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Spectrum of thyroid lesions on fine needle aspiration cytology

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Abstract:

The incidence of thyroid lesions is increasing significantly nowadays. Many a times, differentiation between physiological, inflammatory, autoimmune, hyperfunctioning and hypofunctioning of thyroid gland, benign and malignant tumor poses diagnostic difficulty. Fine needle aspiration cytology (FNAC) with clinical correlation, along with ultrasonography and thyroid function tests are done in relevant cases. Final diagnosis requires morphological examination of the lesions. FNAC is widely accepted and has become the cornerstone in evaluation of the thyroid lesions, as unnecessary surgery can be avoided. We studied a total of 251 cases in the age range of 3 years to 72 years, who presented with thyroid swelling over a period of one year and got a spectrum of thyroid lesions on cytology. Incidence was more in females 230 cases (91.63%) compared to males 21 cases (8.36%). Nodular goiter was the commonest disease constituting 127 cases (50.59%) followed by Hashimoto's thyroiditis 93 cases (33.05%) and malignancy was reported in 7 cases (2.78%).

USG guided FNAC for optimization of results is necessary for the location of target lesion. Careful searching for malignant cells and repeat FNAC are the key to a successful diagnosis and to plan a proper surgical procedure. Follow-up is necessary in case of a benign mass.

Key words: Fine needle aspiration cytology (FNAC), Thyroid lesions, Benign, Malignant

Introduction:

Thyroid gland enlargement is a common presentation in the general population and in the FNAC OPD, but all thyroid enlargements do not require surgery.[1] Thyroid nodules are common but thyroid cancer is uncommon.[2] FNAC is a very useful modality to decide on the patients requiring surgery from those who need not be operated.[3] Introduction of FNAC in the field of thyroid diagnostic tests has reduced thyroid surgeries considerably.[4] The main requirement for thyroid FNAC is to differentiate neoplastic from non neoplastic lesions and get a definite diagnosis of the enlargement.[5] FNAC is usually the first line of investigation followed by ultrasound examination, thyroid function tests and antibody levels.[6]

Aims and Objectives:

- To study the overall prevalence of various causes responsible for thyroid enlargement.
- To study the distribution of various lesions among the age and sex groups.
- To emphasize the limitations and pitfalls.

Materials & Methods:

Patients presented with thyroid swelling to the OPD of Bowring and Lady Curzon Hospital, Bangalore were included in the present study over a period of one year from July 2012 to June 2013. A total of 251 patients presented with thyroid swelling were assessed clinically, along with laboratory investigations like thyroid function tests, ultrasonography and by FNAC study. Patients presenting with thyroid swelling of all age and sex groups were included in the study.

A detailed history pertaining to neck swelling and relevant questions pertaining to the etiological factors, duration, symptoms of hypothyroidism or hyperthyroidism, previous surgery were elicited from all the patients.

Patients were examined clinically for thyroid swelling; following features were noted like size of thyroid gland, type of enlargement (diffuse/nodular), consistency (firm/soft), movement on deglutition and protrusion of tongue and any associated cervical lymph node enlargement. Thyroid function test reports were available only in 54 cases.

FNAC of the thyroid swelling was done for the diagnosis of pathological lesions. FNAC of thyroid swelling was performed under aseptic precautions using 23G-24 G needle. Needle was inserted into the gland by non aspiration technique, to and fro movement of the needle was done, material collected in the hub of the needle was taken on the slide and smears were made. In those patients with no aspiration, negative suction was given with 10 ml syringe, and the material obtained. The aspirated material was expelled on the glass slides, smears were made, slides were air dried and stained by Giemsa stain, and also the remaining slides were fixed in alcohol, then stained with haematoxylin and Eosin stain for evaluation in each case. In fluid aspirates, material was centrifuged and slide was prepared with the sediment. Aspiration was done at 2-3 sites and in some suspicious cases and elderly patients, USG guided FNAC was done. In 15 cases where aspirate was unsatisfactory, repeat FNAC under USG guidance yielded adequate material. For all cases of solitary thyroid nodule, either solid or cystic USG examination was done mandatorily in order to get satisfactory material and not to miss cystic papillary carcinoma.

