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Cytological Evaluation of Thyroid Lesions Based on the Bethesda System.

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Abstract :
Background :*Fine Needle Cytology (FNC) is a safe, cost effective and reliable technique for diagnosing diseases of the thyroid gland.*
Objectives*: (1) To categorize the cytological pattern according to The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). (2) To correlate the results of fine needle cytology with histopathological diagnosis wherever possible.*
Methods: *Patients with thyroid swellings referred for FNC of thyroid were included. The lesions were classified according to TBSRTC. In cases where surgery was performed, the specimens sent to histopathology were studied. Age, sex, cytological features and histological types were studied. Statistical analysis was done. False positive and false negative diagnosis were reanalysed.*
Results: *A total of 171 cases were available for FNC, of which specimens of 51 cases were received. On cytological examination, the majority of the cases belonged to category II of the Bethesda system. On subsequent histopathological examination, 43 cases belonged to the benign and non-neoplastic category and 8 cases were found to be malignant. The risk of malignancy in categories II, III, IV, V, VI was 3.3%, 50%, 7.6%, 100%, 100% respectively. The sensitivity of FNAC diagnosis was found to be 87.5 %, specificity was 84.8 %, positive predictive value was 73.6 %, negative predictive value was 93.3%, and accuracy was 84 %.*
Conclusion*: The present study suggests that fine needle cytology gives good positive correlation with histopathology with high sensitivity and specificity. False negative and false positive results can be reduced by repeat aspiration, correct sampling from the lesions with meticulous examination and reporting. TBSRTC improves clinical significance and the predictive value of thyroid FNC.*
Keywords*: Fine needle cytology, The Bethesda system for reporting thyroid cytopathology.*

I. Introduction

Fine needle cytology (FNC) has been an effective tool for the evaluation of thyroid nodules and thyroid diseases. It reduces the rate of unnecessary thyroid surgery for patients with benign nodules and appropriately triages patients with thyroid cancer to appropriate surgery. The prevalence of goiter is more than 40 million in India with more than 2 billion globally [(1)]. To address terminology and other issues related to thyroid FNAC, The National Cancer Institute (NCI) proposed the six tiered "The Bethesda System for Reporting Thyroid Cytopathology" (TBSRTC). It helps to communicate thyroid fine needle aspiration interpretations to referring physicians in terms that are succinct, unambiguous and clinically helpful and the source of information for pathologists as well [(2)]. It is a flexible framework and has standardized the cytomorphological criteria and diagnostic approach in reporting thyroid cytology.

The use of a standardized reporting system for thyroid cytology, such as TBSRTC, improves reproducibility, clinical significance, and the predictive value of thyroid FNA. [(3)]

This study aims correlating the cytological diagnosis with the final histopathological diagnosis (except the unsatisfactory category) and to evaluate the sensitivity, specificity, predictive values and accuracy, thereby to assess its role in preoperative diagnosis and planning of proper management of thyroid swellings.

II. Materials and Methods

The study was undertaken in the Department of Pathology, NKP Salve Institute of Medical Sciences and Research centre, Nagpur comprising of 171 cases.

Patients with clinically diagnosed thyroid swellings referred to the Department of Pathology for FNC of thyroid and the patients referred for guided FNC were included in the study. All the patients were clinically examined in detail and a careful palpation of the thyroid was done to guide precisely the location for doing aspiration. Details of the procedure were explained to the patients and consent was taken. FNC was done from the thyroid swelling using a 24-26-gauge needle attached to a 10-ml syringe under aseptic precautions. Both

non-aspiration and aspiration techniques were followed. Then 4-5 smears were prepared and promptly fixed in a fixative containing 95% ethyl alcohol. These were stained with Haematoxylin and Eosin (H&E) stain. Air dried smears were also prepared and stained with May- Grunwald- Giemsa stain. The cytological features were evaluated and the reporting was done according to The Bethesda System.

Histopathological specimens, wherever available, were processed as per standard methods. The histological diagnoses were classified into non-neoplastic and neoplastic

Cytological diagnoses were correlated with histopathology wherever possible and efficacy of FNAC was estimated.

