#### ©Borgis

## \*Magdalena Grajewska-Ferens<sup>1</sup>, Joanna Cielecka-Kuszyk<sup>2</sup>

# The use of fine needle aspiration biopsy in the diagnosis of thyroid nodules

## Zastosowanie biopsji cienkoigłowej w diagnostyce guzków tarczycy

<sup>1</sup>Department of Pediatrics and Endocrinology, Medical University of Warsaw Head of Department: Beata Pyrżak, MD, PhD <sup>2</sup>Department of Virology, National Institute of Public Health – National Institute of Hygiene, Warsaw Head of Department: prof. Bogumiła Litwińska, MD, PhD

#### Key words

children, thyroid nodule, fine needle aspiration biopsy

#### Słowa kluczowe

dzieci, guzek tarczycy, biopsja aspiracyjna cienkoigłowa

### Address/adres:

\*Magdalena Grajewska-Ferens Department of Pediatrics and Endocrinology Medical University of Warsaw ul. Marszałkowska 24, 00-576 Warszawa tel. +48 (22) 522-73-60 leszek.ferens@kliniczny.pl

#### Summary

**Introduction.** Fine needle aspiration (FNA) is a simple, inexpensive, easily performed outpatient procedure which can provide a rapid diagnosis. It is eminently suitable for the investigation of superficial palpable lesions in many sites, including the thyroid gland. Cy-tological examination of aspirated material can detect thyroiditis, toxic hyperplasia and colloid goiters as well as neoplastic processes, epithelial, lymphoid and metastatic changes.

**Aim.** The aim of this study was the analysis of the results of FNAB in thyroid nodules in children, the usefulness of FNAB in the therapeutic procedures and comparison of the cytologic changes with the postoperative changes of the thyroid.

**Material and methods.** Thirty seven patients (33 females and 4 males) of the Clinical Department of Endocrinology and Pediatrics in the Warsaw University of Medicine, were qualified to FNA because of the presence of thyroid nodules. The age of patients varied from 7 to 18 years old. The microscopical changes were described according the cytological picture and graded by recommended diagnostic categories using Bethesda System.

**Results.** In most patients (31/37) the results of FNA were consistent with the grade 2 according to Bethesda System, in one patient with the grade 1, in two patients with the grade 3, in another two patients with the grade 5, and finally in one patient with the grade 6 corresponding to papillary carcinoma. The patients presented in the article did not follow the core needle biopsy, but we have demonstrated that in our group of patients FNA was a sensitive test. The results of FNA coincided with the histopathological results of surgical specimens.

**Conclusions.** We have demonstrated that the main purpose of this technique is to provide a differential diagnosis between benign and malignant changes enabling appropriate therapeutic management and the determination of the correct surgical procedure when surgery is required.

#### Streszczenie

Wstęp. Biopsja cienkoigłowa (FNA) jest inwazyjną, jednak stosunkowo prostą i niedrogą procedurą medyczną łatwo wykonywaną w warunkach przychodni bez konieczności hospitalizacji pacjenta. Ma zastosowanie głównie w diagnozie wyczuwalnych palpacyjnie guzków, w szczególności guzków tarczycy. Badanie cytologiczne aspirowanego materiału pozwala na wykrycie zmian towarzyszących zapaleniu tarczycy, hiperlazji i wola koloidalnego, jak również zmian nowotworowych o podłożu nabłonkowym, limfoidalnym i zmian metaplastycznych.

**Cel pracy.** Celem pracy była analiza wyników biopsji cienkoigłowej guzków tarczycy u dzieci, użyteczność FNAB przy wyborze odpowiedniego leczenia i korelacja wyników cytologicznych z wynikami histopatologicznymi pooperacyjnymi tarczycy.

Materiał i metody. Trzydziestu siedmiu pacjentów (33 dziewczynki i 4 chłopców) hospitalizowanych w Oddziale Endokrynologii i Pediatrii Uniwersytetu Warszawskiego zostało zakwalifikowanych do FNA z powodu palpacyjnie wykrytych guzków tarczycy. Wiek chorych wynosił od 7 do 18 lat. Zmiany mikroskopowe były opisywane w zależności od obrazu cytologicznego, stosując kryteria diagnostyczne według skali Bethesda.

