



The importance of using fine-needle aspiration cytology in the diagnosis of thyroid nodules

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ABSTRACT

Background: Thyroid nodules are common diseases, frequent in middle-aged women; only 5%–30% are malignant. Fine needle aspiration cytology is a simple, rapid and non invasive diagnostic test, performed to predict malignancy and avoid unnecessary surgery.

The aim of this study is to evaluate the accuracy of fine needle aspiration in the management of thyroid lesions. **Materials and methods:** Our study was retrospective, including all cases of thyroid fine needle aspiration between January 2010 and December 2017, which were verified by microscopic examination, Data was obtained from the files of Pathology and ENT Department of Farhat Hached Hospital of Sousse and from nuclear medicine department of Sahloul Hospital of Sousse, Tunisia.

Results: A total of 58 cases were studied, the main age was $40 \pm 15,57$ years and the sex ratio was 0.03 with female predominance. Concordance between fine needle aspiration and histology was seen in 45 cases. The sensitivity was 60% and the specificity was 100%. The negative and positive predictive values were 100 and 92%, respectively. The concordance index Kappa was of 0.67.

Conclusion: Thyroid fine needle aspiration in experienced hands is an easily performed diagnostic procedure with very little associated risk. It should be performed in suspect nodules for treatment stratification.

1. Introduction

Thyroid nodules are common disorders with a prevalence ranged from 4 to 7% in adult population, 5%–30% are malignant [1]. The fine needle aspiration cytology (FNAC) is the most accurate diagnostic test, performed to determine malignancy and reduce the number of unnecessary surgery for benign nodules [2] (see Fig. 1).

The aim of this study is to access the accuracy of fine needle aspiration cytology in the diagnosis and management of thyroid lesions with a literature review.

2. Materials and methods

This was a retrospective study, performed between January 2010 and December 2017, including all cases of thyroid fine needle aspiration cytology, which were verified by microscopic examination by an

experimental cytologist (20 years of experience) and pathologist assistant (7 years of experience). Data obtained from the files of Ear Nose Throat department and Pathology Department of Farhat Hached Hospital of Sousse, and from nuclear medicine department of Sahloul Hospital of Sousse, Tunisia.

The FNAC was carried out with a 22 to 27 gauge needle attached to a 20-mL needle with two to six passes in each nodule. The smears were air-dried and fixed by 95% alcohol. Then, the slides were stained with May-Grunewald-Giemsa (MGG). Cytological classification was done according to the guidelines of the European Thyroid Association Bethesda 2017 (Table 1).

The data were captured using Statistical Package for the Social Sciences (SPSS) software version 21. For descriptive analysis, we calculated frequencies and percentages for qualitative variables. For the concordance analysis we used the kappa test (κ). The study of the FNAC was the diagnostic test to be evaluated by calculating its sensitivity, specificity,

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positive predictive value (PPV) and negative predictive value (NPV) in comparison to the surgical specimen. All statistical tests were bidirectional with a significance level of 0.05.

The concordance between FNAC and surgical specimens was analyzed by determining the kappa coefficient (95% CI) using the kappa (k) test. Concordance of 0–0.2 was defined as negligible, 0.21–0.40: as weak, 0.40–0.60: as moderate, 0.60–0.80: as good, and 0.80–1.00: as perfect. We had follow the instruction of 2020 scare guidelines [3].

3. Results

A total of 58 cases were studied in 57 patients, the mean age of the patients was 40 ± 15 , 57 years, ranged from 12 to 76 years. The sex ratio was 0.03 with a female predominance.

Familial history of thyroid cancer was found in one case (1,8%), goiter in 7 cases (12,3%) and personal history of thyroid surgery was noticed in one case (1,8%). The major symptom was dysphagia (60%). Thyroid function tests including thyroid-stimulating hormone and L thyroxine was practiced in all patients, 39 patients was hypothyroid (68,42%).