Results:

Among 251 patients, the age ranged from 3 yrs to 72 yrs (**Table I**). Two Hundred and thirty cases were female (91.63%) and 21 cases were male (8.36%). Among the diagnostic outcome, 242 (96.4%) were Benign (non-neoplastic), 7(2.78%) were malignant & 2 (0.79%) were inconclusive.

Overall prevalence of various lesions: Nodular goiter was the commonest-78 (31.07%), colloid goiter- 20 (7.96%), nodular goiter with cystic change- 19(7.56%), thyroid cyst- 17(6.77%), nodular goitre with hyperplasia- 10 (3.98%). Hashimoto's thyroiditis accounted for 93(37.05%), papillary carcinoma and papillary carcinoma with Hashimoto's thyroiditis- 07(2.78%), diffuse hyperplasia- 02(0.79%), lymphocytic thyroiditis- 02(0.79%), follicular neoplasm- 01(0.39%) and inconclusive group which includes Follicular/ nodular goiter 02(0.79%). (**Table II**)

Four (1.59%) cases were in 1- 10 yrs age group; of them maximum were cyst 2 (50%), followed by nodular goiter 1 (25%) and nodular goiter with hyperplasia 1(25%). Forty three (17.13%) cases were in 11-20 yrs age groups; of them, Hashimoto's thyroiditis were 19 (44.1%), nodular goiter were 11(25.58%), colloid goiter were 10 (23.2%), nodular goiter with cystic change, cyst and nodular goiter with hyperplasia were 01(2.3%) each. Seventy two cases (28.68%) were in 21 – 30 yrs age groups; of them Hashimoto's thyroiditis were 34 (47.2%), nodular goiter were 18(25%), colloid goiter, nodular goiter with cystic change and cyst were 04(5.55%) each. Nodular goiter with hyperplasia were 02(2.77%) and Hashimoto's with papillary carcinoma were 02(2.77%), diffuse hyperplasia, lymphocytic thyroiditis were 01(1.38%) each, papillary carcinoma 01(1.38%) and follicular / nodular goiter were 01(1.38%). Sixty three cases (25.09%) were in 31 – 40 yrs age group, of them nodular goiter 23(36.5%), Hashimoto's thyroiditis 21(33.3%), nodular goiter with cystic change 05(7.93%), cyst 04(6.34%), colloid goiter, nodular goiter with hyperplasia

were 03(4.76%) each, papillary carcinoma 02(3.17%), and diffuse hyperplasia and follicular neoplasm / nodular goiter 01(1.58%) each. Thirty five cases (13.94%) were in 41-50 yrs age group, of them nodular goiter were 12(34.28%), Hashimoto's thyroiditis 11(31.42%), nodular goiter with cystic change 06(17.14%), cyst 03(8.57%), nodular goiter with hyperplasia 02(5.71%), colloid goiter 01(2.85%). Twelve cases (4.78%) were in 61-70 yrs age group, of them nodular goiter and Hashimoto's thyroiditis were 04(3.33%) each, colloid goiter, cyst, lymphocytic thyroiditis and follicular neoplasm/ nodular goiter were 01(8.33%) each. Four cases (1.59%) were in more than 71 yrs of age, of them nodular goiter 2(50%) and Hashimoto's thyroiditis and nodular goiter with hyperplasia 01(25%) each.

In around 15 cases, aspirate was unsatisfactory i.e. showing only haemorrhage; in such cases repeat FNAC under USG guidance yielded adequate material.

