

APPLICATION OF THE BETHESDA CLASSIFICATION IN THE HISTOPATHOLOGICAL CHARACTERISTICS OF PATIENTS WITH THYROID NODULES

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Abstract. *Background.* The Bethesda Classification for Reporting Thyroid Cytopathology (BSRTC) was developed in 2010 to provide a standardized framework for interpreting and reporting FNA cytology, and its use is recommended for the evaluation of thyroid nodules in both adults and children.

Material and methods. A retrospective analysis of 51 patients with thyroid nodules was performed. Of the 51 patients, 33 were men and 18 were women.

Research methods - general clinical, biochemical (bilirubin, direct, indirect, ALT, AST, PTI, coagulogram, CRP), hormonal (TSH, free thyroxine, antibodies to thyroid peroxidase, to thyroglobulin and thyrocyte receptors, prolactin in the blood) and instrumental: ECG, Ultrasound of the thyroid gland, internal organs, chest x-ray, as well as fine-needle aspiration biopsy (FNA).

Research results. The patients were divided into 2 groups: group 1 - patients with one nodular thyroid formation - 35 patients, group 2 - patients with multinodular thyroid formations - 16 patients. 20 healthy individuals made up the control group.

Conclusions. 1) The majority of patients, a total of 22 out of 51 patients, belonged to Bethesda category II (43.1%), while 2 - category I (3.9%), 6 - category III (11.8%), 12 - category IV (23.5%), 7 - category V (13.7%) and 2 patients belonged to category VI (3.9%) respectively. 2) When analyzing the cytological response, the Bethesda classification must be used for correct prognosis and treatment.

Keywords: thyroid gland, nodules, formations.

Background. Thyroid nodules (TN) are common. Their importance lies in the need to assess thyroid function, the degree and future risk of mass effect, and also exclude thyroid cancer, which occurs in 7-15% of thyroid nodules. Evaluation of thyroid nodules consists of four key components: medical history and examination, serum thyroid-stimulating hormone (TSH) measurement, ultrasound, and, if indicated, fine-needle aspiration (FNA) biopsy. If serum TSH is suppressed, a thyroid scan with Tc or J131 can differentiate between a solitary hot nodule, a toxic multinodular goiter, or, less commonly, thyroiditis or Graves' disease within a coexisting thyroid nodule. Cartographically, cold nodules are assessed in the same way as normal or elevated serum TSH levels.

For the diagnosis of thyroid nodules, fine-needle aspiration biopsy (FNA), large-needle aspiration biopsy and large-needle biopsy were used [1, 2]. In the 1980s, FNA became the standard diagnostic method for the thyroid gland, replacing large-needle biopsy, due to its high diagnostic

accuracy and low complication rates [3]. Thus, core needle biopsy, performed without ultrasound guidance using a large-bore needle, is currently not recommended for thyroid nodules due to local pain and the risk of cervical bleeding [4,5]. Although FNA demonstrates high diagnostic specificity and safety, it has several limitations: 1) the average reported diagnostic sensitivity is about 83% with a false-negative rate of 2–18% [6,7]. 2) the rate of nondiagnostic results with initial FNA is about 10% and an even higher rate of up to 50% with repeated FNA [8,9], 3) the rate of atypia (follicular lesion) of uncertain significance is about 10–20% with high rates of inconclusive results with repeat FNA in particular has 1–7% nondiagnostic rates and 3.8–31.0% atypia (follicular lesion) of undetermined significance [10–12]. and 4) low accuracy in diagnosing follicular lesions [13, 14]. These limitations of TAB lead to repeat TAB or unnecessary surgery [15]. Therefore, additional diagnostic tools are needed to overcome the limitations of FNA for thyroid nodules.

With the development of thick biopsy devices, single- or double-action spring needles began to be used to diagnose thyroid nodules. In addition, the widespread use of high-resolution ultrasound makes it possible to make an accurate diagnosis and minimize complications [16]. Thus, it has been reported that needle biopsy is an effective and safe method for biopsy of thyroid nodules [17].

Interpretation of cytological results of FNA is a key element in the evaluation of thyroid nodules and allows one to estimate the approximate risk of malignancy. Since its inception, the Bethesda Thyroid Cytopathology Reporting System (TBSRTC) has created a standardized reporting system with a limited number of diagnostic categories for thyroid fine-needle aspiration (FNA) specimens. Using TBSRTC, cytopathologists can communicate their interpretations to the treating physician in concise, unambiguous, and clinically useful terms. TBSRTC has become widespread in the United States and many countries around the world and is approved by the American Thyroid Association [17].

The above was the reason for the present study.

Purpose of the study-evaluate the histopathological characteristics of patients with thyroid nodules according to the Bethesda system.

Material and methods. Based on the Department of Endocrine Surgery Republican Specialized Scientific and Practical Medical Center of Endocrinology of the Ministry of Health of the Republic of Uzbekistan named after academician. Y.H. Turakulov from 2016 to 2020, 130 case histories of patients with thyroid nodules were studied retrospectively. Of these, 51 patients underwent TAB. Of the 51 patients, 33 were men and 18 were women.