At the ultrasound exam, the size of nodules ranged between 0,1 and 9,5 cm. All nodules were unique except in one patient who had two. Forty-seven nodules were sharply demarcated (87,04%) and seven were poorly demarcated (12,96%). Regarding the echogenicity, thirty-three

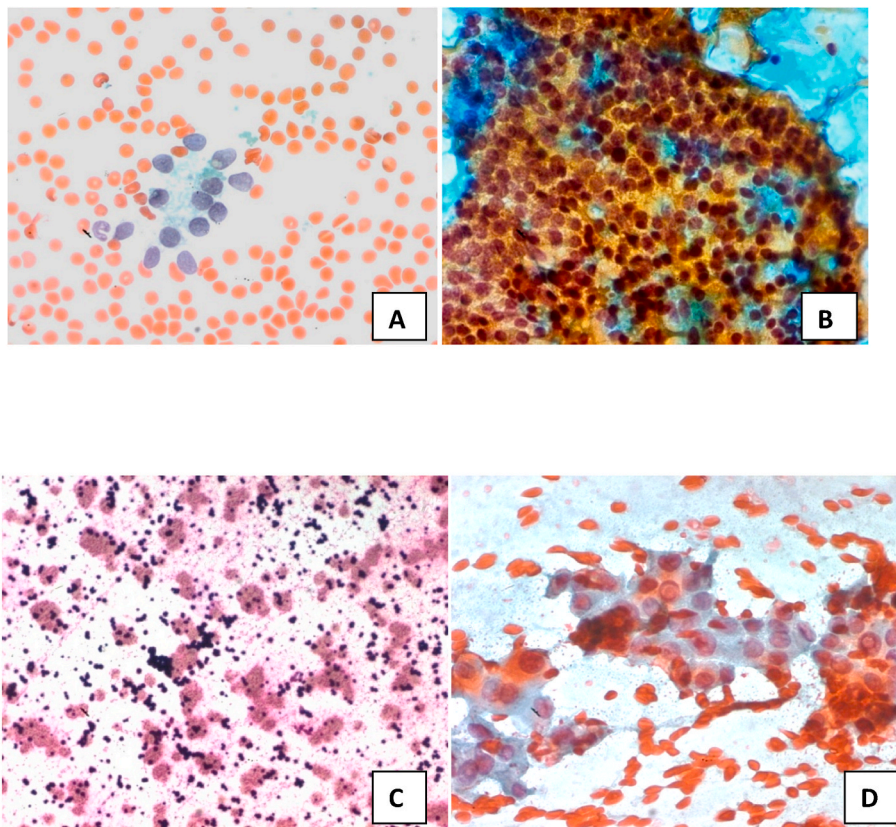
nodules were anechoic (61,11%), nineteen were hypoechoic (35,19%) and two were hyperechoic (3,7%). According to European - Thyroid Imaging and Reporting Data System (EU-TIRADS) Classification 2017, ten (17,24%) nodules were suspicious for malignancy (EU-TIRADS 4 or 5) and forty-eight were benign (82,76%) (EUTIRADS 2 or 3).

Cytologically, the 58 cases were classified as unsatisfactory (Bethesda I) in 2 cases (3,45%), benign in 43 (Bethesda II) (74,14%) (Figure A), suspicious for follicular neoplasm in 7 cases (Bethesda IV) (12,07%) (Figure B et C) and malignant (Bethesda VI) in 6 cases (10,34%) (Figure D).

All of our patients underwent surgery, 10 patients had total thyroidectomy with lymph node dissection and 48 patients had lobectomy. The histology revealed 48 benign nodules (82,76%) and 10 malignant ones (17,24%) corresponding to nine cases of papillary carcinoma and one case of follicular carcinoma.

Cyto-histological correlation showed that the unsatisfactory cases were all benign. Out of 43 benign cytological nodules (Bethesda II), only 4 were malignant with three papillary carcinomas and one follicular carcinoma. The suspicious cases for follicular neoplasm (Bethesda IV) were all benign. The 6 cases cytologically malignant (Bethesda VI) was confirmed by histology and all cases were papillary carcinoma (Table 1).