Discussion:

FNAC is not a substitute for conventional surgical histopathology, it is regarded as an extremely valuable complement in diagnosis and it is becoming just as indispensable.[7]

The FNAC procedure is performed without local anesthesia with the help of the non-aspiration technique, using 23-25 gauge needles.[8] In all cases, first FNAC was done by non-aspiration technique. In lesions of colloid goiter, nodular goiter, hyperplasia and neoplasia adequate aspirate was obtained. In those cases where adequate aspirate was not obtained by non-aspiration technique, then negative suction was given with a syringe and aspiration was done. This was usually needed in cases of Hashimoto's thyroiditis. This can be explained due to the solidification of the thyroid tissue by the dense lymphocytic infiltration and reduced vascularity when compared to the other thyroid lesions. The false negative FNAC results may occur because of sampling error.[4] Inadequate sampling is seen with inexperience of the cytopathologists, may also often results from sclerotic calcified nodules,nodules with cystic degeneration and calcified nodules. [8,9]

In a study of 514 patients by Filip Gabalec et al, a change from benign results to suspicious/ malignant in 13% of cases was seen on repeat FNAC. Repeating FNAC in patients with benign cytology in about 1 year horizon can reduce the rate of undiagnosed tumors.[5]

FNAC can be performed with or without ultrasound guidance but diagnostic accuracy improved with sonographic needle localization due to decreased number of inadequate specimens and false negative results.[10] In the thyroid glands with multiple nodules, each nodule can vary in the cytological appearance and one of them could be neoplastic. In such cases, USG guided FNAC is very useful in determining the area and nodule to be aspirated which is suspicious of neoplasms.

In our study, aspirates negative for cells (unsatisfactory aspirates) underwent ultrasound guided FNAC and good aspirates were obtained in most of the cases. Many a times, on blind FNAC neoplasms are missed due to sampling errors and on subsequent thyroidectomy, follicular and papillary neoplasms were identified. This can be minimised by guided FNAC. The ultrasound features of thyroid malignancy includes irregular edges, solid lesion, hypoechogenicity and being a single nodule respectively.[11] Thyroid nodule size must not be considered as a criteria for malignancy and thyroid nodule of any size may be suspected malignant.[11]

False negative rate can be reduced by repeating the FNAC.[5] In a study of 5017 patients with initially benign results who underwent repeat FNAC, thyroid carcinoma were detected in 2.3% in the initially benign cases at an interval of 6-

12 months.[5] Diffuse, mild to moderate enlargement is seen in Hashimoto's thyroiditis and colloid goiter. Diffuse enlargement with nodularity is seen in multinodular goiter. Solitary enlargement is seen in thyroid cyst, neoplasms and sometimes in nodular goiter with single prominent nodule. On palpation, cases of Hashimoto's thyroiditis were more firm in consistency when compared to other types of thyroid enlargements. Haemorrhagic fluid mixed with colloid aspirate was seen in thyroid cyst in cases associated with secondary hemorrhage in nodular goiter and follicular neoplasm. Maximum number of thyroid enlargement was seen in age group of 21-30 yrs (28.68%), second highest constituted in 31-40 yrs (25.09%). Nodular goiter (78) was the most commonest lesion encountered in our study constituting (127 cases, 50.59 %) associated with cystic change(19) and with hyperplasia (10) cases. Maximum number of nodular goiter cases were seen in 31- 40 yrs, one case was seen below 10 yrs and few cases after 52 yrs. The cytological features of nodular goiter observed were abundant thick and thin colloid, follicular cells were few in groups, monolayered sheets (**Figure I**)and showed variation in cell size.