Wyniki. Większość pacjentów wykazywała zmiany łagodne określone jako 2 stopień skali Bethesda (31/37 pacjentów). U jednego pacjenta materiał pobrany za pomocą FNAB był niediagnostyczny, 2 pacjentów wykazywało zmiany atypowe określone jako 2 stopień skali Bethesda, a 3 pozostałych pacjentów zmiany rakowe określone jako 5 i 6 stopień wg skali Bethesda. Zmiany łagodne i rakowe rozpoznane za pomocą FNAB zostały potwierdzone w materiale histopatologicznym pooperacyjnym.

Wnioski. W pracy wykazano, że głównym celem tej metody jest umożliwienie diagnostyki różnicowej pomiędzy łagodnymi i złośliwymi zmianami w tarczycy, co w konsekwencji ułatwia podjęcie decyzji odnośnie leczenia i ewentualnego zabiegu chirurgicznego.

## INTRODUCTION

Fine needle aspiration (FNA) is a simple, inexpensive, easily performed outpatient procedure which can provide a rapid diagnosis. It is eminently suitable for the investigation of superficial palpable lesions in many sites, including the thyroid gland. Thyroid FNA has a high diagnostic accuracy rate  $\sim$  about 90 to 100% and its role is either diagnostic or therapeutic (1). The main purpose of thyroid FNA is to provide a rational approach to management to determine the appropriate surgical procedure in cases of thyroid cancer. It is important in pre-operative diagnosis by identifying the disease process in both solitary nodules and in diffuse enlargement of the thyroid gland. A specific diagnosis cannot always be arrived at as sampling is variable and not always representative, but the surgeon is provided with information which helps in deciding management options. Cytological examination of aspirated material can detect thyroiditis, toxic hyperplasia and colloid goiters as well as neoplastic processes, epithelial, lymphoid and metastatic changes. The Bethesda System for reporting cervical cytology interpretations, was first developed at the National Center Institute (NCI) workshop in 1988 and widely adopted in the United States for reporting Papanicolaou test results (2). The notes and recommendations were updated in 2007 improving the clarity of communication among cytopathologists and other health care providers, predicting the cancer risk and reducing unnecessary surgery for patients with benign nodules (3). The 6 general diagnostic categories are shown in bold type in the table 1. Each of the categories has an implied cancer risk (ranging from 0 to 3% for the benign category to virtually 100% for the malignant category) that links it to a rational clinical management guideline.

## AIM

The aim of this study was the analysis of the results of FNAB in thyroid nodules in children, the usefulness of FNAB in the theeupeutic precedures and comparison of the cytologic changes with the postoperative changes of the thyroid.

## MATERIAL AND METHODS

Thirty seven patients (33 females and 4 males) of the Clinical Department of Endocrinology and Pediatrics in the Warsaw University of Medicine, were qualified to the fine needle aspiration biopsy (FNA) because of the presence of thyroid nodules. The age of patients varied from 7 to 18 years old. The material obtained by FNA was immediately fixed in 96% ethanol with naphthol ether (1:1) and stained with Hematoxilin and Eosin. The microscopical

**Table 1.** The Bethesda System for Reporting Cytopathology:

 Recommended Diagnostic Categories (2).

