ORIGINAL RESEARCH PAPER

Volume-7 | Issue-2 | February-2018 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

DIAGNOSTIC EVALUATION OF BETHESDA SYSTEM FOR REPORTING THYROID CYTOPATHOLOGY WITH CORRELATION OF HISTOPATHOLOGY IN THYROID NODULES

Pathology

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ABSTRACT

Background: Fine needle aspiration cytology is a common and excellent procedure for the evaluation of thyroid lesions that require surgical resection. It is simple, cost effective and with negligible side effects. The purpose of the our study is to classify the fine needle aspiration cytology (FNAC) by Bethesda system for reporting of thyroid cytology and its correlation of histopathology (HPE) of the excised nodule or specimen and also assess the diagnostic accuracy of FNAC in the diagnosis of the thyroid nodules.

Materials and Methods: This is a prospective study conducted at the Department of ENT, Surgery, Pathology-Government Medical College, Kannauj and Department of Pathology-SGPGIMS, Lucknow, January 2009 to December 2011.

Results: It includes 200 patients, 147 were females and 53 males, age ranged from 11-65 years. FNAC of benign thyroid lesion showed 93.6% sensitivity, 88 % specificity and 92% diagnostic accuracy . Likewise, results for malignant thyroid lesions showed 97.0, 98.0 and 96.0% respectively.

Conclusion: FNAC has high diangostic accuracy in the diagnostic evaluation of thyroid lesions.

KEYWORDS

Solitary thyroid nodule, PTC, FNAC, Histopathology.

Introduction:

Thyroid nodular (TN) lesions are among the commonest endocrine disorders in developed and developing countries including India.[1] Epidemiologic studies have shown the prevalence of palpable thyroid nodules to be approximately 5% in women and 1% in men living in iodine-sufficient parts of the world.[2,3] It has been reported that about 42 million people in India suffer from thyroid diseases in which the prevalence of palpable thyroid nodule is about 12.2%.[4] However, The relative frequency of thyroid cancer among all the cancer cases in India was reported to be approximately 0.1%–0.2% in 1999.[5] Most of thyroid nodules are asymptomatic and the fraction of malignant nodule is only about 5 percent of all palpable nodules.The diagnostic guidelines are available to differentiate benign from malignant thyroid nodules. It is reported that ultrasonography may not provide reliable information including internal calcification, hypoechogenity and centrally increased blood flow which are suspicious for malignancy.[6] Other diagnostic tests include radionuclide (Isotope) scan, FNAC and histopathology. Hence the combined use of FNAC, radionuclide scanning, hormonal study and histopathology of nodules may be the best diagnostic strategy.[7] Fine needle aspiration cytology may be cost effective screening tool to reduce large number of unnecessary operations of benign nodules. Bethesda System for Reporting Thyroid Cytopathology recommends that each report have begin with a general six diagnostic categories.[8] Orell (1992) Silverman (1986) suggested that fine needle aspiration cytology is not the same as histology, therefore in present study we evaluated the diagnostic accuracy, Bethesda system of thyroid cytology reporting, sensitivity, specificity and limitations of fine-needle aspiration cytology with correlation of histopathology in the diagnosis of thyroid nodular lesions.

Materials and Methods :

This prospective study was planned to evaluate the fine needle aspiration cytology by Bethesda system and correlated with histopathology in the diagnosis of thyroid nodules. Two hundred ten subjects were enrolled for the purpose out of which two hundred FNA with thyroid nodules finally selected for the study. Informed consent was taken and purpose of the study was explained to each patients.

All the patients underwent FNAC which was performed by the cytopathologists. The site of needle piercing was cleaned with spirit and betadine. A 23-gauge needle with 10/20 ml. syringe fitted to a syringe holder which was quickly attached, the aspiration procedure was performed and inserted into the lesion. A minimum of 1-2 FNA passes were taken from each lesion and the slides were immediately checked for adequacy of representative material. Both air-dried (2-3 smears stained for May-Grünwald-Giemsa(MGG), and alcohol-fixed smears (1-2 smears for PAP and 1-2 smears hematoxylin-eosin) were made in each case. In case of cystic nodule, material was centrifuged and sediments were taken for smear preparation.