III. Results

A total of 171 cases, comprised of 141 women (82.4%) and 30 men (17.5%), were included in this study. The female/male (F/M) ratio was 5:1. Most of the patients i.e. 70 were in the age group of 21 to 40 years. Thyroid status was evaluated in 135 cases. Euthyroid status was observed in 122 cases, 8 patients were hyperthyroid and 5 patients were hypothyroid.

The distribution of the FNC cases according to the Bethesda categories was as given in TABLE.1

There were 28 cases in non-diagnostic or unsatisfactory category. Benign and non-neoplastic were 109 cases (63.7%), including 93 cases of nodular goitre, ten cases of chronic lymphocytic thyroiditis and three cases each of Grave's disease and Hashimoto thyroiditis. There were ten cases (5.8%) in the category III Atypia of undetermined significance/Follicular lesion of undetermined significance. Furthermore, 19 cases (11.1%) were in the category IV i.e Follicular neoplasm/Suspicious for follicular neoplasm. Also, one case (0.5%) was suspicious for medullary carcinoma. Lastly, there were four malignant cases (2.3%), including 2 cases of papillary carcinoma, one case of medullary carcinoma, and one case of lymphoma. (TABLE.1.)

Table.1

BETHESDA CATEGORIES	NO. OF CASES IN EACH CATEGORY
Non-diagnostic or unsatisfactory	28
Benign	
Nodular goitre	93
Chronic lymphocytic thyroiditis	10
Hashimoto thyroiditis	3
Grave's disease	3
AUS/FLUS	10
Follicular neoplasm/suspicious for follicular neoplasm	19
Suspicious for malignancy	
Medullary carcinoma	1
Malignant	
Anaplastic carcinoma	2
Papillary carcinoma	1
Lymphoma	1
TOTAL	171

The frequency of histological types after thyroidectomy was as given in TABLE.2.

Table. (2)

Histologicaldiagnosis	Types	No. Of Cases
Non-Neoplastic (35 Cases)	Nodular Goitre	33
	Chronic Lymphocytic Thyroiditis	2
Neoplastic (16 Cases)	Follicular Adenoma	8
	Papillary Carcinoma	3
	Follicular Carcinoma	2
	Medullary Carcinoma	1
	Anaplastic Carcinoma	1
	DLBCL	1
	Total	51

DLBCL- diffuse large B cell lymphoma

TABLE (3) gives the correlation between FNAC and histological diagnoses and shows the accuracy of FNC in diagnosis of malignancy. As can be seen, there were two cases of False negative diagnosis (which were cytologically diagnosed as benign and on histopathology confirmed to be malignant) and 5 cases of false positive diagnosis (which were cytologically diagnosed as malignant and on histopathology found to be benign).

Table (3)

BETHESDA CATEGORIES	HISTOLOGICAL SUBTYPES	NO. OF CASES	TRUE/FALSE DIAGNOSIS	RISK OF MALIGNANCY
BENIGN (II)	NODULAR GOITRE	27	TN	3.3%
	PAPILLARY CA	1	FN	
	FOLLICULAR ADENOMA	1	FN	
	CHRONIC LYMPHOCYTIC THYROIDITIS	1	TN	
AUS/FLUS(III)	PAPILLARY CARCINOMA	1	TP	50%
	NODULAR GOITRE	1	FP	
FN/SFN (IV)	FOLLICULLAR ADENOMA	8	TP	7.6%
	FOLLICULAR CARCINOMA	1	TP	
	ADENOMATOUS GOITRE	4	FP	
SUSP FOR MALIGNANCY (V)	MEDULLARY CARCINOMA	1	TP	100%
MALIGNANT (VI)	ANAPLASTIC	1	TP	100%
	DLBCL	1	TP	
	PAPILLARY	1	TP	

TN-true negative, FN-false negative, TP- true positive, FP-false positive.

The sensitivity of FNC diagnosis was found to be 87.5 %, specificity was 84.8 %, positive predictive value was 73.6 %, negative predictive value was 93.3%, and accuracy was 84 %.