The patients were divided into 2 groups: group 1 - patients with one nodular thyroid formation - 35 patients, group 2 - patients with multinodular thyroid formations - 16 patients. 20 healthy individuals made up the control group.

Inclusion criteria: patients with nodular diseases of the thyroid gland, men, women

Exclusion criteria: other thyroid diseases, severe diseases of autoimmune origin, vasculitis.

Research methods - general clinical, biochemical (bilirubin, direct, indirect, ALT, AST, PTI, coagulogram, CRP), hormonal (TSH, free thyroxine, antibodies to thyroid peroxidase, to thyroglobulin and thyrocyte receptors, prolactin in the blood) and instrumental: ECG, Ultrasound of the thyroid gland, internal organs, chest x-ray, as well as fine-needle aspiration biopsy (FNA).

The analysis included American recommendations for thyroid nodules according to the ACR-TIRADS (American College of Radiology-Thyroid Image Reporting and Data System) classification. [18, 19].

FNA was performed in all patients with a thyroid nodule larger than 1 cm. Thyroid cytology was assessed according to a unified classification Bethesda (2010) or The Bethesda System For Reporting Thyroid Cytopathology (TBSRTC) to determine treatment and prognosis [20]. Currently, WHO recommends using a single terminological classification to unify the description of the results of cytological examination Bethesda, developed in the clinic Bethesda (USA) in 2010. The classification identifies six categories of diagnoses, allowing the endocrinologist to determine the order of further actions. Each category reflects the expected (from 0-3%) or obvious (up to 100%) risks of malignancy, and the patient management tactics are determined.

Statistical software / Microsoft Excel and STATISTICA_6 was used for statistical analysis, and $p < 0.05$ was considered a significant difference. Normally distributed quantitative data were expressed as mean and standard deviation ($M \pm SD$).

Analysis and results. Table 1 shows the distribution of patients by gender and age.

Table 1.

Distribution of patients by gender and age

Age, years	Number men	Number of women	Total
18-44 young	eleven	8	19
44-60 average	12	6	18
60-75 elderly	10	3	13
75-90 senile	-	-	
90+ years long-lived	-	-	
Total: n = 51	33	18	51

As can be seen from Table 1, most of the patients were aged from 18 to 44 years - 19 patients (37.2%). Table 2 shows the characteristics of the histopathological analysis.

Table 2

Characteristics of histopathological analysis according to the system Bethesda

Cytology	1 group n=35	2nd group n=16	Total
Unsatisfactory punctate	2 (5.7%)	-	2 (3.9%)
Benign node	25 (71.4%)	12 (75%)	37 (72.5%)
Atypia of unknown origin	3 (8.5%)	3 (18.8%)	7 (13.7%)
Follicular tumor	2 (5.7%)	-	2 (3.9%)
Suspicion of malignancy	2 (5.7%)	1 (6.2%)	3 (5.9%)
Malignancy	1 (2.8%)	-	1 (1.9%)
Total	35	16	51

As can be seen from Table 2, in group 1 of patients in 2 (5.7%) cases, unsatisfactory punctate was noted, in 25 (71.4%) - benign node, 3 (8.5%) - atypia of unknown origin, in 2 (5.7%) - suspicion of a follicular tumor, in 2 (5.7%) - suspicion of malignancy and in 1 (2.8%) case - malignancy.

In group 2 patients, 12(75%)– benign node, 3x(18.8%)- atypia of unknown origin, in 1(6.2%)- suspicion of malignancy.

According to the results of histopathological analysis according to the system Bethesda, we analyzed the relevant recommendations for patients (Table 3).

Table 3

Characteristics of histopathological analysis according to the system Bethesda

Cytology	Risks of malignancy (number of patients)	Recommendations
Unsatisfactory punctate	2(3.9%)	Repeat TAB under ultrasound guidance
Benign	22 (43.1%)	Clinical observation
Atypia of unknown origin	6 (11.8%)	Repeat TAB
Follicular tumor	12 (23.5%)	Hemithyroidectomy
Suspicion of malignancy	7 (13.7%)	Subtotal thyroidectomy or hemithyroidectomy (lobectomy)* * It is necessary to evaluate the histology of intraoperative material
Malignancy	2 (3.9%)	Subtotal thyroidectomy or hemithyroidectomy (lobectomy)*

Thus, The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) has proven to be a very good screening platform for dividing patients with thyroid nodules into benign and malignant groups, as this is directly related to the risk of malignancy in each category. This helped to correctly plan surgical intervention in 96.4% of patients [20, 21]

Studies around the world have proven that the inclusion of The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) in diagnostic algorithms for patients with thyroid nodules reduces the number of unnecessary thyroidectomies and also improves the quality of detection of thyroid malignancies. In 93% of patients, TBSRTC correlated with final histopathology and was inconsistent in only 7% of cases [20, 21]

Conclusions. 1) The majority of patients, a total of 22 out of 51 patients, belonged to Bethesda category II (43.1%), while 2 were category I (3.9%), 6 were category III (11.8%), 12 were category IV (23.5%), 7 - category V (13.7%) and 2 patients belonged to category VI (3.9%), respectively. 2 patients with Bethesda category I underwent repeat FNA, and later they had category II. 2) When analyzing the cytological response, the Bethesda classification must be used for correct prognosis and treatment.