Table I: Age distribution of thyroid lesions

Age	No of cases	Percentage
0-10 yrs	4	1.59%
11-20 yrs	43	17.13%
21-30 yrs	72	28.68%
31-40 yrs	63	25.09%
41-50yrs	35	13.94%
51-60yrs	18	7.17%
61-70 yrs	12	4.78%
>70yrs	4	1.59%

Table II: Prevalence of various lesions

Disease	Number	Percentage
Hashimoto's thyroiditis	93	37.05
Nodular goiter	78	31.07
Colloid goiter	20	7.96
Nodular goiter with cystic change	19	7.56
Cyst(colloid/ thyroid)	17	6.77
Nodular goiter with hyperplasia	10	3.98
Papillary carcinoma and papillary carcinoma with Hashimoto's thyroiditis	07	2.78
Diffuse hyperplasia	02	0.79
Lymphocytic thyroiditis	02	0.79
Follicular neoplasm	01	0.39
Inconclusive (follicular neoplasm/nodular goitre)	02	0.79
Total no. of cases	251	100

Cases with few cyst macrophages, hemosiderin laden macrophages also observed along with nodular feature were labeled as nodular goiter with cystic change. Presence of increased number of follicular cells with abundant cytoplasm, fire flares were reported as nodular goiter with feature of hyperplasia.

Nineteen cases (7.56%) of nodular goiter showed cystic change, and the aspirate was mainly brownish fluid. Ten cases of

Table III: Distribution of lesions in various age groups

Diagnosis	0-10yrs	11-20yrs	21-30yrs	31-40yrs	41-50yrs	51-60yrs	61-70yrs	>71yrs	Total
Nodular goiter	01	11	18	23	12	07	04	02	78
Hashimoto's thyroiditis	00	19	34	21	11	03	04	01	93
Colloid goiter	00	10	04	03	01	01	01	00	20
Nodular goiter with cystic change	00	01	04	05	06	03	00	00	19
Cyst(colloid/thyroid)	02	01	04	04	03	02	01	00	17
Diffuse hyperplasia	00	00	01	01	00	00	00	00	02
Nodular goiter with hyperplasia	01	01	02	03	02	00	00	01	10
Lymphocytic thyroiditis	00	00	01	00	00	00	01	00	02
Papillary carcinoma	00	00	01	02	00	02	00	00	05
Hashimoto's with papillary carcinoma	00	00	02	00	00	00	00	00	02
Follicular/nodular	00	00	01	01	00	00	00	00	02
Follicular neoplasm	00	00	00	00	00	00	01	00	01
Total	04	43	72	63	35	18	12	04	251

nodular goiter (3.98%) showed features of hyperplasia. The centrifuged smears of this fluid usually did not show any follicular cells. Only background of colloid and cyst macrophages was seen. Colloid goiter was seen in 20 cases (7.96 %), commonest age group of 11-20 yrs and few cases in 21-40 yrs age group. Microscopy showed moderate amount of thin colloid, benign follicular cells. Thyroid cysts were seen in 17 cases (6.77%), and maximum number was in 21-40 yrs age group. Nodular goiter with cystic change and simple cyst are difficult to differentiate on cytology as the microscopic features are almost similar in presence of abundant thin colloid, cyst macrophages and hemosiderin laden macrophages, follicular cells in clumps are more commonly seen in nodular goiter. However in inconclusive cases, USG examination proves to be helpful in categorizing the lesion.

Hashimoto's thyroiditis was the second most common lesion encountered in our study constituting 93 cases (33.05 %) more frequently seen in 21 – 30 yrs age group and occurs in the span of 11-50 yrs age

Figure I: Nodular goiter showing thyroid follicular cells in monolayered sheets (Giemsa stain 10 X).

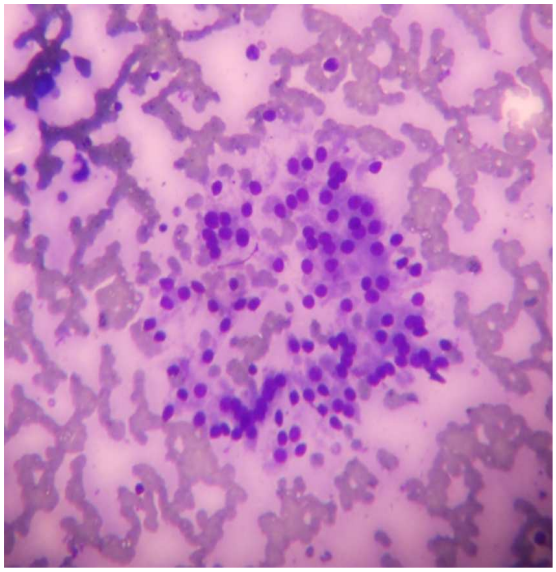


Figure II: Hashimoto's thyroiditis showing follicular infiltration by lymphocytes (Giemsa stain 40X).

