

ORIGINAL PAPER

THE DIAGNOSIS OF CANCER IN THYROID FINE NEEDLE ASPIRATION BIOPSY. SURGERY, REPEAT BIOPSY OR SPECIMEN CONSULTATION?

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Fine needle aspiration biopsy (FNA) is the only diagnostic method that allows a preoperative diagnosis of thyroid carcinoma. An unequivocal diagnosis of a malignant change is achievable only in cases in which all cytological criteria of carcinoma are met. The aim of the study was to evaluate the necessity of repeat thyroid FNA in patients with papillary thyroid carcinoma verified on consultative examination (CE).

We analyzed cytology reports of thyroid FNA and CE that resulted in the diagnosis of papillary carcinoma. Evaluation of the correlation of the cytological diagnosis with the histopathology report was based on data obtained after the surgery.

Between 2010 and 2015 in the Institute of Oncology (IO) there were 184 cancers diagnosed on CE or in thyroid FNA performed primarily in IO. Additionally, 74 patients were subjected to repeat biopsy after confirmation of cancer in CE. Histopathological diagnosis of cancer was obtained in 62 (100%) cases that were doubly confirmed with cytological examination. The remaining 12 patients were operated on outside the institute. From 110 FNA primarily performed in the IO, histopathological verification was achievable in 92 cases, from which 92 (100%) provided a confirmation of cancer, and the remaining 18 patients were operated on outside the institute.

High (100%) specificity of cancer diagnosis in FNA established primarily and verified on CE (second independent assessment) indicates that repeat FNA in order to confirm the diagnosis is unnecessary.

Key words: thyroid nodule, thyroid cancer, biopsy, fine-needle.

Introduction

The routine use of fine needle aspiration (FNA), a diagnostic technique introduced in 1960 in Sweden and further developed in the USA, and the progress of imaging methods have resulted in a decrease of unnecessary surgical interventions in benign lesions and an increase in detection of thyroid neoplasms [1, 2, 3, 4, 5, 6, 7].

In 2007 the implementation of the Bethesda System for Reporting Thyroid Cytopathology (BSRTC), which classifies the cytopathological reports into 6 categories, clearly divided the thyroid lesions verified in FNA into groups in which the surgical intervention is either inadmissible, possible, recommended or necessary [5, 8, 9].

This is all the more significant as 3% to 7% of thyroid nodules are malignant and the only method

Table I. Comparison of the risk of malignancy of the NCI Bethesda System for Reporting Thyroid Cytopathology diagnostic categories and the risk of malignancy proposed in Polish guidelines (on the basis of [5], with minor modifications)

BSRTC CATEGORY	ROM IN BSRTC (%)	ROM IN POLISH GUIDELINES (%)
I – non-diagnostic	1-4	5-10
II – benign	0-3	< 1
III – FLUS	5- 15	~5
IV – SFN	15-30	5-20
V – SM	60-75	30-50
VI – malignant	97-99	95-100

BSRTC – Bethesda System for Reporting Thyroid Cytopathology; ROM – risk of malignancy; FLUS – follicular lesion of undetermined significance; SFN – suspicious for follicular neoplasm; SM – suspicious for malignancy

that allows a preoperative (PO) qualification for the concrete malignancy risk group is FNA. The report of “malignancy” – diagnostic category VI (DC VI) of BSRTC – carries the risk of malignancy of 97-99% (95-100% in Polish guidelines), and, what is equally important, most of these lesions are papillary thyroid carcinomas (PTC) (Table I) [1, 5, 8, 10, 11, 12, 13]. The number of PTC variants (WHO classification) and changes that mimic PTC in cytology cause the need of preoperative confirmation of cytological diagnosis of papillary carcinoma by another pathologist. Repeating the FNA unnecessarily prolongs the diagnostic process by causing irrelevant doubts when the result of the second FNA is different than DC VI.

The aim of the study was to evaluate the necessity of repeat thyroid fine needle aspiration in patients

with papillary thyroid carcinoma verified on consultative examination.