The diagnostic categories proposed by the Bethesda System, all the cytologic criteria used to properly place an aspirate into the correct diagnostic category. With this in mind, the general categories recommended by the Bethesda System are 1) non-diag nostic or unsatisfactory, 2) benign, 3) atypia of undetermined significance (or follicular lesion of undetermined ignificance), 4) follicular neoplasm (or suspicious for a follicular neoplasm), 5) suspicious for malignancy and 6) malignant. The risk for malignancy in all category is also described. The cytological diagnosis was correlated with histopathologic reports when ever available. Histopathology was taken as gold standard.

Results

A total of 200 patients were included in the study; 147 were females and 53 males, age ranged from 11-65 years. It includes benign (146 cases) and malignant (44 cases) and inadequate for aspirates in 10 cases. Twenty five (12.5%) subjects were repeated for FNAC before proceeding to surgery, among which the repeated FNAC sample was definitively recognized as malignant in three (1.7%) of these patients. Comparisons between FNAC by Bethesda system and histological diagnosis are shown in **Table 1**.

Table 1: The Bethesda System for Reporting ThyroidCytopathology (n=200)

Diagnostic Categories		Male (n=53)	Female (n=147)	Histopathological Diagnosis (n=140/200)	Total (n=200)
I	**Nondiagnostic or Unsatisfactory**	5	5	1	10
II	**Benign**				
	Adenomatous colloid nodular goiter	10	48	45	58
	Colloid nodule with cystic changes	8	38	32	46
	Hashimoto Thyroiditis	3	15	7	18
	Granulomatous Thyroiditis	2	3	0	5
III	**Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance**	2	4	6	6

IV	**Follicular Neoplasm or Suspicious for a Follicular Neoplasm**	8	13	18	21
V	**Suspicious for malignancy**	2	1	3	3
VI	**Malignancy**				
	Papillary carcinoma	7	8	13	15
	Follicular carcinoma	1	5	6	6
	Anaplastic carcinoma	1	2	2	3
	Medullary carcinoma	2	3	4	5
	Poorly differentiated carcinoma	1	1	2	2
	Thyroid Lymphoma	1	1	1	2

Table 2 : Description of The Bethesda System for Reporting Thyroid Cytopathology with Confirmed histopathological diagnosis (N=200)				**Risk of malignancy (%)**
Bethesda Diagnostic Categories		**Histopathological diagnosis (n=140/200)**	**Total (n=200)**	
I.	**Nondiagnostic or Unsatisfactory**	1	10	
II.	**Benign**			**2.8%**
	Adenomatous colloid nodular goiter	45	58	
	Colloid nodule with cystic changes	Benign Colloid nodule (28)	46	
		Malignant PTC (4)		
	Hashimoto Thyroiditis	7	18	
	Granulomatous Thyroiditis	0	5	
III.	**Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance**	Adenomatous nodule (3)	6	**16.0%**
		Follicular adenoma (1)		
		HCL (1)		
		FVPTC (1)		
IV.	**Follicular Neoplasm or Suspicious for a Follicular Neoplasm**	Follicular adenoma (14)	21	**19.0%**
		Malignant FTC (2)		
		FVPTC (2)		
V.	**Suspicious for malignancy**	PTC(2)	3	**66.6%**
		Follicular adenoma(1)		
VI.	**Malignancy**			**100%**
	Papillary carcinoma	13	15	
	Follicular carcinoma	6	6	
	Anaplastic carcinoma	2	3	
	Medullary carcinoma	4	5	
	Poorly differentiated carcinoma	2	2	
	Thyroid lymphoma	1	2	

PTC : Papillary thyroid carcinoma, FVPTC : Follicular variant of Papillary thyroid carcinoma, FTC : Follicular thyroid carcinoma, HCL : Hurthle cell Lesion

In our study, 10/200 cases were inadequate aspirated material for diagnosis(5.0%), 146/200 cases were benign including suspicious for malignancy (73.0%) and 44/200 cases were malignant (22.0%). Histopathological correlation was seen in 140 of 200 cases of thyroid nodules.

