THYROID FINE NEEDLE ASPIRATION CYTOLOGY IN MORECAMBE BAY

A retrospective audit

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INTRODUCTION

Thyroid malignancies are relatively rare. According to the Office of Statistics the incidence of thyroid malignancy is 1.3 per 100,000 in men and 3.3 per 100,000 in women in the UK (2000). Therefore, in University Hospitals of Morecambe Bay (UHMB) we would expect to diagnose 16 cases per annum based on a population of 350,000.

Patients usually notice a lump in the neck and are then referred to a neck lump/thyroid clinic. Though there is national variation of incidence of thyroid malignancies of those patients who attend a fast track clinic up to 10% prove to be a thyroid malignancy, of which 90% are differentiated tumours (80% papillary and 10% follicular carcinoma), 5% medullary and 3% anaplastic carcinoma, and 1% lymphoma.

Current guidelines⁽¹⁾ recommend that the assessment and diagnosis of thyroid lumps or swellings involves clinical assessment, radiological imaging (ultrasound scanning), and cytological analysis of cells obtained from the swelling by fine needle aspiration (FNA). The latter involves using a small gauge needle ($\pm$ syringe) to aspirate cells from within the lump or swelling during the outpatient assessment, transferring them either into cytology fluid for preservation or onto a glass slide and air drying the cells or applying alcohol fixative to preserve them.

The cytologist will then analyse the sample for both adequacy and cytological abnormalities, provide a descriptive report and grade the sample as shown in table 1.

Obtaining an accurate, adequate sample can be troublesome, and may lead to a delay in the diagnosis of the

nature of the thyroid lump. It can be difficult explaining to patients the likelihood of requiring a repeat FNA, and the true value of the cytological aspirate result as part of the consent process prior to performing FNA. Inadequate results (Thy 1) are defined as less than six groups of ten thyroid epithelial cells within a given aspirate and should be repeated. Inadequacy rates vary between individual clinicians and centres, but there are currently no national guidelines for what is an acceptable rate. Studies report Thy 1 as occurring in between 5% and 41% of cases. Even where the sample was obtained with the pathologist immediately available and able to request a repeat sample, the rate of Thy 1 sampling was quoted at 12%.^(2,3)

Not only is the non-diagnostic 'inadequacy rate' important but also the 'suspicious rate' of FNA (results classified as abnormal cytology: Thy 3, 4, 5) and the overall malignancy detection rate (histologically proven cancer). The suspicious rate should be higher than the malignancy rate but again there are no national guidelines on acceptable rates. Surgical excision is recommended for suspicious cytology or inadequate cytology and equivocal swellings, but the procedure recommended may be affected by the cytology grade and patient wishes after discussion.

METHODS

A list of patients who had undergone thyroid FNA cytology from 1 January 2000 until 30 June 2006 was obtained from the UHMB pathology database (Systematised nOMenclature of MEDicine (SOMMED)) for procedures that had been carried out at the Royal Lancaster Infirmary (RLI), Furness General Hospital (FGH) and Westmorland General

Cytological Grade	Cytological Analysis	Clinical interpretation
Thy 1	Non-diagnostic or Inadequate	Inadequate (insufficient) thyroid epithelial cells or where technical artefact or inadequate cellular preservation precludes interpretation to permit lesion characterisation
Thy 2	Non-neoplastic	Sufficient normal thyroid epithelial cells to permit confident diagnosis of colloid nodule or thyroiditis
Thy 3	Equivocal	1. Follicular cells: unable to distinguish benign from malignant follicular neoplasm 2. Other: slightly atypical cells, inflammatory cells etc, not Thy 2 or Thy 4. Possibly consistent with thyroiditis, lymphoma, malignant thyroid or other pathology
Thy 4	Suspicious of malignancy	Abnormal cells with nuclear features suspicious but not diagnostic of malignancy (papillary, medullary, anaplastic carcinoma or lymphoma)
Thy 5	Malignant	Diagnostic of malignancy (papillary, medullary, anaplastic carcinoma, lymphoma or metastatic tumour): definite malignant cellular features

