

Clinico - Pathological Correlation of Thyroid Swellings

Jain S¹, Nayak R², Totade S³, Shukla N⁴

¹Dr. Sharad Jain, Associate professor, ²Dr. Rashmi Nayak, Assistant professor, ³Dr. Sanjay Totade, Professor and head, ⁴Dr. Neelam Shukla. All are affiliated with department of Pathology, NSCB Medical College, Jabalpur, MP, India

Address for Correspondence: Dr Rashmi Nayak, E mail: vijaynayak123@gmail.com

Abstract

Introduction: Thyroid being an actively functioning gland is subjected to series of disturbances, both physiological and pathological. It may be affected by various disorders like developmental, inflammation, hyperplastic and neoplastic that may present with similar sign and symptoms. Almost any disorder of thyroid can present as a nodule. The thyroid nodule is common problem faced by the clinicians as they cause apprehension due to their unpredictable behaviour. **Method:** A total of 110 patients were studied. All patients underwent FNAC after prior consent. FNAC was done with aseptic precautions by using 23 gauge needles, non-aspiration technique. Material obtained was smeared on 2 glass slides, air dried and stained with Leishmann's stain. Remaining wet slides fixed by using ethanol and were stained with hematoxylin and eosin (H&E) method. Pre-operative FNAC results were then compared with the definitive histological diagnosis. **Result:** Incidence of malignancy in thyroid nodules was 8.18%. Sensitivity and specificity in the present study was 85.7% and 96.4%, respectively with PPV, NPV and diagnostic accuracy of 92.3%, 93.1% and 92.9%, respectively. False positive and false negative error rate was 2.4 and 4.8 respectively. **Conclusion:** Definitive diagnosis of either benign or malignant can be suggested by FNAC and accordingly line of management can be planned. So we can avoid unnecessary surgeries for benign lesions and reduce the cost of hospitalisation.

Key words: Fine Needle Aspiration Cytology, Thyroid Function Tests, Follicular Neoplasm of thyroid

Introduction

Thyroid being an actively functioning gland is subjected to series of disturbances, both physiological and pathological. It may be affected by various disorders like developmental, inflammation, hyperplastic and neoplastic that may present with similar sign and symptoms. Almost any disorder of thyroid can present as a nodule. The thyroid nodule is common problem faced by the clinicians as they cause apprehension due to their unpredictable behaviour.

Prevalence of palpable thyroid nodule in non-iodine deficient area is about 4-7% in general adult population and 0.2 to 1.5 % in children [1,2]. Now a days due common use of USG in clinical practice the incidence of thyroid nodule has rises to 14- 50% [2,3,4]. Benign lesions are more common in thyroid and less than 5% are actually malignant [2, 4].

In India the scenario is quite different. India has world's biggest "goitre Belt" in the subhimalayan region and the

average prevalence of goiter is around 40%. Though goiter is quite common, cancer of thyroid is comparatively rare constituting less than 1% of cancer [5].

Both benign and malignant lesions of thyroid commonly present with a nodule. Since most of the thyroid nodules are benign it is essential to identify patients who are likely to be benefited from surgery and thus avoid essential diagnostic surgery in all cases. This has been attempted on the basis of several diagnostic tools like clinical examination, TSH level, ultrasound, Thyroid scan and FNAC. Among the diagnostic tools currently available fine needle aspiration is considered as the most reliable tool and is often used as the first screening test for the diagnosis of thyroid nodule. Fine needle aspiration cytology is the study of cells obtained by fine needle under vacuum. Some cells with little tissue fluid are sufficient to make a morphological diagnosis. It has emerged as the most accepted, accurate diagnostic procedure which is easy, quick, cost effective and cosmetically sound [1,6,7,8]. But there are some limitations of FNAC; the most important is the

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indeterminate or suspicious results i.e. inability to distinguish between follicular adenoma and carcinoma, other includes inadequate or nondiagnostic smear, sampling error due to large nodule or very small ones and inexperience of the cytopathologist [4,9]. Some of these problem can be solved by USG guided FNAC which helps in taking sample from more representative area.

