

I declare that I have no conflict of interest

Abstract

Background: Correlation of cytologic and ultrasound findings is extremely valuable for the cytopathologist in management of thyroid nodules.

Methods: Ultrasound scans (US) of all thyroid FNA taken over a 13 month period and reported by a single cytologist were reviewed at the time of reporting, focusing on aspirates that were non-diagnostic/unsatisfactory, Bethesda Class I, UK Royal College of Pathologists Class Thy1 or Thy1c.

Results: 68 (40.7%) FNA cases were classified as Thy1, equivalent to Bethesda Class I. US of 3 Thy1 cases were not available for review. On cytologist US review 9 cases were classified as *pure cystic*, 28 as *mixed cystic/solid*, 12 as *predominantly solid/focally cystic*, and 16 as *purely solid*. 27 (41.5%) of cases on cytological assessment were Thy1 and showed no evidence of a cyst on US, 17 (26.1%) were Thy1/Thy1C showing features suggestive of a possible cyst and 21 (32.3%) were Thy1c showing definite features of a cyst. 15 of 16 (93.7%) of *pure solid* cases on US were Thy1, equivalent to Bethesda Class I and all 9 (100%) of cases that were *pure cystic* on US were reported as Thy1c- equivalent to Bethesda Category I- *cyst fluid only* ($p < 0.001$).

Conclusion: Cytopathologist review of thyroid ultrasound scans is extremely useful and can be helpful in triaging patients for further management in cases of solid, mixed cystic and or/solid, and pure cystic thyroid lesions with non-diagnostic/unsatisfactory thyroid FNA.

Background

FNA of the thyroid is the principal method for preoperative investigation of thyroid nodules. While traditionally thyroid FNA was performed freehand, the majority of thyroid FNAs in modern practice are now performed under ultrasound guidance. Although institutional practices vary there is a trend toward some cytopathologists undertaking their own thyroid ultrasound examinations, extending the role of the cytopathologist [1-3]. However, the majority of practicing cytopathologists do not perform thyroid ultrasound examinations at the time of aspiration. There is a wealth of information that can be obtained from review of ultrasound scans, available to the ultrasonographer, radiologist or clinician undertaking the ultrasound scan although not all of this information is easy to convey to the cytopathologist. In North America ultrasound scans can be classified using AACE [4], or ATA [5] sonographic criteria which convey the ultrasound features and a clinical suspicion risk of an individual nodule or lesion. In the UK the 2014 British Thyroid Association Guidelines for Management of Thyroid Cancer classifies nodules on a sonographic index of suspicion/risk scale of U2 to U5 [6]. Frequently however this does not necessarily convey all the relevant information to the cytologist. The author instituted cytopathologist review of all thyroid ultrasound scans for patients undergoing thyroid fine-needle aspiration in June 2016. The data presented here represents a personal 13 month experience describing the results achieved and the value of cytopathologist performed review of thyroid nodule ultrasound scans for non-diagnostic/unsatisfactory thyroid FNA.

Materials and Methods

The Department of Pathology and Cytopathology at The Queen Alexandra Hospital, Cosham, Portsmouth, UK serves a patient population of around 650,000, approximately 2-3% of the UK population. The hospital is a major cancer centre. All thyroid fine-needle aspirates are taken by a team of consultant radiologists or trainee radiologists working under consultant supervision in the ultrasound rooms in the Department of Radiology at Queen Alexandra Hospital, Cosham, Portsmouth. The fine-needle aspirates are taken with 23 or 25 gauge needles using capillary action, and/or simple suction and direct smears are made onto glass slides and are stained with conventional cytological techniques, air dried Giemsa and Papanicolaou stains. Liquid-based cytology techniques are not used. Typically 2 to 3 needle passes are taken with 3 to 4 slides air dried or alcohol fixed prepared per case. Rapid on-site assessment of FNA is not available. As this article describes the results of routine day-to-day clinical practice and the results for the patients concerned are anonymised it did not require institutional ethical approval. The results presented comprise all the fine-needle aspirates personally reported by the author over a 13 month period from July 1st 2016 to 31st July 2017. For each patient the author personally reviewed the ultrasound scans and also the written report of the radiologist. The nodules were classified by the cytologist on the basis of the sonographic nature of the nodule(s) as follows

- (i) *pure cystic* lesion
- (ii) *mixed cystic/solid* nodule
- (iii) predominantly solid nodule with occasional foci of cystic change/and or hemorrhage – *predominantly solid/focally cystic*
- (iv) purely solid nodule- *pure solid*

The cytopathologist also referred to the radiologist's written ultrasound examination report for confirmation. FNA's reported by other cytopathologists at the Department of Pathology Queen, Alexandra Hospital were not included as these patients did not undergo review of their ultrasound scans by a cytopathologist prior to reporting of the thyroid fine-needle aspiration. The fine-needle aspirates were classified using The UK Royal College of Pathologists terminology. [7] This subdivides the non-diagnostic category for cytological diagnosis, Thy1/Thy1c, in a similar manner to other terminology systems such as The Bethesda System for Reporting Thyroid FNA Cytology. An FNA is considered of adequate epithelial cellularity using the Royal College of Pathologists terminology if a sample from a solid lesion has at least 6 groups of thyroid follicular epithelial cells across the submitted slides, each with at least 10 well-visualised epithelial cells. The reason(s) for a non-diagnostic sample may be that either

- (i) the sample consists entirely of blood or it is so heavily bloodstained that the epithelial cells or colloid cannot be visualised
- (ii) the sample is acellular or too low in follicular epithelial cell yield to allow diagnosis
- (iii) the sample cannot be evaluated e.g. due to poor spreading, delayed air drying, or fixation artefact, prominent crush artefact or cells trapped in fibrin