Diagnostic categoryRisk of malignancyUsual managementI. Nondiagnostic or unsatisfactory0Repeat FNA with ultrasoundCyst fluid onlyVirtually acellular specimenOther (obscuring blood, clotting artifact, etc)0-3Clinical follow-upII. Benign0-3Clinical follow-upConsistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)Consistent with lymphocytic (Hashimoto) thyroiditis in the proper olinical contout
I. Nondiagnostic or unsatisfactory0FNA with ultrasoundCyst fluid onlyVirtually acellular specimenOther (obscuring blood, clotting artifact, etc)II. Benign0-3Clinical follow-upConsistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)Consistent with lymphocytic (Hashimoto) thyroiditis in the proper
Virtually acellular specimen       Virtually acellular specimen         Other (obscuring blood, clotting artifact, etc)       Clinical follow-up         II. Benign       0-3       Clinical follow-up         Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)       Consistent with lymphocytic (Hashimoto) thyroiditis in the proper
Other (obscuring blood, clotting artifact, etc)       Clinical follow-up         II. Benign       0-3       Clinical follow-up         Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)       Consistent with lymphocytic (Hashimoto) thyroiditis in the proper
artifact, etc)       Clinical follow-up         II. Benign       0-3       Clinical follow-up         Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)
II. Benign     0-3     follow-up       Consistent with a benign follicular nodule (includes adenomatoid nodule, colloid nodule, etc.)
nodule (includes adenomatoid nodule, colloid nodule, etc.) Consistent with lymphocytic (Hashimoto) thyroiditis in the proper
(Hashimoto) thyroiditis in the proper
clinical context
Consistent with granulomatous (subacute) thyroiditis
III. Atypia of undetermined significance/follicular lesion5-15Repeat FNAof undetermined significance5-151000000000000000000000000000000000000
IV. Follicular neoplasm/"suspicious" for follicular neoplasm Specify if Hürthle cell type
V. Suspicious for malignancy 60-75 60-75 60-75 8urgical lobectomy
Suspicious for papillary carcinoma
Suspicious for medullary carcinoma
Suspicious for metastatic carcinoma
Suspicious for lymphoma
VI. Malignant 97-99 Near-total thyroidec- tomy
Papillary thyroid carcinoma
Poorly differentiated carcinoma
Medullary thyroid carcinoma
Undifferentiated (anaplastic) carcinoma
Squamous cell carcinoma
Carcinoma with mixed features
Metastatic

FNA – fine needle aspiration

changes were described according the cytological picture and graded by recommended diagnostic categories using Bethesda System (tab. 1). The results of FNA have been compared with the histopathological examination of the specimens after lobectomy and total thyroidectomy.

## RESULTS

The results of the reporting thyroid cytopathology are shown in the table 2.

In most patients (31/37) the results of FNA were consistent with a benign follicular nodule, grade 2 according to Bethesda System (fig. 1).

In one patient (1/37) FNA was evaluated as nondiagnostic, grade 1 according to Bethesda System. Two FNA smears (2/37) were categorized as grade 3 according to Bethesda System revealing the feature of thyreocytes with hyperplastic and degenerative changes and oncocytic type cells with trabecular formations, respectively. In another two patients (2/37) FNA were evaluated as grade 5 according to Bethesda System, both features were consistent with papillary structures and cellular atypia. Atypical thyreocytes, without papillary formations consistent with grade 6 according to Bethesda System were described in one FNA (1/37). The results of FNA coincided with the histopathological results of surgical specimens. In the case of non diagnostic smear, the colloid cyst was found by surgical procedure.

## DISCUSSION

FNA is the most common method for evaluation of a suspicious thyroid nodule and has been one of the most useful, safe and accurate tool in the diagnosis

Table 2. Diagnosis made by fine needle aspiration biopsy in patients with thyroid nodule.

