

CLINICAL STUDY

Fine needle cytology of complex thyroid nodules

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Abstract

Objective: To evaluate whether a preliminary aspiration (ASP) of the cystic component and/or using spinal needles in complex thyroid nodules (CTN) could improve the adequacy of cytological sampling. **Methods:** Between January 2004 and December 2006, 386 consecutive patients with CTN were enrolled in this prospective investigation. Ultrasound (US) fine needle aspiration cytology (FNAC) of the solid component of the nodule (one nodule per patient) was performed using two different 25 gauge needles, with (Yale Spinal, YS) or without (Neolus, NS) a stylet, in alternate sequence on consecutive patients. In addition, a subgroup of patients presenting larger cystic component (~50%) was submitted to total aspiration of the cystic component (ASP+) or not submitted (ASP-) before US-FNAC, in alternate sequence within each needle type group. All the samplings were performed by a single endocrinologist.

Results: Adequate specimens were observed in 163 (84.5%) and 183 (94.8%) nodules investigated by NS and YS respectively. Sampling with the stylet needle was associated with an overall significant reduction of non-diagnostic specimens (15.5% vs 5.2% by NS and YS respectively, $P < 0.001$). The favourable result obtained with YS was independent from preliminary aspiration of the cystic component (ASP+: 14.8% vs 5.7% by NS and YS; ASP-: 16.2% vs 4.8%, not significant). A logistic regression analysis, taking into account nodule size and presence of intranodal vascularity at eco-colour evaluation of the solid component, confirmed that needle type was the only significant predictor of successful sampling (odds ratio 3.6 (95% confidence interval 1.7–7.6), $P < 0.001$).

Conclusions: Our data show that adopting stylet needles to perform FNAC in CTN may significantly improve the percentage of adequate sampling. On the other hand, preliminary aspiration of CTN with large cystic component does not add any advantage.

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Introduction

Ultrasound (US) fine needle aspiration cytology (FNAC) is the best available diagnostic procedure to evaluate thyroid nodules to submit to surgery (1–3), with accuracy in distinguishing between benign and malignant thyroid nodules approaching 95%. FNAC is safe, cost effective and may be performed in an outpatient setting. The major limit of this procedure is the high rate of inadequate specimens, reportedly from 10% to 31% (1, 4–6); in this respect, complex thyroid nodules (CTN, i.e. cystic nodules with significant solid components, ~40% of all thyroid nodules) represent a major challenge for cytological diagnosis due to a particularly high rate of non-diagnostic specimens (7–14). We have reasoned that the relatively high pressure of the fluid in CTN may exert a negative effect on FNAC performance. We have also recently shown that the use of needles with a stylet significantly reduces inadequate cytological sampling in solid nodules (2). The purpose of the present study was to examine whether an improvement in the adequacy of cytological sampling in

CTN could be accomplished by preliminary aspiration (ASP) of the cystic component and/or using spinal needles.

Materials and methods

We enrolled in this prospective investigation 386 consecutive patients with CTN, selected from 2877 patients (2244 females, 633 males, mean age 51.2 ± 11.9 years old) referred to our department for US-FNAC between January 2004 and December 2006. US investigation was performed using an ultrasonographic scanner (Logic 9, General Electric, Milwaukee, WI, USA) equipped with a 10–14 MHz linear transducer for morphological study and 4–7 MHz for colour Doppler evaluation. Vascular pattern was evaluated using sagittal and transverse scans performed along the maximum diameter of solid part of the nodule; as previously specified, an absence of flow signals or intranodular flow with multiple vascular images were classified as types 0 and 2 respectively (15).

US-FNAC of the solid component of the nodule (one nodule per patient) was performed using two different 25 gauge needles, with (Yale Spinal, YS) or without (Neolus, NS) a stylet, in alternate sequence on consecutive patients. In addition, a subgroup of patients presenting larger cystic component ($\sim 50\%$) was submitted (ASP+) or not submitted (ASP-) to total aspiration of the cystic component before US-FNAC, in alternate sequence within each needle type group. All the samplings were performed by a single endocrinologist.