Benign nodules can be caused by adenomas, colloid nodules, cysts, infectious nodules, lymphocytic or granulomatous thyroiditis, hyperplastic nodules, and congenital anomalies. Malignant nodules are classified as: Differentiated: a) papillary adeno-carcinoma, and b) follicular adeno-carcinoma, medullary carcinoma, undifferentiated – a) small cell, b) giant cell, and c) carcinosarcoma, and miscellaneous - a) lymphoma/sarcoma, b) squamous cell carcinoma, c) fibrosarcoma, d) mucoepithelial carcinoma, and e) metastatic tumors.

The present study was conducted in Netaji Subhash Chandra Bose Medical College and Hospital, Jabalpur (M.P) during September 2012 to October 2013 with the aims of evaluating accuracy of FNAC in the diagnosis of nodular lesions of thyroid in comparison to other diagnostic modalities, and to make early and accurate differentiation of benign and malignant thyroid nodules so that unnecessary surgery in benign cases can be avoided.

Materials and Methods

The present study was a prospective study carried out in the Department of Pathology, N.S.C.B Medical College Jabalpur, M.P (India), on both indoor and outdoor patient requiring FNAC of the thyroid lesions between September 2012 to September 2013

A total of 110 patients were studied. Inclusion criteria included all patients with thyroid enlargement irrespective of age and sex. In all patients detail clinical findings, USG, and TFT were recorded. All patients underwent FNAC after prior consent.

Technique of FNAC: FNAC was done with aseptic precautions by using 23 gauze needles, non-aspiration technique. Material obtained was smeared on 2 glass

Results

During the study period 110 fine needle aspirations were carried out for thyroid lesion. Out of which 42 cases were subjected to histopathological study. Age group of these 110 patients ranged between 10-75 yrs with the mean age of 38+/- 13.9yrs. Majority of patients were in the age group of 31-40yrs, predominantly patients were females accounting for 92(83.6%) of total 110 cases with male to female ratio of 1: 5.1.

slides, air dried and stained with Leishmann's stain. Remaining wet slides fixed by using ethanol and were stained with hematoxylin and eosin (H&E) method. Adequate aspirates were taken, when cytology smears contain five to six groups of well-preserved follicular cells, with each group containing 10 or more cells [10].

However, adequacy also depends upon the lesion being aspirated. For example, in case of colloid goitre, FNAC may yield only colloid with scanty cells, but it is adequate, if the lesion is taken into consideration. No serious complications occurred in our study. Only the pain for few minutes after aspirations was noted in few cases. Out of 110 cases 42 patients underwent thyroid surgery. FNAC smears results were divided into four categories-Benign (Negative), Suspicious (Intermediate), Malignant (Positive) and Non-diagnostic (Unsatisfactory).

Patients with benign cytodiagnosis did not have malignancy. The epithelial elements showed uniformity of cell size, shape and nuclear structure. Colloid was present in large amount and cellularity was low. Benign nodules included multi-nodular goitre, hyperplastic goitre, colloid goitre, Grave's disease, Hashimoto's thyroiditis, Dequervain thyroiditis and colloid cysts. Suspicious (Intermediate) cytodiagnosis was made when smear was hypercellular and a pattern suggestive of follicular or hurthle cell neoplasm or atypical features suggestive of but not diagnostic for malignancy was present. Malignant smear had cytological finding indicating the presence of malignant cells consistent with primary or metastatic thyroid cancer. Malignant nodules included papillary carcinoma, medullary carcinoma, poorly differentiated carcinoma, anaplastic carcinoma, and lymphoma.

Non-diagnostic (Unsatisfactory) specimens were found to be inadequate for proper cytopathologic interpretation due to presence of cystic fluid or haemorrhagic material and very few cells or excessive drying. Pre-operative FNAC results were then compared with the definitive histological diagnosis. The sensitivity, specificity, diagnostic accuracy, positive predictive value (PPV) and negative predictive value (NPV), false positive and false negative error rate of FNAC in diagnosing thyroid malignancy was calculated.