IV. Discussion

Fine needle cytology is a safe, simple and inexpensive, rapid technique that has emerged as a valuable and popular adjunct in the diagnosis and management of various thyroid lesions. The present study was undertaken to evaluate preoperatively with the help of FNC, the type of thyroid lesions and to correlate the observations with the histopathological examination in order to determine the usefulness and diagnostic accuracy of this technique.

In present study, a total of 171 cases, comprising of 141 women(82.4%) and 30 men (17.5%), were included.

The age group which was studied ranged from 16 years to 68 years. A female preponderance was noted with female to male ratio of 5:1. Similar observations were noted by Muratli et al [(4),] Sinna et al [(5),] Hajmoochehri et al[(6)]

In the present study, majority of the cases were in Category II followed by Category IV which correlates well with the studies conducted by Mehrotra et al [(7)], Yang et al [(8)] and Yassa et al [(9)]

Category I or non-diagnostic had 28 cases (16.3%) in which sufficient material was not available, only cyst fluid, obscuring blood or only macrophages were present. (Fig.1)

Category II or Benign: Majority of cases in our study were benign, maximum number of cases were nodular goitre 93 cases (54.3%), followed by chronic lymphocytic thyroiditis 10 cases (5.8%), Grave's disease 3 cases (1.75%) and Hashimoto thyroiditis 3 cases (1.75%).

Thirty cases were available for histopathological examination and there were two cases of false negative diagnosis, one was ultimately diagnosed as papillary carcinoma and the other one as follicular adenoma. It should be noted that in the false negative papillary carcinoma case, the tumor was deeply seated and therefore missed on FNAC as shown in Fig.7.The other false negative case was a follicular adenoma and had been reported as adenomatous goiter on FNC, as follicular neoplasm and adenomatous goiter are close differential diagnosis of each other [(10).] The risk of malignancy in this category was 3.3%.

Category III or Atypia of undetermined significance/ Follicular lesion of undetermined significance: Thyroid FNCs that do not fit into benign, suspicious for malignancy or malignant categories are included here. AUS/FLUS is reserved for specimens that contain cells (follicular, lymphoid) with architectural atypia that is not sufficient to be classified as suspicious for a follicular neoplasm or malignancy and on the other hand atypia is more marked than benign change. There were 10 such cases. But only two cases were available for histopathological examination. Out of these, one was false positive diagnosis (Fig.5) which was

diagnosed as nodular goiter on histopathology. On reanalysis, the patient gave history of radioiodine therapy, that resulted in nuclear enlargement and grooving which can occur after radioiodine therapy(2)

The risk of malignancy in this category was 50%. The increased risk of malignancy in this category was due to the fact that only two specimens were available for histopathological examination and even though the patients were advised repeat aspiration, they were not willing for it.

Category IV or Follicular Neoplasm/Suspicious for Follicular Neoplasm: The aim of this category is to identify a nodule that might be a follicular carcinoma. Follicular carcinomas have cytomorphologic features that distinguish them from benign follicular nodules but do not permit distinction from a follicular adenoma.They are reportable as Follicular neoplasm or Suspicious for follicular neoplasm. There were 19 such cases. (Fig.6)

Thirteen cases were available for histopathological examination and there were four false positive cases which were diagnosed as adenomatous goiter.Reanalysis showed that FNAC suggestion of follicular neoplasm was due to the fact that adenomatous goiter and follicular neoplasm may show similar cytological features. The risk of malignancy in this category was 7.6%

Category V or suspicious for malignancy: If there is 1 or 2 characteristics of malignancy present and they are only focal and not widespread throughout the follicular cell population, or if sample is sparsely cellular, a diagnosis cannot be made with certainty. In our study, there was only one such case which was suspicious for medullary carcinoma which turned out the same on histopathology. The risk of malignancy in this category was 100%

Category VI or Malignant: The malignant category is used whenever the cytomorphologic features are indicative of malignancy. In our study, there were 4 such cases, 2 cases of anaplastic carcinoma and one case each of papillary carcinoma and lymphoma. (Fig.9)

In three cases histopathology was done, diagnosis was positively correlated with the cytological diagnosis. The risk of malignancy in this category was 100%

The accuracy in the present study was 84%, which is comparable to the accuracy reported by Ko et al [(11)] and Mehrotra et al [(7)], 84.4% and 85.29% respectively.