Two passes for each nodule were performed and the material was obtained by capillary action. Cytological specimens were evaluated in blind by the same cytopathologist and according to the guidelines of the Papanicolaou Society of Cytopathology, the smear was considered adequate if there were at least five groups of well-visualized follicular cells, each group containing ten or more cells (16). All patients with suspicious or malignant cytology underwent surgery.

Written informed consent was obtained from all subjects.

Statistical analysis

ANOVA or χ^2 test were used for between-group comparisons of continuous or categorical variables respectively. Logistic analysis was performed to examine the influence of the experimental factors (needle type and preliminary aspiration of the cystic component) and the potential confounders (nodule size and vascularity of the solid component) on cytological sampling adequacy.

All data were analysed using SPSS version 11.5 (SPSS Inc., Chicago, IL, USA). Data are mean \pm s.d. Statistical significance was considered at $P < 0.05$.

Results

Out of 386 patients (285/101 females/males, mean age 53.1 ± 11.8 years old) with complex thyroid nodule, 145 females and 48 males (mean age 53.7 ± 13.2 years old) were submitted to US-FNAC by NS whereas the others, 140 females and 53 males (mean age 52.5 ± 13.5 years old), by YS.

Overall, in 156 patients the CTN was embedded in a multinodular goitre, while the others presented a single CTN. In addition, 176 patients (45.6%) presenting CTN with a larger cystic component were submitted to US-FNAC of the solid component of the nodule, alternatively with NS or YS needles, preceded by near total aspiration of the cystic component.

The principal US characteristics of the two groups are reported in Table 1.

Adequate specimens were observed in 163 (84.5%) and 183 (94.8%) nodules respectively, investigated by NS and YS (Table 2).

Sampling with the stylet needle was associated with an overall significant reduction of non-diagnostic

Table 1 Ultrasound characteristics of nodules submitted to fine needle aspiration cytology (FNAC) by different needles.

	Neolus needle	Yale needle
No. of patients (nodules)	183	183
Single nodule/embedded in multinodular (<i>n</i>)	117/76	113/80
Mean diameter of all complex nodule (mm)	17.8 ± 3.3	17.7 ± 3.8
Mean diameter of solid component (mm)	9.6 ± 2.1	9.8 ± 2.3
Vascular type 2 (<i>n</i>)	96	92

specimens (15.5% vs 5.2% by NS and YS respectively, $P < 0.001$). The favourable result obtained with YS was not statistically significant when the analysis was limited to nodules presenting vascular pattern type 0 (rate of inadequate sampling 9.3% vs 5.9% by NS and YS, not significant) and was independent from preliminary aspiration of the cystic component (8.3% vs 6.7%, ASP- and ASP+ respectively, not significant). Logistic regression analysis taking into account needle type, vascularity pattern, aspiration of the cystic component and nodule size showed that needle type was the only significant predictor of successful sampling (odds ratio 3.6 (95% CI 1.7–7.6), $P < 0.001$; Table 3).

In this series, there were no relevant complications (s.c. haematoma, infection) with either of the needles, and local pain or discomfort, though not formally assessed, was generally limited and similar with both procedures.

Cytological results obtained by each needle are summarized in Table 3; a diagnosis of papillary carcinoma was histologically determined in 19 of the 28 nodules that were submitted to surgery based on suspicious or neoplastic findings at cytological evaluation (see Table 4).

Discussion

The results of our study show that fine needle aspiration cytology of CTN performed with a stylet needle (YS) significantly improves the percentage of adequate sampling

Table 2 Percentage of inadequate sampling obtained with the two different needles.

