Thy3 cytology: what to do next?

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ABSTRACT

INTRODUCTION Cytological analysis of thyroid fine needle aspiration (FNA) is aided by the ‘Thy’ classification. However, there is often confusion surrounding the management of patients with a Thy3 classification. A subdivision of Thy3 has been created to help reduce this dilemma but its use within the UK appears to be infrequent. This paper analyses the management of patients with Thy3 cytology from FNA of a thyroid nodule in a UK case series and reviews the relevant literature. It also describes the results of a survey of selected UK ENT departments on the use of the Thy3 classification and its subdivisions.

PATIENTS AND METHODS A retrospective analysis of a case series of patients was undertaken. In addition, a telephone survey of local/regional pathology departments was conducted to assess the utilisation of the Thy classification and to assess the awareness and usage of the Thy3 subdivisions.

RESULTS A total of 39 Thy3 results (11 males, 28 females) were identified from 2007 to 2009. Of these, 24 patients went on to have surgery, 8 had a further FNA, 2 had a Tru-cut biopsy and 5 were lost to follow-up. Eleven (28.2%) patients were subsequently diagnosed with a thyroid malignancy. The survey identified that none of the departments had adopted the Thy3 subclassifications and only 40% were aware of them.

CONCLUSIONS Thy3 results from thyroid FNA have a significant risk of malignancy but there remains confusion surrounding their management. This district general hospital has adopted and recommends the use of the Thy3 (i) and Thy3 (ii) subdivisions in order to assist decision-making and avoid delays in treatment or unnecessary surgery.

KEYWORDS

Thy3 classification – Cytology – Thyroid

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It is estimated that 4–7% of the adult population has a palpable nodule and significantly more than this show nodules on ultrasound imaging.¹ Fine needle aspiration (FNA) is the mainstay of diagnosis in thyroid nodules and has decreased the number of patients undergoing thyroid surgery. Furthermore, it has been proven to increase the malignancy yield when used in addition to ultrasound imaging as a diagnostic tool.^{1–4}

In 2007 the ‘Thy’ classification for FNA of the thyroid was introduced by the British Thyroid Association (BTA) to guide management of the thyroid nodule. They suggested a management plan for each of the Thy1 to Thy5 results. These are summarised in Table 1.

The general recommendations made by the BTA regarding FNA of the thyroid are also important.⁵ These state that FNA should be used in planning of surgery with or without ultrasound guidance but the diagnosis is not always possible with FNA alone. They also state that the cytopathologist assessing the FNA should, ideally, have a specialist interest in the thyroid.

Of particular interest are those FNAs with a Thy3 result that is considered ‘indeterminate’. Deciding whether to manage these patients by performing another FNA or referring them directly for surgery can be difficult. The BTA

has subdivided this group into Thy3 (i) and Thy3 (ii) to help guide decisions regarding subsequent management. Thy3 (i) lesions are classified as a follicular lesion/suspected follicular neoplasm. The descriptive text should indicate the level of suspicion of neoplasia. Most of these cases will proceed to surgery. With regard to Thy3 (ii) lesions, there are a small number of cases where cytological evidence is not sufficient to justify inclusion into either Thy2 or Thy4, for example samples with worrying features but cells too scanty to qualify for a Thy4.⁵ The BTA guidelines suggest that Thy3 (ii) lesions should be discussed in the multidisciplinary team meeting to decide on the appropriate course of action.

It is estimated that 5–10% of all thyroid nodules are malignant^{6,7} and review of the literature shows that between 20% and 52% of Thy3 results are malignant.^{8,9,10} Thy3 results from FNA of the thyroid pose a problem as there is no clear guidance regarding the management of these potentially malignant lesions, which are reported to account for around 9% of FNA results from the thyroid.¹⁰

Following discussion in our ENT department, concerns had been raised over there being a lack of definitive protocol for the management of Thy3 nodules. At the time, the Thy3 subclassification was not being utilised. Therefore,

Table 1 Misleading arguments used against a regulated system of compensated donation

	Description	Action
Thy1	Non-diagnostic	Repeat FNA
Thy2	Non-neoplastic	2 x Thy2 3–6 months apart to exclude neoplasia
Thy3 (i)	Follicular lesion/follicular neoplasm (descriptive text to address level of suspicion)	In most cases lobectomy
Thy3 (ii)	Thy2/4 (insufficient features of neoplasia to warrant inclusion in Thy4)	Discussion with multidisciplinary team
Thy4	Suspicious of malignancy	Discussion with multidisciplinary team, possible surgical intervention
Thy5	Diagnostic of malignancy	Multidisciplinary team, possible surgical intervention

the aims of this study were threefold: first, analyse the outcomes for all Thy3 results from FNA over a set period of time in the dedicated lump in the neck clinic at a district general hospital; second, determine the malignancy rate in this group of patients; and third, survey ten regional/local pathology departments as to whether or not they employ the Thy3 subclassification in the cytological analysis of thyroid FNA results.

In addition, this study aimed to summarise BTA and American Thyroid Association (ATA) guidelines for the management of FNA from the thyroid and review the literature regarding Thy3 results and their management.

Materials and Methods

A retrospective review of all Thy3 results was conducted by assessing all the FNAs performed on the thyroid gland between January 2007 and January 2009. The data set was then analysed to determine which patients went on to have surgery or undergo further investigation. The results of histology were compared to the initial cytology in the surgical group.

A telephone survey of ten regional/local pathology departments was also conducted to assess the utilisation of the Thy classification and to assess the awareness and usage of the Thy3 (i) and (ii) subdivisions.

