

"A Cytomorphological Study of Thyroid Lesions with Special Reference to Macrophages"

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Abstract

Background and Objectives : Fine needle Aspiration cytology (FNAC) plays an important role in the evaluation of the nodules in the thyroid gland & selection of patients for surgical treatment. The present study was undertaken with the following aims and objectives:-

1. To study morphological features in thyroid aspirates.
2. To study the cytomorphologic attributes useful in distinguishing between neoplastic and non-neoplastic lesions.
3. To identify conditions associated with presence of macrophages

Methodology : The current study comprised 240 cases with FNA smears from patients with enlarged thyroid (diffuse/nodular). Fine Needle Aspiration Cytology was done and the slides were stained with routine stains plus special stains as and when required.

Results & Conclusion : The results of this study illustrate that if PTC and Hurthle cell neoplasms are excluded, the presence of macrophages strongly supports the diagnosis of benign colloid nodule ($P < 0.0001$). FNAC proved to be a safe, inexpensive, repeatable and rapid procedure in which no hospitalization or anaesthesia is required.

Keywords: Colloid goiter; fine needle aspiration cytology; thyroid; thyroid neoplasms;

I. Introduction

Fine needle aspiration (FNA) is a rapid, cost-effective, safe, and simple means of diagnosing thyroid nodules. [Gharib, 1994 Gerhard and Da Cunha Santos, 2007]. Fine needle Aspiration cytology (FNAC) plays an important role in the evaluation of the nodules in the thyroid gland & selection of patients for surgical treatment. However, it needs to be interpreted together with all the other factors that are of important for the assessment of the thyroid nodule's true nature. Thyroid nodules can be due to a large number of causes, the most common of which is a benign colloid nodule.[Welker et al, 2003]. The main differential diagnosis of benign colloid nodule includes follicular neoplasms (adenoma and carcinoma, of either follicular or Hürthle cell types) and papillary thyroid carcinoma. The current criteria for distinguishing follicular neoplasms from benign colloid nodules have stressed microfollicular architecture, scant colloid and high cellularity relative to colloid content.[Baloch et al 2008, Chan et al, 2003]. These three features are necessarily interdependent, because a microfollicular arrangement necessarily makes the amount of colloid low, relative to the number of follicular cells. Validation of additional diagnostic discriminators between benign colloid nodules and follicular neoplasms would therefore, be useful.

II. Aims And Objectives

The present study was undertaken with the following aims and objectives:-

1. To study morphological features in thyroid aspirates.
2. To study the cytomorphologic attributes useful in distinguishing between neoplastic and non-neoplastic lesions.
3. To identify conditions associated with presence of macrophages.

III. Material And Methods

This was a prospective study on 240 subjects with incidental thyroid swelling attending the surgery and ENT outpatient department (OPD) at our institute. A detailed clinical history and physical examination was

taken in all cases with special reference to features of toxicity. All patients were subjected to Fine Needle Aspiration Cytology (FNAC) in department of Pathology, and their cytomorphology was studied in Giemsa, Papanicolau and Perl (done wherever feasible) stained smears. All cases were studied with specific attention to the occurrence of macrophage..

IV. Results

In this study maximum number of cases belonged to third, fourth & fifth decades accounting for 23.33%, 28.33% & 20% respectively. Overall incidence of thyroid lesions was approximately 10 times more common in females. Out of 240 cases, macrophages were noted in 90 cases. Macrophages containing lesions were also maximum in numbers in 3rd & 4th decade accounting for 26.66% & 35.55% respectively. However no such lesion was seen in 1st & 8th decade of life.

Table 1. shows frequency of various lesion in Thyroid FNAC (Total 240 cases). In this study maximum cases were of colloid goitre 150 cases (i.e. 62.52%) followed by Hashimoto's thyroiditis 65 cases (i.e. 27.08%).