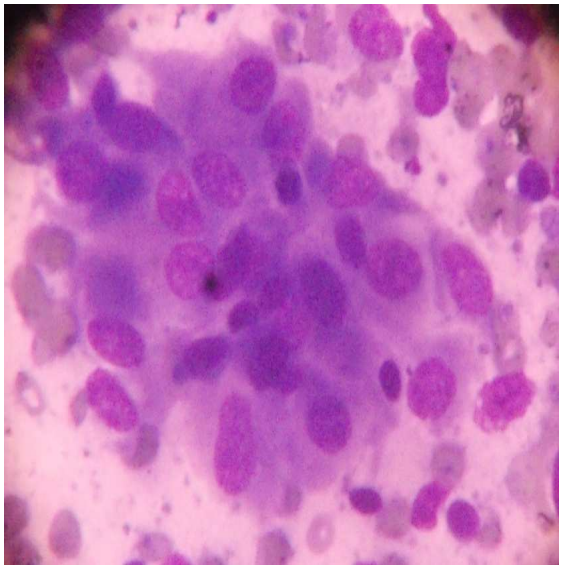


Figure III: Nuclear inclusions seen in Papillary Carcinoma of thyroid (Giemsa stain 40X)

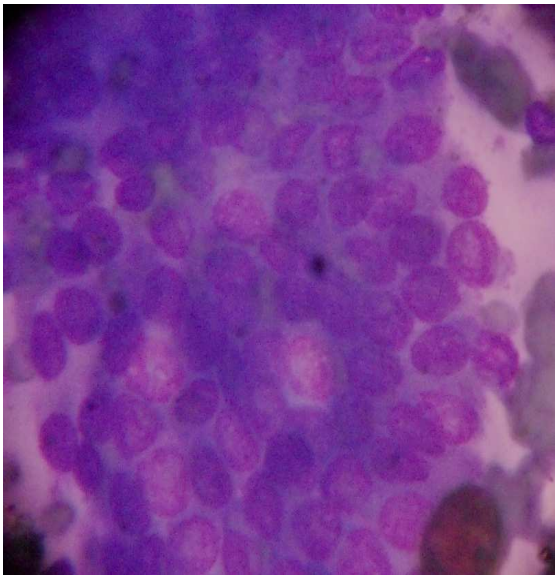
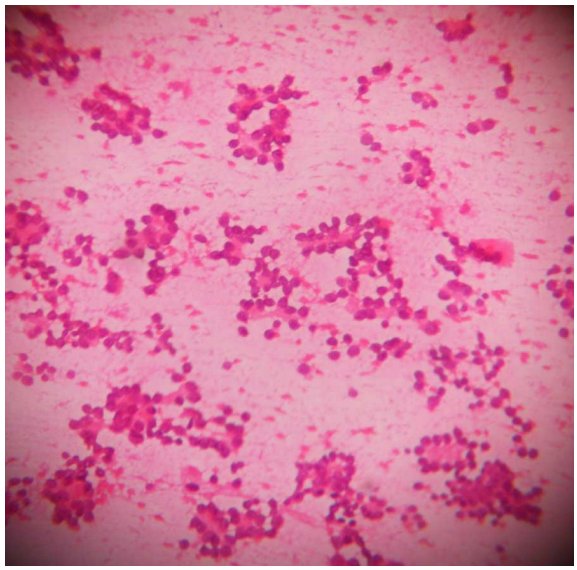


Figure IV: Follicular neoplasm showing repetitive follicular pattern (H&E stain 10X)



group. The incidence seems to reduce after 50 yrs. The cytological features are presence of thyroid follicular cells infiltrated by the lymphocytes, Hurthle cell change, occasional multi nucleated giant cells with scant or no colloid in the background (**Figure II**).