The sensitivity of thyroid FNAC ranges from 65% to 99% and its specificity from 72% to 100% [(12-14)]. In our study, the sensitivity for cytological diagnosis of neoplasia was 87.5%, specificity of 84.8%, and diagnostic accuracy was 84%. This shows that FNC is more sensitive than specific in detecting thyroid malignancy. Similar observations were also made by, Richa Sharma et.al [(1)],Bagga PK et al[(15)] and Naresh Pahuja et al [(16)].

The percentage of risk of malignancy obtained in our research were Category II – 3.3%, Category III-50%, Category IV- 7.6%, Category V & VII- 100%. These observations were similar to the study of Hajmanoochehri et al. [(6)].

V. Conclusion

The present study suggests that FNC gives good positive correlation with histopathology with high sensitivity and specificity. False negative and false positive results can be reduced by FNC with multiple passes from different areas of lesion and guided repeat aspiration from the lesions with meticulous examination and reporting. As TBSRTC is uniform reporting system, it is helpful for both clinicians and pathologists. However, to compare risk of malignancy more larger study will be helpful.

V. Figures

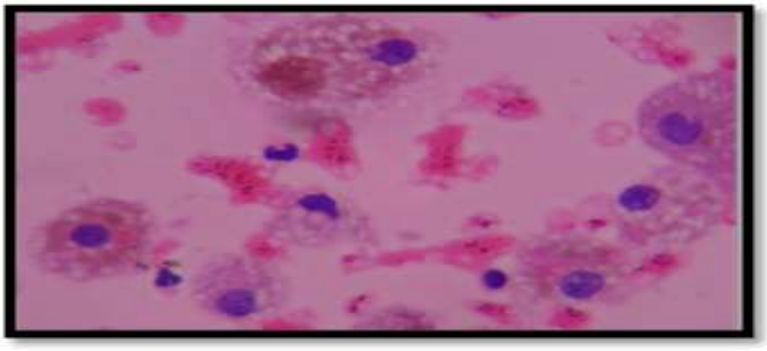

Fig.1 CATEGORY I Cyst macrophages

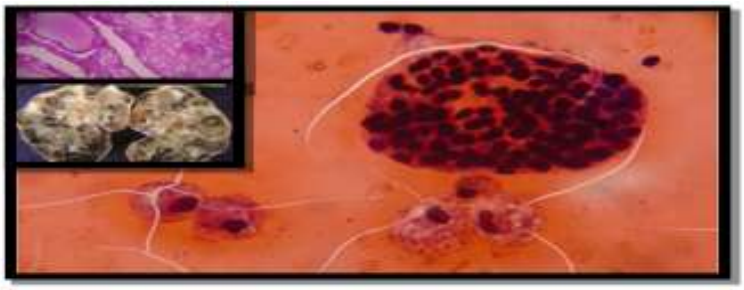

Fig.2 Nodular Goitre

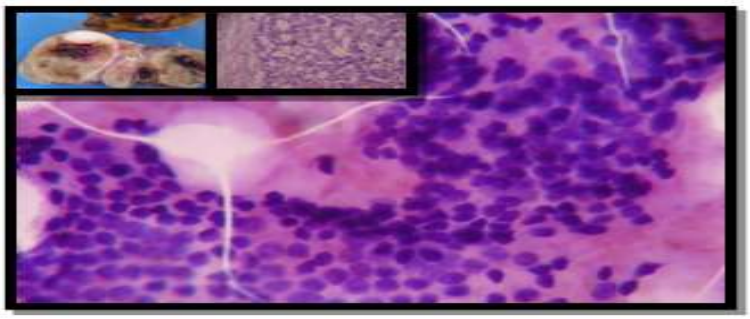

Fig.3 Adenomatous goitre

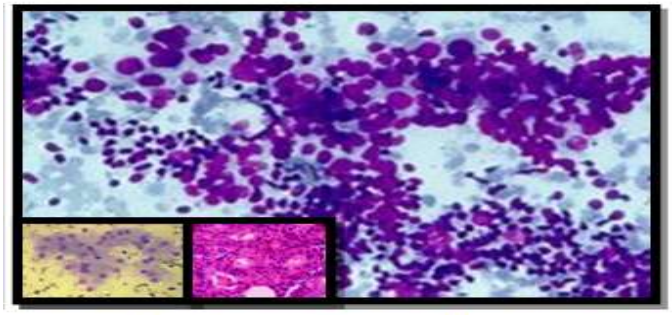

Fig.4 Hashimoto Thyroiditis.