Table 1: Age & sex distribution of the cases

Age group	Male	Female	Total
10-20	3	7	10
21-30	2	27	29
31-40	6	29	35
41-50	1	13	14
51-60	4	11	15
61-70	2	4	6
71-80	0	1	1
Total	18	92	110

All cases (110) presented with midline swelling in front of neck, 24(21.8%) had associated dysphagia and 20(18.2%) had hoarseness of voice. Duration was less than a year in most of the patients 74 (67.2%). In present study 100 (91%) case were in clinical euthyroid state, 6(5.4%) had hyperthyroidism and 4(3.6%) were in a hypothyroid state. FNAC yielded adequate cell samples in 108(98.1%) cases and inadequate in 2(1.9%).

On cytological study out of 110 cases with thyroid lesions, 95(86.3%) were classified as benign; 2(1.8%) as malignant; 11(10%) as suspicious and 2(1.8%) aspirates as inadequate. Among the 95 non-neoplastic lesions, colloid goiter was the commonest 84(76.4%) followed by Dequervain's Thyroiditis 2(1.8%), Lymphocytic Thyroiditis 2(1.8%) and Nodular Goiter were also 2(1.8%). Other less common lesions were Adenomatous Goitre, Hyperactive colloid Goitre and colloid cyst. Among the malignant lesions (n=2) all were papillary carcinoma 2(1.8%) and all the suspicious lesions 11(10.0%) were follicular neoplasm on cytology.

Table 2: Shows correlation of clinical and FNAC diagnosis.

Clinical diagnosis	FNAC Diagnosis								
	Colloid goitre	Adenomatous goitre	Nodular goitre	Thyroiditis	cyst	Graves disease	FN	Papillary carcinoma	US
Colloid goitre(92)	80	1	2				7		2
Thyroiditis(5)	1	-	-	4	-	-	-	-	-
Graves disease(2)	-	-	-	-	-	1	1	-	-
Solitary nodule(5)	-	-	-	-	3	-	2	-	-
Malignancy(6)	3	-	-	-	-	-	1	2	-
Total(110)	84	1	2	4	3	1	11	2	2

Table 2 show correlation between clinical and FNAC diagnosis. Clinico-cytological correlation is highest in case colloid goitre (87%), in case of thyroiditis 80% and least in malignancy (33%).

Table 3-FNAC and Histological correlation

	FNAC diagnosis		Histopathological Diagnosis	
	Colloid goitre	Follicular adenoma	Follicular carcinoma	Papillary carcinoma
Colloid goitre(29)	27	2	-	-
Follicular neoplasm(11)	1	3	7	-
Papillary carcinoma(2)	-	-	-	2
Total(42)	28	5	7	2

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Table 3 shows correlation between FNAC and Histology. Among 95 non-neoplastic lesions diagnosed by cytology, histopathological study was done in 29 cases of these 29 cases diagnosed cytologically as colloid goitre, histological examination confirmed the diagnosis of colloid goitre in 27 cases. Two cases which were diagnosed as colloid goitre on FNAC turned out to be follicular adenoma on histology. Cyto-histological concordance rate in colloid goitre was 93.1%.

Out of 110 cases 42 were operated. Histopathological diagnosis in these 42 operated cases showed malignancy in 09(21.4%) and benign lesions in 33(78.6%). Most common benign lesion on histopathological report was colloid goitre (66.7%) and the most common malignancy was follicular carcinoma (16.7%) while papillary carcinoma constitutes only 4.7%.

Cytological diagnosis of papillary carcinoma was made in 2 cases. Histopathological study carried out in both cases and it was concurrent in both cases. Thus the concordance rate in case of papillary carcinoma was 100%. Of the 11 suspicious cases, histopathological studies were possible in all 11 cases. Among these, 7(63.6%) were follicular carcinoma, 3(27.3%) follicular adenoma and 1(9.1%) adenomatous goitre. Cytohistologic correlation in this group were not considered due to its cytologically indeterminate-nature. The incidence of suspicious cases in the present study was 10%. And the incidence of malignancy in suspicious cases was 63.6%. Overall, cytohistological correlation in all categories excluding the suspicious group was 93.5%.