In a study by Shirish Chandanwale et al[12], a study of 150 cases from Pune showed colloid nodular goiter to be the commonest lesion constituting 65.3% of the total lesion. Thyroiditis was seen in 12.6% of cases whereas in our study, nodular colloid goiter was the commonest seen in 55.7% of cases and increase in incidence in Hashimoto's thyroditis / autoimmune thyroditis 38%, was seen associated compared to study in Pune where 12.6% of autoimmune thyroiditis was identified. 6.75% malignancy was seen in above study and our study showed 3% (8 cases) of malignancy; one was follicular neoplasm and 7 were papillary carcinoma.

Two cases (0.79%) represented abundant colloid, follicular cell showing repetitive pattern which were inconclusive on cytology and hence reported as follicular neoplasm/ nodular goiter. On cytology, features of nodular goiter and follicular neoplasm are sometimes difficult to report.[12] A study by Arup Sengupta et al from Sikkim[7] showed colloid nodular goiter constituting 75.84% of the total cases followed by autoimmune thyroditis 8.5%, neoplastic lesion seen in 11.24%.[7]

Diffuse hyperplasia 2 cases (0.79%) were seen in 21-40 yrs age group, these patients showed clinical features of hyperthyroidism, correlated with TFT findings (increase in T3,T4 and decrease TSH level). Two cases (0.79%) diagnosed as lymphocytic thyroiditis in the presence of lymphoid cells rich background and absence of follicular infiltration by lymphocytes.

Ten cases (3.98%) were classified under neoplastic category, 9 cases (2.78%) were reported as papillary carcinoma of thyroid. Neoplastic lesions were seen in the age group of 21- 60 yrs, 2 cases (0.79%) of papillary carcinoma also showed features of Hashimoto's thyroditis. The cytological features showed cellular smears with sheets and syncytial aggregates of follicular cells showing distinct anatomical border, nuclear grooves, overlapping and crowding, papillaroid fragments with or without fibrovascular core. Some showed multiple distinct nucleoli, intranuclear cytoplasmic inclusions (**Figure III**) and thick scanty chewing gum colloid. One cases (0.39%) of follicular neoplasm were diagnosed with cytological features of high cellularity and repetitive follicular pattern (**Figure IV**).

Two cases (0.79%) shows presence of large amount of colloid along with repetitive follicular pattern; hence diagnosis of follicular neoplasm/ nodular goiter was suggested which was inconclusive on cytology. Similar experiences was encountered by Bhatta S et al study where it was difficult to differentiate follicular neoplasm and colloid goiter.[13]

A study of comparison of FNAC with isotope scanning with I-131 scintigraphy by Rabia Basharat et al found FNAC to be more specific than sensitive whereas thyroid isotope scan is more sensitive than specific in detecting thyroid malignancy. Therefore, FNAC should be adopted as an initial investigation of thyroid disease in all tertiary hospitals.[14]

Molecular markers on FNAC smears can aid in diagnosing presence of neoplasm in inconclusive cases. Genetic mutations implicated in the development of differentiated thyroid carcinoma alter the DNA sequence encoding tyrosine kinase receptors (RET/PTC, NTRK), nuclear proteins (PAX-8-PPARγ), and signaling proteins (RAS, BRAF). RET/PTC rearrangements occur only in papillary thyroid carcinoma, but NTRK and BRAF mutations are also common.[15] Greater than 70% of papillary thyroid carcinomas will have mutations in the BRAF,RAS, or RET/PTC genes.[16] The BRAF V600E mutation is associated with more

aggressive forms of papillary carcinomas [17,18]. The mutations in the RAS proto-oncogenes (HRAS, NRAS, KRAS) or PAX-8-PPARγ rearrangement are found in approximately 70% of follicular carcinomas.[19] Finding the BRAF mutation, RET/PTC, or PAX-8-PPARγ rearrangements in an indeterminate FNAB specimens has been correlated with a 100% specificity of thyroid cancer.[10] Patients who has cytological diagnosis suspicious of malignancy and who score positive on molecular tests should directly undergo total thyroidectomy instead of diagnostic lobectomy.[15]