Material and methods

The analyzed material consisted of cytological reports of thyroid carcinoma diagnosed in FNA and consultative examinations (CEs) performed in the Department of Tumor Pathology of Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch. The research concerned the period from January 2010, when the Bethesda System for Reporting Thyroid Cytopathology (BSRTC) was implemented in Poland, to April 2015. FNAs performed at the study institution were performed in 2-person teams of a pathologist and radiologist, under ultrasound guidance. The material was obtained by 25-gauge needles. The smears were fixed in 95% alcohol and stained with hematoxylin-eosin (HE). Each case consisted of at least two smears (more specimens were taken if there was scanty material). The material remaining in the aspiration needle was collected for molecular analysis. Each test contained a description of the site of the biopsy with the size of the nodule and ultrasound photography. Our material included 16 656 FNAs in which there were 110 cases of papillary carcinoma (DC VI) (Fig. 1).

Histopathological verification was available in 92 cases; the remaining patients were operated on in other institutions. Additionally, we analyzed 74 cytological CEs. The CEs (from 2 to 4 smears stained with HE) consisted of primary papillary carcinoma diagnosis and the description of the site of the lesion. In all 74 consulted cases, after the confirmation of the diagnosis, repeat biopsy was performed for a molecular test and another evaluation. In this group, histopathological follow-up was obtainable in 62 cases, while 12 patients were lost from observation.

Based on data collected after the surgical resection performed in our institution, the cytohistologic correlation was evaluated.

Results

One hundred eighty-four cytological diagnoses of thyroid malignancy were made from 2010 to 2015 in the Department of Tumor Pathology of the Institute of Oncology (IO), either in FNA performed in IO or on CE.

For 110 FNAs performed in IO, histopathological (HP) verification was accessible in 92 cases, from which in 92 (100%) cases a malignancy was confirmed. The remaining 18 patients were treated surgically in other institutions. From 92 malignant neoplasms, papillary thyroid carcinoma (PTC) comprised 83.7%. Among 77 PTC we obtained 57 reports of the classical (CVPTC) and 20 reports of the

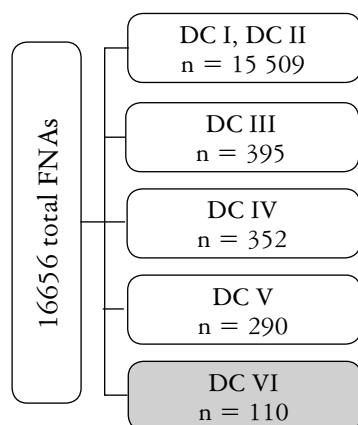


Fig. 1. Proportion of particular diagnostic categories in the study group

follicular variant of PTC (FVPTC), including 1 report of non-invasive follicular variant of papillary thyroid carcinoma (NI-FVPTC).

On CE, the diagnosis of PTC was confirmed in 100% of cases. Repeat FNA supported the primary and consultative diagnosis in 100%. Histopathological examination confirmed the diagnosis of PTC in 62 cases (100%), including 32 FVPTC (1 NI-FVPTC). The remaining 12 patients were subjected to excision at another institution. Altogether in our analysis there were 138 PTC – 84 CVPTC, 52 FVPTC (2× NI-FVPTC), 1 Warthin-like variant of PTC and 1 diffuse sclerosing variant of PTC.

Discussion

Fine needle aspiration is invariably the best method of preoperative diagnostics and rational triage of patients to surgical treatment or observation [5, 14]. In the case of DC VI (“malignant” diagnosis), the recommended treatment is thyroidectomy. When the interpretation is provided by an experienced pathologist who strictly follows the diagnostic guidelines, the cytohistologic (CH) correlation of the DC VI with post-operative outcome is very high. If a biopsied nodule is malignant on cytological examination, then according to the BSRTC it is malignant in 97-99% of cases on final pathology. The CH correlation is the highest in this category. This opinion is shared by many researchers.

Mekel *et al.* retrospectively analyzed 1197 FNAs of patients operated on in the period 2002-2013. The CH correlation was assessed at 94%. In this study the PTC comprised 100% of malignancies [15].