Table 4: Presence of metastasis in cases of thyroid carcinoma

	Metastasis Present	Absent	Total
Follicular carcinoma	4 (57%)	3 (43%)	7
Papillary carcinoma	0	2	2

Table 4 show out of 7 cases of follicular carcinoma, 4 cases had metastasis at the time of diagnosis. Out of 4, 1 showed lung metastasis, 1 vertebral metastasis, 1 orbital metastasis, 1 orbital and cutaneous metastasis. Patients of orbital metastasis presented with progressive enlarging mass and proptosis with duration < 6 months. Both were involving left orbit. Patient of cutaneous metastasis presented with slowly enlarging erythematous mass in right side of face since one year. Orbital and cutaneous metastasis was confirmed by cytology and vertebral by the histopathology.

Sensitivity and specificity in our study was 85.7% and 96.4%, respectively. Positive predictive value which measures true positive, was 92.3% in present study and Negative predictive value which measures true negative was 93.1% in present study. Both false positive and false negative rate was <5% giving high diagnostic accuracy of 92.9%. It shows FNAC is simple, safe screening as well as diagnostic test in evaluating thyroid swelling with some limitations. The major limitation of thyroid cytology is that it cannot differentiate between follicular adenoma and carcinoma.

Discussion

Fine needle aspiration is the initial modality in the investigation of thyroid lesions. It is most accepted, accurate diagnostic procedure which is easy, quick, cost effective and cosmetically sound. It reduces the incidence of unnecessary surgery.

Ages of the patients ranged between 10-75 years. In present study as well as in various other studies, it was most common in the 3rd and 4th decades [11,12,13,14].

Median age was 38+_{13.9} yrs in the present study which was comparable to A. Martinek [12]. In the present study 92 were female and only 18 were males with male to female ratio (M:F) of 1:5.1. Sex distribution was comparable to study by E.A Sinna et al whose study showed M:F ratio of 1:5.2, and Sreaton NJ et al also showed M:F=1:5.2.[8,15]. It has been well

documented in various studies that all types of thyroid lesions occur more commonly in the females [11,13,16].

In the present study 100(91%) cases were in clinical euthyroid state, 6(5.4%) had hyperthyroidism and 4(3.6%) were in a hypothyroid state. Out of 6 hyperthyroid cases, 3 cases were of colloid goitre, one case was of Grave's disease, one case was of Follicular neoplasia and one case was of Hashimoto's thyroiditis on FNAC. Out of 4 hypothyroid cases, all were diagnosed as colloid goitre on FNAC. Other authors had also reported most patients of thyroid nodule as euthyroid [18,19,20].

These findings suggest that TFT is just a preliminary tool in evaluation of nodular lesions of thyroid and lacks sensitivity and specificity in the diagnosis of thyroid nodule.

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In the present study FNAC results were broadly categorised into four groups- benign, malignant, suspicious and unsatisfactory. Out of 110 cases 95(86.3%) were benign; 2(1.8%) malignant; 11(10%) suspicious and 2(1.8%) were inadequate. The reported rate of benign cytological results ranged from 51 to 90%, rate of malignant cytological findings ranged from 1% to 16%, rate of suspicious results ranged from 4% to 23% and the rate of nondiagnostic results varied from 1.6% to 31% [5,6,9,21,22,23,24]. Our results also fall within the reported range.

In the present study incidence of adequate sample was 98.1% and the incidence of inadequate samples was 1.8%. Number of factor are important in affecting the adequacy of thyroid aspirate sample. Mandrekar et al 1995 observed that selection of cases with prior investigations such as thyroid scan and ultrasonography will yield a lower number of inadequate samples as compare to FNAC as initial modaliyt [21].

Burch et al reported a high insufficiency rate of 31%, which they attributed to relative inexperience of many of the aspirators. Another contributor to the higher insufficiency rate was inconsistent reporting of cytology results by a large number of staff pathologists [22]. Raabs et al gave the reason for inadequate FNAC was

different criteria of adequacy used by cytologist and because of poor sampling by the radiologist and clinician [25].