Table 1 Cytological descriptions of thyroid aspirate

Hospital (WGH). For patients from the RLI or WGH, SOMMED code B6 was used as FNAs were recorded using

“30% of patients with a histologically proven thyroid malignancy did not undergo FNA prior to surgery”

Thy 1 to Thy 5 protocol. At FGH all thyroid specimen reports were obtained (SOMMED code F6) as the cytology gradings were not always used when entering the data into the database. From the

record of these patients if the laboratory number ended in ‘e’ this was a cytology report, therefore, this patient had undergone an FNA and was entered into the audit.

Each FNA result had a specific pathology laboratory number, and from this all cytology and histology results for that patient could be accessed via the Trust’s pathology database. The cytology results gave the date, result, requester, pathologist and the hospital. This was entered into the data collection spreadsheet (Microsoft EXCEL®). If the patient had undergone surgery then the histology results could also be accessed and the results were entered into the database to correspond to that patient. A histology report would include the results, the date, the surgeon and the pathologist.

Once collected the data results were analysed and inadequacy, suspicious and malignancy rates for thyroid FNA determined. In addition the sensitivity, specificity and positive and negative predictive values for each cytology class were calculated using the Quality Assurance Standard Report.

RESULTS

From January 2000 until June 2006, 369 patients underwent thyroid FNA; 316 (86%) were female, and the average age was 53.4 years (range 16 to 100 years).

	Mean age (range)	Female	Male
RLI	54 (18-89)	171	29
WGH	51 (16-86)	76	3
FGH	53 (16-100)	69	21
Overall	53 (16-100)	316	53

Table 2 Demographic data

Hospital	No. of patients	Total number of FNAs
RLI	196	262
FGH	90	122
WGH	79	115
Unknown	4	5
Total	369	504

Table 3 The procedure is performed on all UHMB sites

Cancer Detection

Of the 40 patients diagnosed with thyroid malignancy 27 were female and 13 were male. The average age to be diagnosed with a malignancy was 53.2 years (range 26.7 to 81.8 years) compared with 51.7 years for benign cytology.

Of the 40 proven malignancies 28 had undergone pre-operative FNA, five patients on two occasions with the following results (see table 4) which highlight the difficulties of FNA sampling: initial Thy 1 results demand repeat FNA. Thy 2 results in clinically suspicious lesions can prove to be ‘false negative’ results.

Hospital	First FNA	Second FNA	Histology
RLI	Thy 1	Thy 3	papillary
RLI	Thy 1	Thy 3	follicular
RLI	Thy 2	Thy 1	papillary
RLI/WGH	Thy 4	Thy 5	anaplastic
FGH	Thy 1	Thy 2	papillary

Table 4 Five patients had cancer diagnosed after a second FNA sample, three of these had Thy 1 on the first sample

Furthermore, 30% of patients with a histologically proven thyroid malignancy did not undergo FNA prior to surgery. The reasons for this are not known, but may be due to variation in individual clinician’s clinical practice with some offering excision of suspicious or symptomatic lesions without performing FNA.

Malignancy and suspicious rates for FNA

Overall 7.6% of patients who had FNA pre-operatively were found to have a malignancy. Assessing all FNAs the suspicious rate (ie, cytology graded Thy 3, 4 or 5) for each FNA test is 9.3% compared with the true cancer rate of 5.5%.

Predictive value of FNA result for differing cytology classes

All Thy 5 results were proved to be malignant, and 60% of Thy 4 results were confirmed to be cancerous, but they were three patients who did not undergo surgery (reason unclear). Thus the positive predictive value of Thy 4 is 86% (see figure 3). Half of Thy 3 results were confirmed to be benign and just over a quarter were malignant. No definitive histology was available for the remainder and thus the positive predictive value of Thy 3 result is 27%.

