how they reached their interpretation might be of value.

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