REFERENCES

1. Pitman MB, Abele J, Ali SZ, Duick D, Elsheikh TM, Jeffrey RB, et al. Techniques for thyroid FNA: a synopsis of the National Cancer Institute Thyroid Fine-Needle Aspiration State of the Science Conference. //Diagnost Cytopathol. 2008;36:407–424.
2. Silverman JF, West RL, Finley JL, Larkin EW, Park HK, Swanson MS, et al. Fine-needle aspiration versus large-needle biopsy or cutting biopsy in evaluation of thyroid nodules. //Diagnost Cytopathol. 1986;2:25–30.

3. Wang C, Vickery AL, Jr, Maloof F. Needle biopsy of the thyroid. //Surg Gynecol Obstet. 1976;143:365–368.
4. Pisani T, Bononi M, Nagar C, Angelini M, Bezzi M, Vecchione A. Fine needle aspiration and core needle biopsy techniques in the diagnosis of nodular thyroid pathologies. //Anticancer Res. 2000;20:3843–3847.
5. Gharib H, Papini E, Garber JR, Duick DS, Harrell RM, Hegedüs L, et al. American Association of Clinical Endocrinologists, American College of Endocrinology, and Associazione Medici Endocrinologi Medical Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules--2016 Update. //Endocr Pract. 2016;22:622–639.
6. 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. Ann Surg. 2007;246:714–720.
7. Wang CC, Friedman L, Kennedy GC, Wang H, Kebebew E, Steward DL, et al. A large multicenter correlation study of thyroid nodule cytopathology and histopathology. //Thyroid. 2011;21:243–251. [
8. Alexander EK, Heering JP, Benson CB, Frates MC, Doubilet PM, Cibas ES, et al. Assessment of nondiagnostic ultrasound-guided fine needle aspirations of thyroid nodules. J Clin Endocrinol Metab. 2002;87:4924–4927.
9. Orija IB, Piñeyro M, Biscotti C, Reddy SS, Hamrahian AH. Value of repeating a nondiagnostic thyroid fine-needle aspiration biopsy. // Endocr Pract. 2007;13:735–742.
10. Nayar R, Ivanovic M. The indeterminate thyroid fine-needle aspiration: experience from an academic center using terminology similar to that proposed in the 2007 National Cancer Institute Thyroid Fine Needle Aspiration State of the Science Conference. Cancer. 2009;117:195–202.
11. Yang J, Schnadig V, Logrono R, Wasserman PG. Fine-needle aspiration of thyroid nodules: a study of 4703 patients with histologic and clinical correlations. //Cancer. 2007;111:306–315.
12. Yassa L, Cibas ES, Benson CB, Frates MC, Doubilet PM, Gawande AA, et al. Long-term assessment of a multidisciplinary approach to thyroid nodule diagnostic evaluation. //Cancer. 2007;111:508–516.
13. Deveci MS, Deveci G, LiVolsi VA, Baloch ZW. Fine-needle aspiration of follicular lesions of the thyroid. Diagnosis and follow-up. Cytojournal. 2006;3:9.
14. Yoo C, Choi HJ, Im S, Jung JH, Min K, Kang CS, et al. Fine needle aspiration cytology of thyroid follicular neoplasm: cytohistologic correlation and accuracy. //Korean J Pathol. 2013;47:61–66.
15. Yeon JS, Baek JH, Lim HK, Ha EJ, Kim JK, Song DE, et al. Thyroid nodes with initially nondiagnostic cytologic results: the role of core-needle biopsy. //Radiology. 2013;268:274–280.
16. Novoa E, Gürtler N, Arnoux A, Kraft M. Role of ultrasound-guided core-needle biopsy in the assessment of head and neck lesions: a meta-analysis and systematic review of the literature. //Head Neck. 2012;34:1497–1503.
17. Liu Q, Castelli M, Gattuso P, Prinz RA. Simultaneous fine-needle aspiration and core-needle biopsy of thyroid nodules. //Am Surg. 1995;61:628–632. discussion 632-633

18. Pires AT, Mustafá AMM, Magalhães MOG. The 2017 ACR TI-RADS: pictorial essay. //Radiol Bras. 2022 Jan-Feb;55(1):47-53. doi: 10.1590/0100-3984.2020.0141.
19. Tessler FN, Middleton WD, Grant EG, Hoang JK, Berland LL, Teefey SA, Cronan JJ, Beland MD, Desser TS, Frates MC, Hammers LW, Hamper UM, Langer JE, Reading CC, Scoutt LM, Stavros AT. ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White Paper of the ACR TI-RADS Committee. //J Am Coll Radiol. 2017 May;14(5):587-595. doi: 10.1016/j.jacr.2017.01.046.
20. Cibas ES1, Ali SZ. The Bethesda System For Reporting Thyroid Cytopathology.// Am J Clin Pathol. 2009 Nov;132(5):658-65. doi: 10.1309/AJCPPHLWMI3JV4LA.; NCI Thyroid FNA State of the Science Conference.