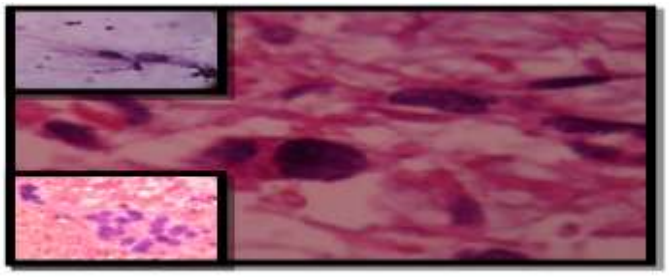

Fig.5 Category III

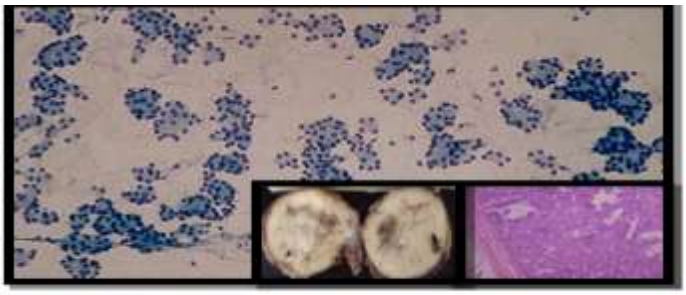

Fig.6 Follicular adenoma

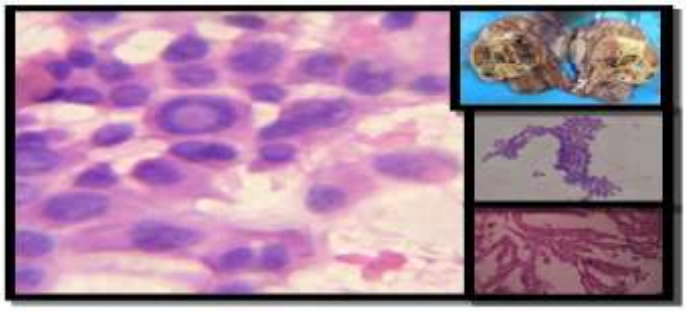

Fig.7 Papillary Carcinoma

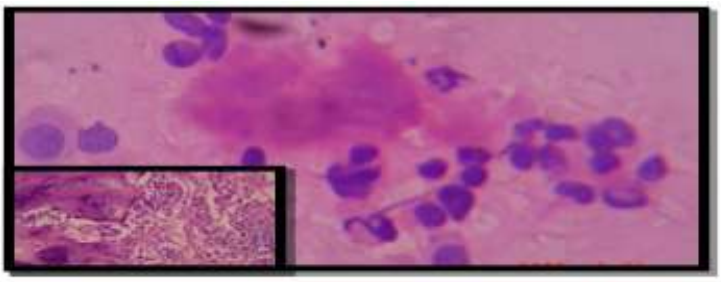

Fig.8 Medullary carcinoma

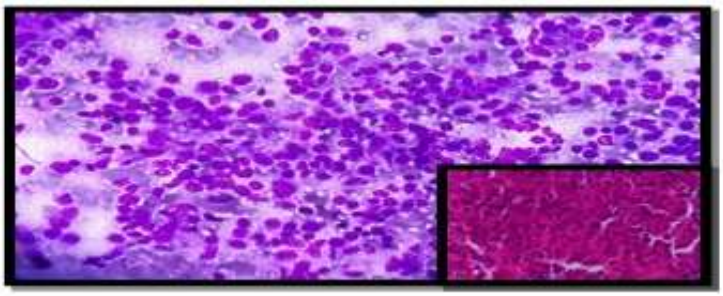

Fig.9 Lymphoma

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