Our observation showed 44 malignant patients in which papillary carcinoma 22cases(50.0%), Follicular carcinoma 8cases(18.0%), Medullary carcinoma 5cases(11.3%), Anaplastic carcinoma 3 cases (6.8%), Poorly differentiated carcinoma 2cases(4.5%) and Lymphoma 2case (4.5%) in **Table 1**. 146 benign cases in which 9(6.1%) cases were diagnosed as carcinoma on histopathology.

According to the Bethesda System, a non-diagnostic/unsatisfac tory thyroid FNA aspirate is a *solid nodule* where there are less than 6 groups of thyroid follicular cells composed of 10 or more cells. In addition, poor cell preservation and/or contamination by obscuring blood or ultrasound gel may warrant a diagnosis of non diagnostic/ unsatisfactory. Finally, an aspirated thyroid cyst should also be signed out as non-diagnostic.

Benign category lesions include 127 cases in which adenomatous colloid nodular goiter (58 cases, Fig 1a&1b), Colloid nodule with cystic changes (46cases, Fig 2a&2b), Hashimoto thyroiditis (18cases Fig 3a&3b) and granulomatous thyroiditis (5cases). 4 of 46 colloid nodule with cystic changes showed PTC on histopathology.The risk of malignancy in the benign group of diagnoses is approximately 2.8%.

Atypia of Undetermined Significance or Follicular Lesion of Undetermined Significance showed 6 cases in which Adenomatous nodule (2cases), Follicular adenoma (2cases Fig 4a &4b) and hurthle cell lesion (1case) and Follicular Variant of PTC (1case, Fig 6a&6b).The risk of malignancy in the benign group of diagnoses is approximately 16.0%.

Follicular Neoplasm or Suspicious for a Follicular Neoplasm showed 21 cases in which FVPTC in 2 cases, follicular carcinoma (Fig 5a &5b) with metastasis in 2 cases and follicular adenoma in 14 cases on histopathology. The risk of malignancy in the benign group of diagnoses is approximately 19.0%.

Suspicious for malignancy showed 3 cases in which papillary thyroid carcinoma in 2 case and follicular adenoma in 1 case on histopathology. The risk of malignancy in the benign group of diagnoses is approximately 66.0%.

Malignant category includes 33 cases of malignancies on smears exhibiting papillary carcinoma (15case Fig 7a &7b), Follicular carcinoma (6case), medullary carcinoma(5case Fig 9a), anaplastic carcinoma (3case, Fig 9b), pooly differentiated carcinoma (2case, Fig 8a &Fig 8b) and thyroid lymphoma (2case). 11 malignant cases were confirmed on histopathology from benign categories (9 case) and suspicious of malignancy (2case). The risk for malignancy is 100% **(Table 2)** in this category. All patients with FNAC samples positive for malignancy were found to have thyroid cancer. The sensitivity, specificity and diagnostic accuracy of FNAC for diagnosing malignancy were 97%, 98% and 96%, respectively in our study.

Discussion

Fine-needle aspiration (FNA) of the thyroid is well stablished procedure in the evaluation of a solitary thyroid nod-ule.[9] In approximately 15% of thyroid FNAs, a cytologic diagnosis of follicular neoplasm is rendered.[10,11] Only 20% of nodules with this diagnosis reveal a malignant thyroid tumor.[10] Benign thyroid nodules includes hyperplastic nodules (HN), colloid nodules (CN), hashimoto's thyroiditis (HT), follicular adenomas (FA) and malignant tumors include classic papillary carcinoma (PTC), follicular carcinoma (FA),follicular variant of papillary carcinoma (FVPTC), Medullary carcinoma, anaplastic carcinoma, poorly differentiated carcinoma and others. Primary benign thyroid nodules or adenomatous nodules resembling tumors are encountered frequently. It has been shown that more than 50% of clinically evident nodules are multinodular goitre or thyroiditis.[12]Primary thyroid cancers constitute 1% of all malignant tumors arising from all organs and are the most common among endocrine system malignancies. More than 80% of the malignancies present in palpable thyroid nodules are papillary thyroid carcinoma (PTC) followed by follicular carcinoma (FC).[13,14,15] In thyroid neoplasms, only a small percentage is malignant, which can histologically mimic benign nodules. The treatment and post-operative management of various types of thyroid nodules depends on the FNA cytologic and/or histologic diagnosis.