	Inadequate samples, n	
	Neolus	Yale spinal
ASP+		
Vascularity type 0	3/44 (6.8%)	3/46 (6.5%)
Vascularity type 2	10/44 (22.7%)	2/42 (4.8%)
Total ASP+	13/88 (14.8%)	5/88 (5.7%)
ASP-		
Vascularity type 0	6/53 (11.3%)	3/55 (5.5%)
Vascularity type 2	11/52 (21.2%)	2/50 (4.0%)
Total ASP-	17/105 (16.2%)	5/105 (4.8%)
All nodules	30/193 (15.5%)	10/193 (5.2%)

Table 3 Logistic regression analysis of successful sampling predictors.

Predictor	Odds ratio (95% CI)	P value
Yale spinal needle	3.6 (1.7–7.6)	<0.001
Vascularity type II	1.8 (0.9–3.5)	NS
ASP+	1.1 (0.6–2.2)	NS
Nodule size (antero-posterior \varnothing)	1.1 (1.0–1.2)	NS

CI, confidence interval.

as compared with a traditional hypodermic needle (NS). This study confirms similar findings obtained by our group in solid nodules (2) and suggests that the advantage offered by stylet needles is similar in cystic nodules.

It is important to underline that the distribution of single nodules, the mean diameter of all the lesions and the mean diameter of all the solid component of the complex nodule, such as the number of nodules with vascularity type 2 was superimposable between the two groups (Table 1). It appears at a subgroup analysis that the cytological results obtained from nodules with vascularity type 0 are independent from the type of needles used.

In addition, we demonstrate that the favourable results obtained by stylet needles are independent of preliminary aspiration of the cystic component of mixed nodules.

The procedure adopting a stylet needle was well tolerated and side effects (discomfort, pain) were superimposable to those observed with a hypodermic needle; no complications (haemorrhage, infections) were observed with either type of needle and regardless of aspiration procedure. In this respect, our results differ from the data reported by Braga *et al.* (17); in fact, they showed a high rate of haemorrhage within the cavity of CTN when performing a partial aspiration of the fluid before FNAC of the solid component. We have no answers to this intrigue point. Obviously, other studies are needed in order to clarify if a total fluid aspiration versus a partial aspiration could indeed reduce the number of haemorrhages, as seen in the present study.

In the past, complex nodules were often regarded as a benign finding that could be managed conservatively, but it is now widely recognized that these lesions have

Table 4 The final cytological results obtained by each needle.

	Neolus	Yale spinal
Cytological diagnosis		
Benign	148 (90.8%)	165 (90.2%)
Suspicious	7 (4.3%)	9 (4.9%)
Cancer ^a	8 (4.9%)	9 (4.9%)
Total	163 (100%)	183 (100%)
Histological diagnosis		
Benign	2 (13.3%)	3 (16.7%)
Follicular adenoma	4 (26.7%)	5 (27.8%)
Cancer ^a	9 (60.0%)	10 (55.5%)
Total	15 (100%)	18 (100%)

^aPapillary cancers.

approximately the same potential for being malignant as does a solid tumour (11–14, 18, 19); moreover, it is also well documented that complex thyroid cancers are commonly papillary tumours, even if follicular, Hurthle cells and medullary histotypes are reported (20–22).

In this study, all the tumours were papillary cancers and the prevalence of malignancy (5.4%) in CTN was in accordance with the literature data and the previous investigations obtained in a larger series of nodules (1, 2, 7).

In our study, we have not taken into account a further option to improve the number of adequate specimens, i.e. the Diff-Quick stain procedure may (7, 23–25). However, the advantage of this procedure has been documented for solid thyroid nodules, whereas in complex lesions the rate of inadequate sampling seems to remains high (7, 26).

In conclusion, this study shows evidence that adopting stylet needles to perform FNAC in CTN may significantly improve the percentage of adequate sampling. On the other hand, preliminary aspiration of CTN with large cystic component, though apparently not limited by higher rate of side effects or complications, does not add any advantage. On this basis, we may suggest the adoption of stylet needle for US-FNAC of both solid and cystic thyroid nodules.

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