According to our study, sensibility of the FNAC was of 60% and specificity of 100%. The negative and positive predictive values were 100 and 92%, respectively. The cyto-histological concordance showed a



A-Benign follicular cells (Bethesda I), MGG x 400

B-Suspicious for follicular neoplasm (Bethesda IV), MGG x400

C- Suspicious for oncocytic neoplasm (Bethesda IV), MGG x400

D-Papillary carcinoma, malignant (Bethesda VI), MGG x 400

Fig. 1. A-Benign follicular cells (Bethesda I), MGG x 400. B-Suspicious for follicular neoplasm (Bethesda IV), MGG x400. C- Suspicious for oncocytic neoplasm (Bethesda IV), MGG x400. D-Papillary carcinoma, malignant (Bethesda VI), MGG x 400.

Kappa index of 0.67, indicating a good concordance.

4. Discussion

Thyroid nodules are a current disease occurring especially in middle-aged female with an estimate of 4–10% in the adult population [4]. There are mostly benign, malignant nodules accounts 5–30% [3–8]. Diagnosing malignant nodules is challenging, FNAC, indicated for clinical, ultrasonographic, and scintigraphic suspected of malignancy nodules, is the most accurate tool, that enable the screening of lesions that should be operated [1,2,5,6]. Indeed, FNAC is a quick, safe, ease of repetition, and low cost diagnostic exam [1,2,5,6]. Its wide use has significantly reduced the number of unnecessary surgeries and in counterpart in the increase of malignant specimens revealed after thyroidectomies [4,7,8].

Currently, it is highly recommended the use of the 2017 Bethesda system for reporting thyroid cytopathology, according to this system, FNAC results are classified in one of six categories: unsatisfactory (Bethesda I), benign (Bethesda II), Atypia of undetermined significance or follicular lesion of undetermined significance (Bethesda III), suspicious for follicular neoplasm (Bethesda IV), suspicious for malignancy (Bethesda V) and malignant (Bethesda VI) [Figure 1](#). For each of these categories is assigned to a risk for malignancy, and treatment option for the patient [8–10] ([Table 2](#)).

In our study, the specificity was of 100%, the sensitivity was of 60%, the negative and positive predictive values were 100 and 92%, respectively. The concordance index Kappa was of 0.67, indicating a good concordance.

Most previous studies reported high degree of specificity (74%–100%) [11–24] and acceptable degree of sensitivity, ranging between 61% and 100% [11–24]. Concordance between FNAC and histological examination of surgical specimen is good to perfect, with Kappa index of 0.67–0.96 [11–13,15–19,21], which is consistent with our findings.

Rare studies have found no encouraging results [14,17,18,22,23], these series were unicentric, considering a small number of cases, and showing a high rate of non diagnostic cytology, reaching 20%, which explain the large number of false negative cases and in consequence the decrease of the sensibility [14,17,18,22,23] ([Table 3](#)).

High rate of false negative rate are explained by sampling errors, occurring mostly in nodules measuring more than 4 cm and less than 1 cm. In fact, FNAC remains an operative dependent technique, it depends on the skill and experience of the clinician as well as the cytopathologist expertise [7].

Another limitation of FNAC related to the histological type of the lesion, indeed, unlikely papillary carcinoma which can be easily diagnosed on FNAC, some lesions may not be identified [25] example of the presence of microfollicular structures or crowded cellular clusters is a challenge to diagnosis, particularly in low-quality specimens; in fact, the distinction between follicular carcinoma and follicular adenoma requires an evaluation of capsular or vascular invasion, findings that necessitate histological assessment [1], this was observed in our study, since a case of follicular carcinoma was cytologically diagnosed as benign.

These limits can be exceeded by using of ultrasound-guided FNAC to avoid sampling errors and the use of immunohistochemical markers as well as molecular testing that has been recently introduced based on

Table 1
Cyto-histologic correlation.

	Non diagnostic	Benign	Atypia of undetermined significance	Suspicious of follicular neoplasm	Suspicious of malignancy	Malignant
Thyroid adenoma	2	26	0	7	0	0
Goiter	0	5	0	0	0	0
Thyroiditis	0	8	0	0	0	0
Papillary carcinoma	0	3	0	0	0	6
Follicular carcinoma	0	1	0	0	0	0
Total	2	43	0	7	0	6

Table 2

The 2017 Bethesda System for Reporting Thyroid Cytopathology: Implied Risk of Malignancy and recommended management.