Fine needle aspiration cytology is a good modality of choice for diagnosis of thyroid nodules. However, diagnosis of thyroid cancer still remains uncertain in a large number of cases. In a review of more than 18,000 thyroid FNABs performed at the Mayo Clinic, FNAB had a reported sensitivity of 83%, specificity of 92%, and accuracy of 95%. [16]

The reporting of thyroid cytology has been subject of much debate for last forty years. Now there is a Bethesda system of thyroid FNA

diagnosis. FNA smear is considered satisfactory if 6 or more groups of 10 follicular cells each are present on a minimum of two slides.[17,18] The overall sensitivity, specificity, and accuracy of FNAC technique is 83%, 92% and 95% respectively. In FNAC, both false positive and negative results occur. [19]

Diagnostic accuracy varies between different series and depends on the method of data analysis. Good aspiration technique and availability of experienced cytologists are of importance in achieving high diagnostic accuracy. In our study, the diagnostic accuracy of FNAC positive for malignancy was comparable to others previous study. The sample diagnosed to have a benign lesion (without atypical cell, follicular cell, or Hurthle cell lesions) do not have a cancer. If they are not symptomatic, surgery could be avoided. Although a positive FNAC result is very useful in selecting patients for surgery, a negative FNAC is sometimes inconclusive and poses diagnostic clinical challenge. Indeterminate FNAC findings were due to difficulty in differentiating benign follicular and Hurthle cell lesions from their malignant counterparts. The diagnosis of follicular and Hurthle cell carcinoma requires identification of capsular or vascular invasion, which is impossible with an FNAC specimen. Patients having an FNAC diagnosis of atypical cell, follicular or Hurthle cell lesions should be advised to undergo surgery, as a significant proportion harbour malignancy. Another limitation of FNAC is inadequate sampling, which gives rise to non-diagnostic results. Insufficient cellular material from cystic or haemorrhagic lesions, the experience of cytopathologists in performing aspirations, the numbers of punctures, and the technique of preparing smears all affect the rate of non-diagnostic results. Use of ultrasound guidance was shown to decrease the proportion of non-diagnostic results as compared to freehand FNAC. However, there was no change in the overall sensitivity or specificity. In our study, 5% (10cases) of the patients had inadequate sampling, which was comparable to other large series, the sensitivity, specificity and diagnostic accuracy in suspicious and malignant lesion were 97.0, 98.0 and 96.0%, respectively The Bethesda System for reporting thyroid fine-needle aspiration (FNA) specimens, undoubtedly represented a major step toward standardization, reproducibility, and ultimately improved clinical significance, usefulness, and predictive value of thyroid FNA. The sensitivity, specificity and diagnostic accuracy were 97, 50.7 and 68.8%, respectively in earlier publication review. The rates of false negatives and false positives were low: 3 and 0.5%, respectively. [20]

Till date Fine Needle Aspiration is considered as the gold standard for screening all thyroid nodular lesions. But it has got its own share of fallacies and pit-falls. Sample adequacy and accuracy is highly dependent upon the skills of the pathologist performing the test.

To conclude, FNAC has high diagnostic values for thyroid cancers. Among those with indeterminate FNAC results, atypical cell lesions and age greater than 40 years were conferred increased risk of malignancy, for whom early surgical intervention should be offered. The result of meta-analysis in thyroid lesions showed high overall accuracy, indicating that TBSRTC represents a reliable and valid reporting system for thyroid cytology.