Results

A total of 59 Thy3 results (11 males, 28 females) were identified from January 2007 to January 2009. The average age in this group was 48.9 years, with a male to female ratio of 1:2.5. Each Thy3 result was discussed in a regular meeting prior to clinic, comprising at least one consultant ENT surgeon, a consultant pathologist with a specialist interest in thyroid pathology and a consultant radiologist with a specialist interest in head and neck ultrasound. The outcome of these patients is summarised in Figure 1.

Of the 24 patients who went straight to surgery, 37.5% were found to have a malignancy. The histology of this group is summarised in Table 2.

However, there were ten patients who were classified as Thy3 but not deemed to have sufficient cytological evidence to justify surgery and were therefore recommended for further FNA or a Tru-cut biopsy. Of these, five had a repeat Thy3 result on cytological analysis. Three of these patients went on to have surgery and histology showed one papillary carcinoma, one follicular carcinoma and one nodular colloid goitre. Of the two patients who did not go on to have surgery, one was diagnosed with lung cancer and underwent no further investigation, the other died of other causes. Regarding the other five patients who had a repeat FNA or a Tru-cut biopsy, two had a Thy1 result, two had a Thy2 result and one was found to have a thyroid cyst. The median time to subsequent FNA/Tru-cut was 52.5 days.

By combining the results for both groups (those that initially had surgery and those that underwent further investigations), the overall malignancy rate was 28.2%. This is summarised in Table 3.

Following a telephone survey of ten regional/local pathology departments, 50% ($n=5$) confirmed that they employed a pathologist with a specific interest in thyroid pathology. The survey identified that 90% ($n=9$) were using the BTA Thy classification. However, none had adopted the Thy3 subclassifications. Furthermore, only 40% ($n=4$) were aware of the subclassifications.

Discussion

It has been reported that there is a malignancy rate of 20–52% for Thy3 results.^{8,9} Despite the undoubted role for an ‘indeterminate’ or Thy3 group,¹¹ there is uncertainty regarding the management of patients with Thy3 results from FNA of the thyroid. In our study, 69.2% ($n=27$) of patients with a Thy3 result went on to have surgery. Overall, there was a 28.2% ($n=11$) malignancy rate.

Table 2 Histology from patients going on to have surgery after Thy3 cytological classification from an initial FNA

Histology	Number
Follicular adenoma	37.5% (n=9)
Papillary carcinoma	16.6% (n=4)
Follicular carcinoma	12.5% (n=3)
Hurtle cell carcinoma	8.3% (n=2)
Multinodular/colloid goitre	8.3% (n=2)
Hashimoto's thyroiditis	8.3% (n=2)
Hurtle cell adenoma	4.2% (n=1)
Atypical adenoma	4.2% (n=1)

Table 3 Malignancy rate overall and in each group

Group	Number	Percentage
Another FNA/ Tru-cut	2/10	20.0%
Straight to surgery	9/24	37.5%
Total	11/39	28.2%

Of the ten Thy3 patients who went on to have further investigations, five had another Thy3 result. Of this subset, three went on to have surgery. Histological analysis of this group demonstrated that two had a malignancy (one papillary carcinoma and one follicular carcinoma).

Data comparing malignancy rates between Thy3 (i) and Thy3 (ii) groups are sparse but there are studies that have looked at the malignancy rate within the Thy3 group as a whole. An audit of FNA across five NHS hospitals looking at Thy3 results and their subsequent management demonstrated that 20–75% of Thy3 cases go on to surgical excision, with a 35% malignancy rate on histological analysis.¹² It is

therefore clear that the rate of patients going on to have surgery and the malignancy rate seen with the Thy3 group in our study is comparable to that quoted in the literature.

To date, this study and the one previously mentioned highlight the potential confusion surrounding the future management of Thy3 lesions. There has been an attempt by the BTA to address this issue with the addition of the Thy3(i) and Thy3(ii) groups. These subdivisions within the Thy3 groups are accompanied by a suggested management protocol. A thyroid lobectomy is advised for Thy3 (i) results whereas discussion within a multidisciplinary team is suggested for a Thy3 (ii) result.⁵

The telephone survey conducted in this study showed that subclassification of Thy3 results has not been adopted by any of the ten hospitals contacted and only 40% (n=4) were aware of it. If this is the case nationwide, then the subclassification is clearly an under-utilised addition to the cytological analysis of Thy3 FNAs that could assist in the management of such patients.

The ATA guidelines differ; they recommend a radio-nuclide scan for a suspicious or follicular lesion. If a hot nodule is found that correlates with the nodule identified on ultrasound imaging, then surgery is not recommended as the malignancy rate is low.¹⁵ However, if a cold nodule is found, the patient should proceed to have surgery.

At an ATA meeting in 2007 a recommendation was made that Thy3 results should be divided into an atypical or borderline group and a follicular neoplasm group. Patients with atypical or borderline results should go on to have repeat FNA in three to six months. If this gives the same result or is more suspicious than the first FNA, they should undergo surgery, whereas those with a follicular neoplasm should go straight on to have surgery.¹⁴ Those with cytology suggesting a follicular neoplasm initially should also go straight on to have surgery.

Interestingly, at the ATA meeting in 2007 a six-tier scheme and associated risk of malignancy was suggested.¹⁵ This scheme was found to be effective for determining which patients needed surgery versus follow-up FNA.¹⁶

Conclusions

Our study showed that the percentage of patients with Thy3 results going on to surgery and the malignancy rate in each group are in keeping with that quoted in the literature. It is therefore clear that Thy3 results from FNA of the thyroid have a significant risk of malignancy but there still remains a grey area surrounding the management of Thy3 results. This lack of clarification of treatment of patients with Thy3 results may lead to a delay in treatment. This district general hospital has adopted and recommends the use of Thy3 (i) and Thy3 (ii) subdivisions in order to assist decision-making and avoid delays in treatment or potential unnecessary surgery.

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