No.	Sex	Age (years)	FNA	BS	Final diagnosis
1	F	14	Thyreocytes, Collodi, numerous lymphocytes	2	Chronic inflammation
2	F	15	Colloid, thyreocytes	2	Colloid nodule
3	F	13	Colloid, thyreocytes	2	Colloid nodule
4	F	9	Colloid, thyreocytes	2	Colloid nodule
5	F	17	lymphocytes	2	Hashimoto thyroiditis
6	F	16	Atypical cells with groove, papillary formations	5	Papillary carcinoma
7	F	16	Colloid, thyreocytes	2	Colloid nodule
8	F	15	Thyreocytes with hyperplastic and degenerative changes	3	Colloid nodule
9	F	13	Lymphocytes, histiocytes, oxyphilic cells, colloid	2	Hashimoto thyroiditis
10	М	15	Groups of hyperplastic thyreocytes, colloid	2	Adenomatoid nodule
11	F	10	Groups of hyperplastic thyreocytes, oxyphilic cells, numerous lymphocytes	2	Chronic thyroiditis
12	F	13	Thyreocytes,	2	Cyst
13	F	14	Thyreocytes, colloid	2	Colloid nodule
14	F	17	Thyreocytes, degenerative changes	2	Adenoimatoid nodule
15	F	16	Histiocytes with hemosiderin	2	Granulomatous thyroiditis
16	F	14	Acellular specimen, blood	1	Colloid nodule
17	F	17	Atypical thyreocytes, without papillary formations	6	Papillary carcinoma
18	F	14	Papillary structures with cellular atypia	5	Papillary carcinoma
19	F	15	Thyreocytes, colloid	2	Colloid nodule
20	F	17	Thyreocytes, numerous lymphocytes	2	Autoimmune disease
21	F	13	Thyreocytes, colloid	2	Benign lesion
22	F	12	Thyreocytes with degenerative changes, epithelioid cells, macrophages	2	Granulomatous subacute thyroiditis
23	М	9	Oncocytic type cells, trabecular formations	3	Adenomatoid nodule
24	F	8	Blood, thyreocytes, Collodi, lymphocytes	2	Hashimoto thyroiditis
25	М	15	Histiocytes, lymphocytes, thyreocytes	2	Chronic thyroiditis
26	F	15	Thyreocytes, colloid	2	Colloid nodule
27	F	16	Thyreocytes, colloid	2	Colloid nodule
28	F	12	Thyreocytes, colloid	2	Colloid nodule
29	F	18	Thyreocytes, colloid	2	Colloid nodule
30	F	17	Thyreocytes, lymphocytes, colloid	2	Hashimoto thyroiditis
31	F	13	Thyreocytes, colloid	2	Colloid nodule
32	F	17	Thyreocytes, lymphocytes	2	Hashimoto thyroiditis
33	F	13	Erythocytes, numerous lymphocytes, eosinophilic granulocytes	2	Thyroiditis
34	F	7	Thyreocytes, colloid, lymphocytes	2	Colloid nodule
35	F	8	Thyreocytes, colloid, lymphocytes	2	Hashimoto thyroiditis
36	М	8	Colloid, macrophages	2	Colloid nodule
37	F	16	Thyreocytes, colloid	2	Colloidal cyst

FNA - thyroid fine needle aspiration biopsy, BS - diagnostic category using Bethesda system



Fig. 1. Benign changes, diagnostics criteria 2 according to the Bethesda System for Reporting Cytopathology (H.E 400x).

of thyroid pathology (4). Although it may be either diagnostic and therapeutic, its fundamental role is to rule out the presence of cancerous cells, specially in elderly. It has a high diagnostic accuracy rate about 90-100% (1). However, considering patients with negative FNA, some authors report the diagnostic sensitivity to be approximately 80%, and FNA could miss up to a third of all thyroid malignancy (1, 5, 6). The use of core needle biopsy can reduce false negative results reported by TNAB but a local anesthetic is administered and patients can refuse this more aggressive diagnostic method. This method enables the final histologic examination and has a diagnostic accuracy significantly higher than that of FNA (7). The patients presented in the article did not follow the core needle biopsy, but we have demonstrated that in our group