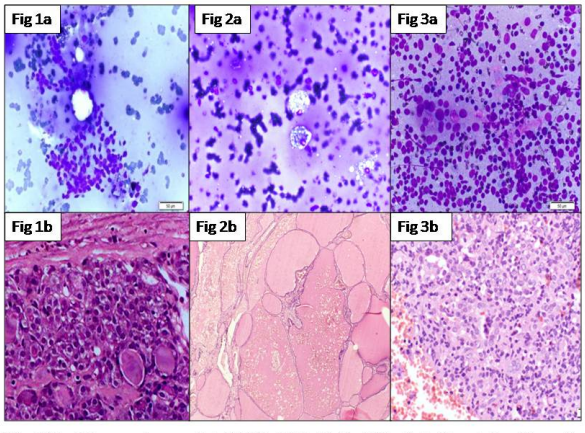

Fig1a &1b: Adenomatous nodule(MGG, H&E), Fig2a & 2b: Colloid nodule with cystic macrophages(MGG, H&E), Fig 3a & 3b: Hashimoto thyroiditis (MGG , H&E)

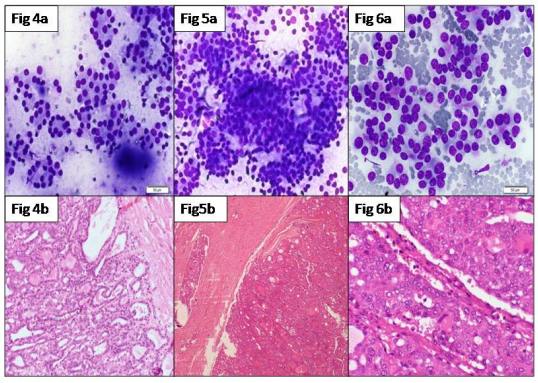

Fig 4a &4b: FLUS (MGG), Follicular Adenoma(H&E), Fig5a & 5b: Follicular neoplasm (MGG), Follicular Carcinoma(H&E), Fig 6a & Suspicious of malignancy (MGG), 6b: Follicular variant of Papillary thyroid carcinoma FVPTC(H&E)

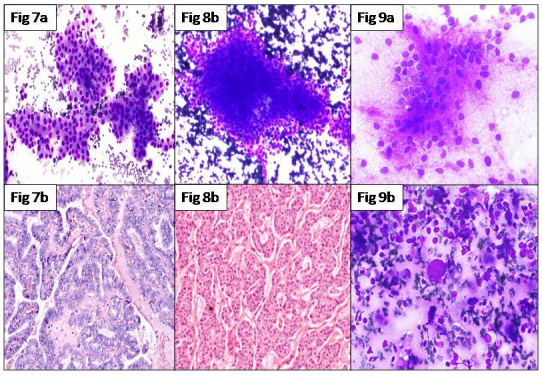

Fig 7a &7b: Papillary thyroid carcinoma (MGG, H&E), Fig8a & 8b: Poorly differentiated carcinoma or insular carcinoma(MGG, H&E), Fig 9a : Medullary thyroid carcinoma (MGG) & Fig 9b: Anaplastic thyroid carcinoma(MGG)

References:

1. Hegedüs L. Clinical practice. The thyroid nodule. N Engl J Med. 2004;351:1764–71.
2. Vander JB, Gaston EA, Dawber TR. 1968. The significance of nontoxic thyroid nodules. Final report of a 15-year study of the incidence of thyroid malignancy. Ann Intern Med 69:537–540.
3. Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, Evans JG, Young E, Bird T, Smith PA. 1977. The spectrum of thyroid disease in a community: the Whickham survey. Clin Endocrinol (Oxf)7:481–493.
4. Usha Menon V, Sundaram KR, Unnikrishnan AG, Jayakumar RV, Nair V, Kumar H. High prevalence of undetected thyroid disorders in an iodine sufficient adult south Indian population. J Indian Med Assoc. 2009;107:72–7.
5. Rao DN. Thyroid Cancer- An Indian Perspective. In: Shah AH, Samuel AM, Rao RS, editors. Thyroid Cancer- An Indian Perspective. Mumbai: Quest Publications; 1999. pp. 3–16.
6. Brito JP, Gionfriddo MR, Al Nofal A, et al. The accuracy of thyroid nodule ultrasound to predict thyroid cancer: systematic review and meta-analysis. J Clin Endocrinol Metab. 2014;99(4):1253–63.
7. Unnikrishnan AG, Kalra S, Baruah M, et al. Endocrine Society of India management guidelines for patients with thyroid nodules: A position statement. Indian Journal of Endocrinology and Metabolism. 2011;15(1):2-8. doi:10.4103/2230-8210.77566.
8. Massimo bonjiovanni, allessandra spitale, William C. Faquin. The Bethesda System for Reporting Thyroid Cytopathology : A Meta-Analysis. Acta cytologica 2012; 56,333-339
9. Silverman JFWR, Larkin EW, et al. The role of ®ne-needle aspiration biopsy in the rapid diagnosis and management of thyroid neoplasms. Cancer 1986;57:1164±117
10. Boyd LA, Earnhardt RC, Dunn JT, Frierson HF, Hanks JB. Preoper-ative evaluation and predictive value of ®ne-needle aspiration and frozen section of thyroid nodules. J Am Coll Surg 1998;187:494±502.
11. Baloch ZW, Sack MJ, Yu GH, LiVolsi VA, Gupta PK. Fine-needle aspiration of thyroid: an institutional experience. Thyroid 1998;8:565± 569.
12. Delellis RA, Williams ED. Tumours of the thyroid and parathyroid. In: The WHO classification of tumours of endocrine organs. Delellis RA, Lloyd RV, Heitz PU, Eng C (eds). IARC Press, Lyon. 2004; 50-133.
13. Yoon-LC, Mi KK, Jin-Won S, Han J, Kim JH, Yang JH, et al. Immunoex-pression of HBME 1, high molecular weight cytokeratin, cytokeratin19, thyroid transcription factor-1, and E-cadherin in thyroid carcinomas. J Korean Med Sci 2005;20(5):853–9
14. Yasuhiro I, Hiroshi Y, Chisato T, Miya A, Kobayashi K, Matsuzuka F,et al. HBME-1 expression in follicular tumor of the thyroid: an inves-tigation of whether it can be used as a marker to diagnose follicular carcinoma. Anticancer Res 2005;25:179–82.
15. Arturs O, Zenons N, Ilze S, Volanska G, Gardovskis J. Immuno-histochemical expression of HBME-1, E-cadherin, and CD56 inthe differential diagnosis of thyroid nodules. Medicina (Kaunas)2012;48(10):507–14.[6] Mauro P, Jaime R, Roberta.
16. Gharib H, Papini E thyroid nodules: clinical importance, assessment and treatment. Endocrinol Metab Clin North Am. 2007;36:707-735.
17. Morgan JL, Serpell JW, Mb BS, Cheng MS, Mb F. Fine-needle aspiration cytology of thyroid nodules: How useful is it? ANZ J Surg. 2003; 73:480.
18. Hamburger JI, Husain M, Nishiyama R, et al. Increasing the accuracy of fine needle biopsy for thyroid nodules. Arch Pathol Lab Med 1989; 113:1035–41.
19. Boey J, Hsu C, Collins RJ. False negative errors in fine needle aspiration biopsy of dominant thyroid nodules: a prospective follow-up study. World J Surg 1986; 10: 623-30.
20. Massimo Bongiovanni, Alessandra Spitale, William C. Faquin, Luca Mazzucchelli, Zubair W. Baloch.The Bethesda System for Reporting Thyroid Cytopathology: A Meta-Analysis. Acta Cytologica, July 25, 2012:56,333-339.