A similar outcome was achieved by Lew *et al.*, who obtained 97% confirmation of a malignant neoplasm in the histopathological report; PTC amounted to 92% (82% CVPTC and 18% FVPTC). The analyzed cases were consulted and classified according to the BSRTC [16]. A similar (98.7%) CH correlation was reported by Strickland *et al.* [17] Mittendorf *et al.* observed 100% CH correlation. For 622 FNAs there were 36 DC VI (6%) [18]. Albuja-Cruz *et al.* submitted a study in which all analyzed patients (1086 FNA) had histopathological verification (lobectomy or thyroidectomy). They received 199 DC VI reports for nodules smaller than 4 cm and 20 for nodules larger than 4 cm. Histopathological examination demonstrated 96% correlation for the “<4 cm” nodules and 100% correlation for the “>4 cm” nodules [19]. Kleiman *et al.* also proved that BSRTC categories are a satisfactory tool for assessment of the risk of malignancy of the biopsied nodules [20].

Our study is particularly noteworthy, because apart from the analysis of our own material, which revealed 100% CH correlation, we also evaluated the material from other institutions. Consultative examination of the FNA was not the end of the diagnos-

tic process. Each patient was subjected to a repeat FNA, which provided 100% compatibility with the primary diagnosis, and 100% compatibility with the post-operative material.

The correlation of FNA and HP reports is high in all publications concerning this matter, and all researchers present similar conclusions. Predictability of DC VI is very high, but mistakes are also likely to occur at this diagnostic stage. The recommendation for DC VI is thyroidectomy, but taking into account that the risk of malignancy is 97-99%, for every 100 thyroidectomies 1-3 are unnecessary. There is a much higher divergence between FNA and HP in the DC V and IV, and the results are even more confounding for DC III [21, 22, 23, 24, 25, 26, 27, 28].

As long as in the case of DC IV or V the risk of malignancy is at the level of 15-30% or 60-75%, respectively, so the premise is that there is no alternative to lobectomy and thorough examination of the whole material, the DC VI imposes instant radical management [5, 8]. The errors occurring at this stage of diagnostics result from a few factors. Pathologists who deal with the preoperative CE have enough experience, but sometimes the material is scanty or not well processed. In such cases we need to consider “taking a step back” from the DC VI diagnosis and report DC V, which will result in lobectomy.

Jang *et al.* analyzed cases which appeared malignant in cytology examination and proved benign on HP verification [29]. In the literature there are many descriptions of changes that may emerge in the thyroid gland as a result of multiple punctures, such as hemorrhage, vascular thrombosis, fibrosis, infarction, fibrinoid necrosis, cystic degeneration, vascular and capsular pseudoinvasion, angioinvasion and cellular atypia [30, 31, 32]. The damage caused in the thyroid gland due to FNAs repeated unnecessarily causes considerable difficulties in establishing the final diagnosis from the post-operative material [30, 33, 34, 35, 36].

Follicular variant of PTC is the second, after CVPTC, most common form of thyroid cancer. Special attention has recently been given to the encapsulated non-invasive follicular variant of papillary thyroid carcinoma: NI-FVPTC due to its indolent course. It is proposed to treat this tumor as an adenoma [14, 17, 37, 38, 39]. It is often difficult, though, to assess the capsular invasion if the patient had multiple biopsies and the capsule has features that cause difficulties in distinguishing between capsular damage and invasion. Treating NI-FVPTC as an adenoma, according to the researchers, reduces the risk of malignancy in all BSRTC categories, with the most considerable decline in DC V and VI, which may have an impact on the extent of the surgery [40, 41].

Altogether in our analysis there were 138 PTCs, including 84 CVPTCs and 52 FVPTCs (2× NI-FVPTC).