Most of the FNA results were Thy 2 as expected, but a small number of Thy 2 results were proven malignant (3%). A quarter of the FNAs were proven histologically to be benign. The negative predictive value of Thy 2 is 97%.

	Differentiated Thyroid Cancers				Undifferentiated		
Hospital	Papillary	Follicular	Medullary	Hurtle Cell	Anaplastic	Lymphoma	Total no. of patients
RLI	9 (3)	5 (2)		1	1	1 (1)	23
FGH	5 (3)	1 (2)	(1)				12
WGH	4			1			5
Total	24	10	1	2	1	2	40

Table 5 Type of malignancy (Number in brackets = patients who did not have FNA prior to surgery)

FNA Result	Number	Proven Ca	Proven benign	No Histology
Thy 1	139	5	37	97
Thy 2	316	10	86	220
Thy 3	37	10	18	9
Thy 4	10	6	1	3
Thy 5	2	2	0	0

Table 6 Numbers of cancer detected compared with total number of FNA by grade of sample

Over 34 doctors of various grades performed FNA of the thyroid nodule. There were 28 procedures that did not have a named aspirator recorded: these may have include radiologists whose name did not appear on a request form. Thirteen doctors performed thyroid FNAs more than five times in the given time period.

DISCUSSION

The demographic results are similar to national results with a varied age range and a female preponderance. Thyroid malignancies are more common in women than men, but men have an increased rate of being diagnosed with a malignancy if presenting with a thyroid swelling. The average age of a thyroid condition and age of diagnosis for a malignant thyroid lesion are also similar to the national average. As expected most tumours (85%) are differentiated cancers.

Suspicious thyroid cytology results have high positive predictive values and knowledge of individual unit results should aid informed discussion with patients regarding surgery. Patients with Thy 5 and 4 should be treated as malignant; however, there is a 10% chance that Thy 4 may prove to be benign. This information can be used in the discussion with the patients as treating Thy 4 aggressively reduces the risk of inadequate primary surgery or need for further surgery (eg, completion thyroidectomy).

Patients with Thy 3 cytology need counselling regarding choice of initial surgery (hemi or total thyroidectomy) and up to a quarter may then require further completion surgery.

Whilst Thy 2 cytology in this series had a high negative predictive value, a substantial false negative rate demonstrates that clinical assessment remains important in the management of nodular thyroid disease. Current national guidelines suggest that patients with a thyroid lump should not be discharged from clinic until there are two Thy 2 results following FNA, and no clinically suspicious features.⁽¹⁾

FNA inadequacy rates (Thy 1) varied amongst the number of clinicians who perform the FNA. Individual clinicians who perform FNA more frequently have a slightly higher inadequacy rate; however, the range and therefore the predictability of the results are more constant. Clinicians who have less experience in performing FNA are also more unlikely to repeat the FNA. Five initially inadequate FNA results subsequently proved to be malignant on histology (12.5% of malignancies), but 70% of patients with initially inadequate FNA did not have a repeat FNA performed or surgical excision.

One in four thyroid FNA samples performed by clinicians are reported inadequate, and patients should be informed of this and the potential need and importance of repeat FNA when consent is obtained. Reasons for the high rate of 'inadequate' FNA samples include the inherent difficulties of obtaining an adequate number of identifiable cells from what

“patients with a thyroid lump should not be discharged from clinic until there are two Thy 2 results following FNA, and no clinically suspicious features”

are often 'bloody' samples as the thyroid gland is very vascular, or the fact that some tumours are relatively acellular or exhibit central necrosis. For these reasons technique or experience are not the only determinants of a successful FNA sample.

Units should establish a quality assurance programme to ensure patients with Thy 1 results undergo repeat FNA performed by clinicians with acceptable, audited FNA results.

Standardised FNA technique, ultrasound-guided FNA and immediate cyto-pathological analysis of FNA sample adequacy/quality have been reported to reduce inadequacy rates. All of these aspects may be best delivered through a dedicated thyroid/neck lump assessment clinic, as recommended in the guidance on cancer services.⁽⁴⁾

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