Diagnostic category	Risk of malignancy if NIFTP ≠ CA (%)	Risk of malignancy if NIFTP= CA (%)	Usual management
Nondiagnostic/ Unsatisfactory (Bethesda I)	5–10	5–10	Repeat FNA with ultrasound guidance
Benign (Bethesda II)	0–3	0–3	Clinical and sonographic follow up
Atypia of undetermined significance or follicular lesion or undetermined significance (Bethesda III)	6–18	10–30	Repeat FNA, molecular testing or lobectomy
Follicular neoplasm or suspicious for a follicular neoplasm (Bethesda IV)	10–40	25–40	Molecular testing, lobectomy
Suspicious for malignancy (Bethesda V)	45–60	50–75	Near-total thyroidectomy or lobectomy
Malignant (Bethesda VI)	94–96	97–99	Near-total thyroidectomy or lobectomy

liquid-based cytology to improve diagnosing of follicular carcinoma [2, 27,9,26].

5. Conclusion

In summary, fine needle aspiration cytology is a valuable test, considered the gold standard diagnostic tool for thyroid nodules [2]. Combination of additional and advanced diagnostic methods such as immunocytochemical studies and molecular pathology techniques enhance the prognostic value of FNAC.

Through this study, we enhance the importance of using FNAC before surgery to predict malignancy and avoid unnecessary one. Studies will be needed to improve the performance of FNAC.

Ethical approval

This study is exempt from ethical approval at our institution.

Availability of data and material

The authors declare that there are that all data and materials are available.

Author's contribution

Bchir Ahlem: Drafting, conception, analysis.

Hamza Zammel, Missaoui Nabih: conception, collecting data.

Bdioui Ahlem: acquisition and interpretation of data.

Hmissa Sihem, Mokni Moncef: revising.

Table 3
Results of thyroid fine needle aspiration cytology in the literature.

Studies	Number of FNAC performed	sensibility (%)	specificity (%)	Kappa index
El Hag IA. et al. [10]	67	85.7	97,6	0,94
Leonard N. et al. [11]	184	88	78	0,8
Ari. D. et al. [12]	349	87	46	0,68
Cheung, YS et al. [13]	179	54	100	–
Çap. J et al. [14]	536	86	74	0,75
Mojghan A. et al. [15]	354	93	96	0,96
Morgan JL. et al. [16]	253	67.2	73,7	0,67
Nicholas J. et al. [17]	199	61	100	0,96
Slowinska D. et al. [18]	3572	69	86	0,86
Lioe TF. et al. [19]	208	91	94	–
Leenhardt L. et al. [20]	450	94	63	0,95
Prades J.-M et al. [21]	202	55,8	99,1	–
Guevara N et al. [22]	252	39,1	100	–
Sellami M et al. [23]	117	100	67	–
Yang et al. [24]	4703	94	98.5	–
Gupta et al. [25]	75	80	86.6	–
Bukhari et al. [26]	120	100	82.5	–
Mondal et al. (28)	1020	86.6	87	–
Muratli et al. (29)	1607	87.1	64.6	–
Mehra et al.(30)	225	76,92	88,46	–
Our study	57	60	100	0.91

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Registration of research studies

1. Name of the registry: N/A*
 2. Unique identifying number or registration ID:N/A*
 3. Hyperlink to your specific registration (must be publicly accessible and will be checked):N/A*
- * Exempt, not a first case report.

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Declaration of competing interest

The authors have no conflict of interest to disclose.

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List of abbreviations

FNAC	Fine needle aspiration cytology
ENT Department	Otolaryngology or Ear Nose and Throat Department
MGG	May-Grunewald-Giemsa
SPSS	Statistical Package for the Social Sciences
PPV	positive predictive value
NPV	negative predictive value

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2021.01.101>.

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