#### BIBLIOGRAPHY

- Arda IS, Yildirim S, Demirhan B et al.: Fine needle aspiration biopsy of thyroid nodules. Arch Dis Child 2001; 85: 313-317.
- Baloch ZW, LiVolsi VA, Asa SL et al.: Diagnostic terminology and morphologic criteria for cytologic diagnosis of thyroid lesions: a synopsis of the National Cancer Institute Thyroid Fine Needle Aspiration State of the Science Conference. Diagn Cytopathol 2008; 36: 425-437.
- Broome JT, Solorzano CC: The impact if atypia/follicular lesion of undetermined significance on the rate of malignancy in thyroid fine needle aspiration: evaluation of the Bethesda System for Reporting Thyroid Cytopathology. Surgery 2011; 150(6): 1234-1241.
- Ogilivie JB, Piatigorsky EJ, Clark OH: Current status of fine needle aspiration for thyroid nodules. Adv Surg 2006; 40: 223-238.
- Corrias A, Einaudi S, Chiorboli E et al.: Accuracy of Fine Needle Aspiration Biopsy of thyroid nodules in detecting malignancy in childhood: Comparison with conventional clinical, laboratory and imaging approaches. J Clin Endocrinol Matab 2001; 86: 4644-4648.
- Tee YY, Lowe AJ, Brand CA, Judson RT: Fine needle aspiration may miss a third of all malignancy in palpable thyroid nodules: a comprehensive literature review. Annn Surg 2007, 246(5): 714-720.
- Trimboli P, Nasrollah N, Guidobaldi L et al.: The use of core needle biopsy as first-line in diagnosis of thyroid nodules reduces false negative and inconclusive data reported by fine needle aspiration. World J Surg Oncol 2014; 12: 61-67.

of patients FNA was a sensitive test, what support an international meta-analysis in the pediatric population (8).

In patients with already diagnosed thyroid cancer, the main purpose of FNA is to provide a definite diagnosis of malignancy, with tumor type, enabling appropriate therapeutic management and to determine the correct surgical procedure when surgery is required. In such a situation, many health care providers are involved thus clear terminology and other issues related to thyroid FNA are of great importance. To address this problem NCI hosted the Science Conference (October 2007) that finally led to the Bethesda Thyroid Atlas Project and form the framework for The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) (2, 4). It was intended as a flexible framework that can be modified to suit the needs of the particular laboratory and the patients it serves. The Report should be in common usage by now, thus we had performed FNA in all presented patients and than evaluated the cytology results according to Bethesda System. Disagreement regarding the use of TBSRTC terminology for classifying the results of thyroid FNA mainly occurred in the most-often criticized categories of atypia/follicular lesion of undetermined significance (AUS/FLUS) and FN/SFN (3, 10). In conclusion the Bethesda System for Reporting Thyroid Cytopathology resulted in more frequent repeat FNA, fewer thyroidectomies and no change in malignancy rate (9, 11, 12).

## CONCLUSIONS

Fine needle aspiration biopsy is a good diagnostic tool in the evaluation of the thyroid nodule in pediatric patients.

- Stevens C, Lee JK, Sadatsafavi M, Blair GK: Pediatric thyroid fine needle aspiration cytology: a meta-analysis. J Pediatr Srg 2009; 44(11): 2184-2191.
- Chen JC, Pace SC, Chen BA et al.: Yield of repeat fine needle aspiration biopsy and rate of malignancy in patients with atypia or follicular lesion of undetermined significance: the impact of the Bethesda System for Reporting Thyroid Cytopathology. Surgery 2012; 152(6): 1037-1044.
- Krane JF, Vanderlaan PA, Faquin WC et al.: The atypia of undetermined significance/follicular lesion of undetermined significance: malignant ratio: a proposed performance measure for reporting in the Bethesda system for thyroid cytopathology. Cancer Cytopathology 2012; 120(2): 111-116.
- Jing X, Knoepp SM, Roh MH et al.: Group of consensus review minimizes the diagnosis of "follicular lesion of undetermined significance" and improves cytohistologic concordance. Diagn Cytopathol 2012; 40(12): 1037-1042.
- Tejinder SB, Rahul M, Mridu M et al.: Reproducibility of "The Bethesda System for reporting Thyroid Cytopathology": a multicenter study with review of the literature. J Clin Daign Res 2013; 7(6): 1051-1054.
- Cibas ES, Syed ZA: The Bethesda System for Reporting Thyroid Cytopathology. Am J Clin Pathol 2009; 132: 658-665.
- McKee G: The role of fine needle aspiration cytology in the diagnosis of thyroid lesions. J R Soc Med 1998; 91 (suppl. 33): 28-32.

received/otrzymano: 02.07.2014 accepted/zaakceptowano: 19.09.2014