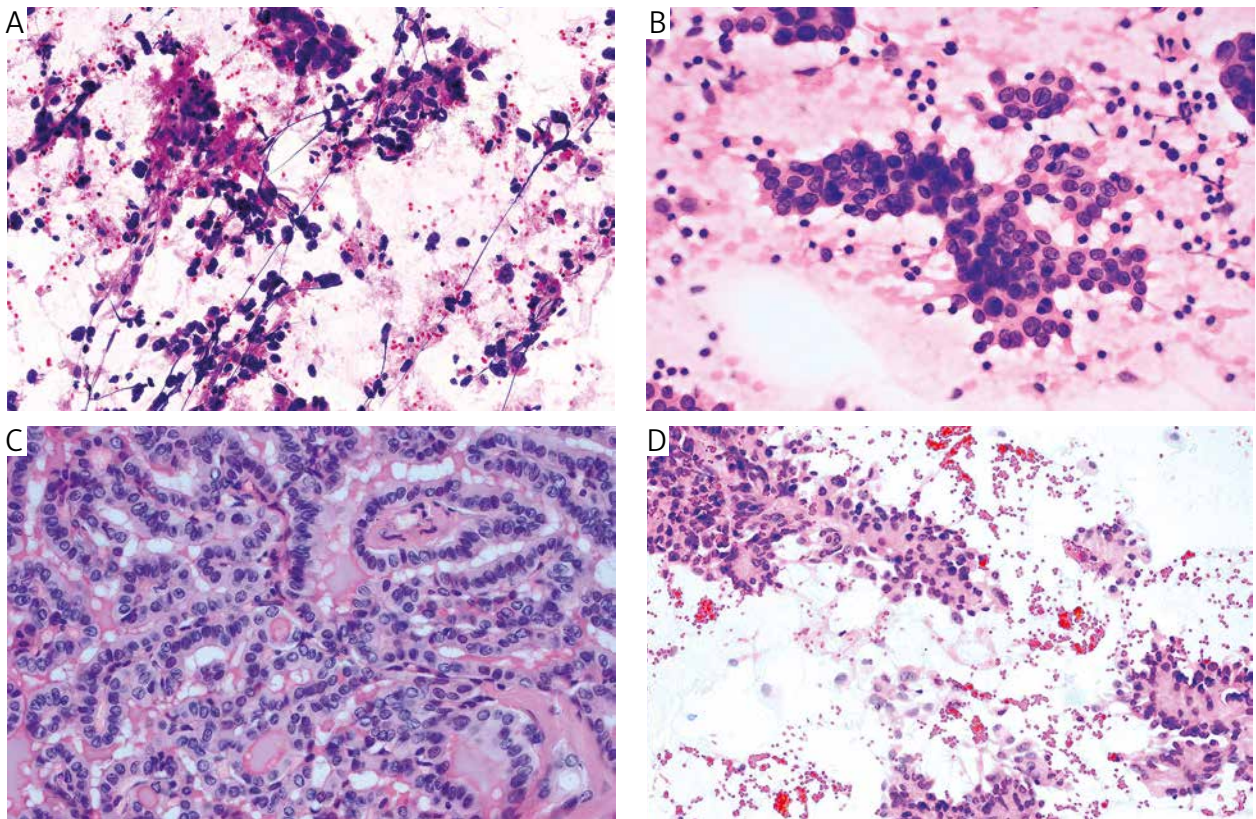


Fig. 2. A, B – examples of DC VI of the Bethesda system: A) microcellular carcinoma (metastatic); B) classical papillary thyroid carcinoma; C) typical histology of PTC and D) its manifestation in cytology of hyalinizing trabecular tumor (HTT) resembling PTC (staining HE)

Another important factor that affects FNA interpretation is the particular character of thyroid nodules. There are many mimics of PTC, such as chronic lymphocytic thyroiditis, benign papillary hyperplastic nodules or papillary hyperplasia in Graves' disease. Rare variants of PTC cannot be omitted: tall cell variant and oncocyctic PTC [36, 40]. We believe that strict following of the guidelines of PTC diagnosis and adopting the rule that we do not diagnose PTC unless all its characteristic features are present in the cytology image minimizes the possibility of an error. However, there is a benign neoplasm that has the cytological characteristics of PTC – hyalinizing trabecular tumor (HTT). It is crucial to remember that if there is abundant material in the cytology smear (much more abundant than in PTC) and in every sheet of cells there are a few inclusions, we should always report DC V with the note that the tumor has to be differentiated between PTC and HTT (Fig. 2). Hyalinizing trabecular tumor is a benign lesion that does not require any treatment, but a lobectomy is necessary to make a definite diagnosis [36].

Bethesda System for Reporting Thyroid Cytopathology in the case of cytological diagnosis of papillary carcinoma is a perfect tool for predicting the HP diagnosis, but it is critical to remember about the abnormal images of the rare lesions [36, 39, 42].

Conclusions

High (100%) specificity of cancer diagnosis in FNA established primarily and verified on CE (second independent assessment) indicates that repeat FNA in order to confirm the diagnosis is unnecessary.

The authors declare no conflict of interest.

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