Pitfalls in FNAC of the thyroid as mentioned by Shah study [20] are adequacy of specimens(quantitative and qualitative), accuracy of specimens (non-homogeneity of needle placement), accuracy of cytopathological interpretation, cysts(difficult with degenerative nodules), follicular lesions(benign v/s malignant), Hurthle cell lesions (benign v/s malignant), and lymphocytic lesions(lymphocytic thyroiditis v/s lymphoma).[20]

The sensitivity of thyroid FNAC ranges from 65 % to 99% and specificity from 72 % to 100 %.[4] A combination of additional, advanced and diagnostic methods such as immunocytochemical studies, molecular pathology techniques enhance the prognostic value of FNAC in patient with atypia of undetermined significance or follicular lesion of undetermined significance, lesions suspicious of malignancy and suspected follicular neoplasm.[9]

Conclusions:

Our study concluded the fact that nodular goiter (42.62%) is the foremost commonest cause of thyroid enlargement followed by Hashimoto's thyroiditis. Most cases of nodular goiter occurred in the age group of 31 – 40 yrs but it is seen in the age group of 11 yrs to > 70 yrs (all age groups). Neoplastic lesions constituted (3.18 %). Incidence of papillary carcinoma was more common than follicular carcinoma. FNAC was found to be simple, safe and convenient test without any record of complications.

FNAC is used to differentiate neoplastic from non-neoplastic lesions. The non-neoplastic lesion especially Hashimoto's thyroiditis can be treated medically hence excluded from undergoing surgery and reduce the number thyroid surgeries.[13] In neoplastic lesion based on the benign nodules and malignant nature of the nodule, the required surgery can be decided. FNAC is not a substitute for conventional surgical histopathology. FNAC should be treated as a first line of diagnostic tool for thyroid swelling and in doubtful cases it should be coupled with ultrasound examination and USG guided FNAC for optimization of results. However, for final diagnosis there is no substitute for histopathology. The location of the target lesion, careful searching for malignant cells and repeat FNAC are the key to successful diagnosis to plan a proper surgery.[21] The distinction of the benign and malignant thyroid nodules is fundamental , as malignancy necessitates surgery, while strict patient follow–up is necessary in the case of a benign mass[7].

References:

1. Guhamallick M, Sengupta S, Bhattacharya NK, Basu N, Roy S, Ghosh AK, Chowdhury M. Cytodiagnosis of thyroid lesions-usefulness and pitfalls: A Study of 288 cases. J Cytol 2008; 25: 6-9.

2. Musani MA, Khan FA, Malik S, Khambaty Y. Fine needle aspiration cytology: sensitivity and specificity in thyroid lesions. J Ayub Med Coll Abbottabad 2011; 23(1): 34-6.

3. Handa U, Garg S, Mohan H, Nagarkar N. Role of fine needle aspiration cytology in diagnosis and management of thyroid lesions: A study on 434 patients. Journal of Cytology 2008; 25:13–17.