In the UK Royal College of Pathologists terminology cyst fluid specimens that do not reach the threshold for adequate follicular epithelial cell yield stated above and that contain mostly macrophages but abundant colloid can be reported as... 'a sample is

in keeping with fluid from a cyst but there are no epithelial cells or colloid to confirm cyst type..' with use of the category *Thy 1c* where 'c' means a cystic lesion. [7]

For the purposes of this study if it was absolutely clear that the lesion was cystic based on the nature of the cells seen in the relevant slides from the sample received it was reported as Thy1c, equivalent to Bethesda Category I *cyst fluid only*. If there was some uncertainty based on the cellular appearances the aspirate was reported as Thy1/Thy1c- implying that it was unclear as to whether or not the aspirate was from a cystic lesion. If the lesion did not show features of a cyst and had less than 6 groups of 10 well preserved epithelial cells across the slides or it was technically unsatisfactory for whatever other reason the case was reported as Thy1, equivalent to Bethesda category I *non-diagnostic*.

Statistical analysis was performed using Statistica Academic version 13.2 Tibco Software Inc., Palo Alto, Ca, USA.

Results

There were, in total, 167 FNA's from 139 patients were reported with ultrasound review over a 13 month period, comprising 68 (40.7%) Thy1 aspirates. 27 (16.2%) were Thy1 and showed no cytological features of a cyst, 17 (10.2%) were Thy1/Thy1c showing features suggestive of a possible cyst although not conclusive for a cyst and 21 (12.6%) were Thy 1c showing definite features indicating a cyst. There were 30 Thy 2 aspirates, 7 Thy2c aspirates, 29 Thy3a, 20 Thy3F, 7 Thy4 and 6 Thy 5 FNA's. In 3 cases the ultrasound images were not available for review as these had not been uploaded onto the computer server at the time of ultrasound examination and these images could not be retrieved. Of the 65 remaining cases that were either Thy1, Thy1/Thy1c or Thy1c and that are the basis of this article; 9 were classified by the author on review of the ultrasound scan as *pure cystic*, 28 were classified as *mixed cystic/solid*, 12 as *predominantly solid/focally cystic* and 16 as *purely solid* (table1). There was no statistically significant trend across the whole group of 65 non-diagnostic thyroid FNAs when cases that were either *mixed cystic/solid* or *predominantly solid/focally cystic* were included, chi-square test NS. If the *mixed cystic/solid* and the *predominantly solid/focally cystic* cases were excluded from the analysis, 15 of 16 (93.7%) of the cases that appeared *purely solid* on ultrasound were reported as Thy1-equivalent to Bethesda class I and all 9 cases (100%) *pure cystic* on ultrasound were reported as Thy 1c, equivalent to Bethesda class I- '*cyst fluid only*', Fisher's exact test $p > 0.001$. Of the 28 cases that on ultrasound appeared *mixed cystic/solid* 5 were reported as Thy1, 12 as Thy1/Thy1c and 11 as Thy1c. Of the *predominantly solid/focally cystic* 7 cases were reported as Thy1, 4 cases as Thy1/Thy 1c, and 1 case as Thy 1c.

Discussion

This brief study suggests that it can be useful for a reporting pathologist with sufficient expertise to review the relevant ultrasound scans of thyroid lesions and thyroid nodules if an FNA is considered *non-diagnostic/unsatisfactory*. The principal reason is that solid thyroid lesions on ultrasound should nearly always yield diagnostic cellular material or show some other specific lesion. If a thyroid nodule is solid and cellular material is absent or lacking this implies that the FNA is likely to be unsatisfactory and that the FNA should be repeated. If the lesion is clearly from a unilocular/simple cyst on ultrasound and the cytopathologist is aware of this and there are no concerning ultrasound features identified by the radiologist or the cytopathologist then the lesion is likely to be of very low risk. However cases that are part cystic/part solid or predominantly solid with occasional cystic areas are potentially more problematic, particularly if the aspirate is taken from a cystic area of a larger lesion that is elsewhere solid. These lesions should not be categorised as Thy 1c in the UK terminology [7] or Bethesda Category I *cyst fluid only* [8] as this may understate the potential risk of malignancy of these lesions. Cases that are interpreted cytologically as purely cystic on FNA cytology, if the ultrasound shows a simple unilocular cyst, may after review of the ultrasound scan by a cytopathologist need no further follow-up. Triage of cases to potentially higher-risk lesions that require further follow-up and/or re-aspiration and/or possible surgery can be achieved. In this small prospective study all the cases that on ultrasound were purely cystic showed appearances in keeping with *cyst fluid only*, and lesions that on ultrasound appeared purely solid on ultrasound were in almost all cases were reported as Thy1.

It is also worth commenting that in the UK Royal College of Pathologists Terminology as also in The Bethesda System for Reporting Thyroid FNA cytology the *nondiagnostic/unsatisfactory* criteria are virtually identical. In the Bethesda system a non-diagnostic/unsatisfactory aspirate typically comprises fewer than six groups of well preserved well stained follicular epithelial cells, or is poorly prepared, poorly stained, or shows obscured follicular cells, or is a cyst fluid, whether without histiocytes or fewer than 6 groups of 10 benign follicular cells [8]. *The Bethesda System for Reporting Thyroid Cytology: Definitions, Criteria and Explanatory Notes* states that in the proper clinical setting e.g. ultrasound evidence of a simple unilocular cyst, cyst fluid only specimens may be considered clinically adequate even though they are reported as non-diagnostic/unsatisfactory [8].

In summary, in the appropriate clinical setting, cytopathological assessment of thyroid FNA can usefully be extended to include the cytologist's review of the ultrasound scans prior to issuing of the cytopathology report, if the cytopathologist sufficient expertise and training in ultrasound scan interpretation.

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