In various studies 0.5 to 9.3% of benign cytological finding turn out to be malignant histopathologically [6,17,21,24,26,27]. In the present study false negative rate was 4.8% which is comparable to recent studies.

This may be due to insufficient sampling, sampling from non-representative area and cytological misdiagnosis. False positive rate was 2.4%. FP diagnosis is mainly due to misinterpretation of cellular atypia.

10 to 56% of suspicious cytological finding proved to be malignant on histopathological examination [6,17,21,24,26,27,28]. In the present study 63.6% of the suspicious cases were malignant following surgical procedure.

Thyroid lesions classified as malignant on FNAC have a high risk of being malignant on surgical follow up was observed in previous studies as well as in the present study. [6,17,21,24,26,28]. Cyto-histopathological correlation was established in 86% to 100% cases. Results of the present study also fall within the reported range.

Series	Year	Sensitivity	Specificity	PPV	NPV	DA
Agrawal S[5]	1995	76.5	95.9	86.7	92.2	90.9
Holleman et al [29]	1995	84	52	53	83	65
Burch et al [22]	1996	80	73.2	55.8	90	75.2
Lopez et al [30]	1997	90	99.8	98	99	99
Leonard& Melcher [27]	1997	88	78	46	97	80
Baloch et al [6]	1998	92	84	73.3	98.7	
Cap et al [31]	1999	86	74	34	97	75
Settakorn J et al [32]	2001	90.4	85.7	83.3	93.7	92.5
Morgan et al [17]	2003	55	73	70	67.4	67.2
Mahar et all [33]	2006	98	70	91	93	91
Haberal [34]	2009	92.6	91.6	83.5	96.5	91.9
Moosa et al [35]	2010	77.7	98.9	87.5	97.8	
Gupta M et al [11]	2010	80	86.6	80	86.6	13.3
Wahid F et al [14]	2011	88.1	77.5	80.4	86.1	82.9
Pandey et al [26]	2012	57.1	90	70.6	83.3	90.3
EA sinna [8]	2012	92.8	94.2	94.9	91.8	93.6
Muratli et al [24]	2014	87.1	64.6	76.1	79.5	77.3
Present study	2014	85.7	96.4	92.3	93.1	92.9

Table 5 is a review of recent series on various statistical indices like sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of FNAC of thyroid.

The sensitivity rate in above series ranged from 76% to 98% with the exception of 55% in the study by Morgan et al (2003), in Australia [17].

Our results were comparable to the series with a sensitivity of 85.7%. The specificity rates varied from 73% to 98.9% with the exception of Holleman et al (1995), who reported the specificity rate as low as 52% [29].

Our results were comparable to the series with specificity rate of 96.7%. Analysis of the above series reveals an overall positive predictive value (PPV) ranging from 34% to 98% which implies presence of malignancy.

A negative predictive value (NPV) i.e. negative for malignancy in the above series ranged from 67.4% to 98.7%.

Our results are comparable with a PPV of 92.3% and a NPV of 93.1%. This confirms FNAC as a good screening procedure for thyroid lesions.

The diagnostic accuracy of FNAC ranged from 65% to 99% depending upon the expertise of the aspirator and cyto-pathologist interpreting the sample [5,6,8,11,14,17,22,24,27,29- 35].

The diagnostic accuracy in present study was 92.9%.

These data suggest that that fine needle aspiration cytology is slightly more specific than sensitive in detecting thyroid cancer and confirm it as a reliable diagnostic test.

Conclusions

FNAC of thyroid lesions is safe, simple, cost effective accurate method for management of palpable thyroid lesions.

Non aspiration technique is superior to other technique; it yields good cellularity and decreases the obscuring effect of blood. No major complication was faced in any case.

The procedure was well tolerated by all the patients and could easily be repeated.

There was a good cytohistopathological correlation with sensitivity of 85.7% and specificity of 96.4%. Thus in more than two third patients a definitive diagnosis of either

benign or malignant can be suggested by FNAC and accordingly line of management can be planned. So we can avoid unnecessary surgeries for benign lesions and reduce the cost of hospitalisation.

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