4. Esmaili HA, Taghipour H. "Fine-Needle Aspiration in the Diagnosis of Thyroid Diseases: An Appraisal in Our

Institution," ISRN Pathology, vol. 2012, Article ID 912728, 4 pages, 2012. doi:10.5402/2012/912728.
5. Gabalec F, Cáp J, Ryska A, Vasatko T and Ceeová V. Benign fine needle aspiration cytology of thyroid nodule: to repeat or not to repeat? European Journal of Endocrinology 2009; 16: 933-37.
6. La Rosa GL, Belfiore A, Giuffrida D, Sicurella C, Ippolito O, Russo G, et al. Evaluation of the fine needle aspiration biopsy in the preoperative selection of cold thyroid nodules. Cancer 1991; 67: 2137-41.
7. Sengupta A, Pal R, Kar S, Zaman FA, Sengupta S, Pal S. Fine needle aspiration cytology as the primary diagnostic tool in thyroid enlargement. J Nat Sc Biol Med 2011; 2: 113-118.
8. Bagga PK, Mahajan NC. Fine needle aspiration cytology of thyroid swellings: How useful and accurate is it? Indian Journal of Cancer 2010; 47:437-42.
9. Muratli A, Erdogan N, Sevim S, Unal I, Akyuz S. Diagnostic efficacy and importance of fine-needle aspiration cytology of thyroid nodules. J Cytol 2014; 31:73-8.
10. Steven R. Bomeli, MD, Shane O, LeBeu, MD, and Robert L Ferris MD, PhD. Evaluation of a thyroid nodule. Otalaryngol Clin North Am 2010; 43(2):229-38.
11. Rahimi M, Farshchian N, Rezaee E, Shahebrahimi K, and Madani H. To differentiate benign from malignant thyroid nodule comparison of sonography with FNAC findings. Pak J Med Sci 2013; 29(1):77-80.
12. Chandanwale S, Singh N, Kumar H, Pradhan P, Gore C, Rajpal M. Clinicopathological correlation of thyroid nodules. Int J Pharm Biomed Sci 2012; 3(3): 97-102.
13. Bhatta S, Makaju R, Mohammad A. Role of fine needle aspiration cytology in the diagnosis of thyroid lesions. Journal of Pathology of Nepal 2012; 2:186-88.
14. Basharat R, Bukhari MH, Saeed S, Hamid T. Comparison of Fine Needle Aspiration Cytology and Thyroid Scan in Solitary Thyroid Nodule.
Patholog Res Int 2011; 2011: 754041. doi:10.4061/2011/754041.
15. Melillo RM, Santoro M, Vecchio G. Differential diagnosis of thyroid nodules using fine-needle aspiration cytology and oncogene mutation screening: are we ready? F1000 Med Rep 2010 Aug 19: 2:62. doi: 10.3410/M2-62.
16. Adeniran AJ, Zhu Z, Gandhi M, Steward DL, Fidler JP, Giordano TJ, et al. Correlation between genetic alterations and microscopic features, clinical manifestations, and prognostic characteristics of thyroid papillary carcinomas. Am J Surg Pathol 2006; 30(2): 216-22.
17. Xing M, Westra WH, Tufano RP, Cohen Y, Rosenbaum E, Rhoden KJ, et al. BRAF mutation predicts a poorer clinical prognosis for papillary thyroid cancer. J Clin Endocrinol Metab 2005; 90(12): 6373-9.
18. Elisei R, Ugolini C, Viola D, Lupi C, Biagini A, Giannini R, et al. BRAF(V600E) mutation and outcome of patients with papillary thyroid carcinoma: a15-year median follow-up study. J Clin Endocrinol Metab 2008; 93(10):3943-9.
19. Nikiforova MN, Lynch RA, Biddinger PW, Alexander EK, Dorn GW, Tallini G, et al. RAS point mutations and PAX8-PPAR gamma rearrangement in thyroid tumors: evidence for distinct molecular pathways in thyroid follicular carcinoma. J Clin Endocrinol Metab 2003; 88(5): 2318-26.
20. Shah AR. Controversies in the management of thyroid nodule. Laryngoscope 2000; 110:183-93.
21. Asotra S, Sharma J. Role of AgNORs in thyroid lesions on FNAC smears. J Cytol 2008; 25:18-22.

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