As seen in Table 2, maximum macrophage containing lesions were of colloid goiter (52%). Macrophages were not seen in cases of Follicular neoplasm, Papillary carcinoma, Medullary carcinoma and Anaplastic carcinoma in this study. Fisher exact test was applied to know the significance of macrophages in non-neoplastic thyroid lesions & neoplastic thyroid lesions & it was found statistically significant (p value = 0.047)

As per table 3, it was observed that all the malignant cases had high cellularity (i.e. 100%). It was observed in this study that out of 90 cases (i.e. 37.50%) of Macrophages containing lesion of thyroid 38 cases (i.e. 42.22 %) had moderate cellularity & 48 cases (i.e. 53.33%) had high cellularity. It was observed that in macrophages containing lesions, 87 cases (i.e. 96.66%) had sheets (Monolayered) as a major pattern, 3 cases (3.34%) had dispersed cells as predominant pattern.

As seen in table 4, Out of 65 cases (i.e. 27.08%) cases of Hashimoto's thyroiditis, all 65 cases had lymphocytes (i.e. 100%).

Table 5 shows presence of giant cells in macrophages containing lesions of thyroid. In 78 cases (i.e. 86.67%) of Macrophages containing colloid goiter only 06 cases (i.e. 7.69%) had giant cells. Almost all cases of Macrophages containing Hashimoto's thyroiditis and granulomatous thyroiditis, had giant cells. While giant cells were not found in Macrophages containing follicular epithelial hyperplasia and other thyroid lesions.

All the cases of Granulomatous thyroiditis had plasma cells (i.e. 100%). Plasma cells were absent in all cases follicular epithelial hyperplasia, Follicular neoplasm, Papillary carcinoma, Medullary carcinoma & Anaplastic carcinoma.

Table 7. shows that out of 240 cases, 18 cases (i.e. 7.50%) had nil to scanty colloid, 78 cases (i.e. 32.50%) had moderate amount & 144 cases (i.e. 60%) had abundant of colloid.

The table 8. shows correlation of colloid in Macrophages containing lesions of thyroid.

V. Discussion

The overall prevalence of thyroid disorders came out to be 12.91 cases per thousand persons who attended the S.V.B.P. Hospital in the present study. But according to a survey done by Tiwari et al (1998), prevalence was 10.4 per thousand female and 2.9 per thousand males. In our present study macrophages were reported in 90 cases out of 240 cases. Jaffar et al (2009) observed that 95 cases out of 165 patients showed macrophages.

In this study only 2.5% cases were malignant. Nguyen et al (2005) also observed that 60-85% cases of thyroid swelling are benign. Colloid goiter was most common lesion diagnosed in this study which had also been reported in other series (Kini 1987, Anantha Krishanan, Rao and Narsimhan et al 1989). Similar observation was made by Welker et al (2003) that most common thyroid lesion are benign colloid goiter.

In present study diagnosis of malignancy was not entertained in any of the 90 cases of macrophages containing lesions. Sirpal et al (1996) who also failed to find malignancy in 50 cases of macrophages containing thyroid lesions.

In present study we observed that all high cellularity colloid goiter had macrophages. All the cases of follicular epithelial hyperplasia with high cellularity had macrophages. Thus, it was observed that presence of macrophages indicated towards benign lesion even in the presence of high cellularity (i.e. presence of macrophages indicates towards benign lesions).

Jaffar et al, (2009) also observed that 11 of 64 cases of follicular neoplasm having macrophages maximum had histological feature equivocal between follicular adenoma & colloid goiter.

In this study, sheets of epithelium as a major pattern favoured non neoplastic lesion (i.e. 89.2%) in total thyroid FNAC and nearly same in macrophage containing lesions. More cellular cohesion was observed in benign lesion than compared to malignant. Ravinsky et al (1988) also observed that the preponderant

arrangement in non neoplastic lesion was in flat sheets and clusters of one or two cell thick. Kini et al (1981) also reported that aspirate from non neoplastic nodular goiter tends to have honeycomb pattern of epithelial cells in contrast to neoplastic lesions.

Fisher (2008), thyroid FNA had experienced that any microfollicles encountered in a benign colloid nodule are more commonly lined with flattened, attenuated epithelium compared to a cuboidal or even slightly columnar epithelium in the microfollicles of follicular neoplasm i.e. benign conditions have sheets were as neoplastic have clusters.

The presence of significant nuclear pleomorphism was not helpful in distinguishing between neoplastic lesions and non-neoplastic lesion in the current study. Similar observation was made by Ravinsky et. al (1992) and vadnouc et al (1992). The finding in Kini et al (1981) were some what different, they observed that the presence of tissue fragments with ill defined cell borders and large pleomorphic nuclei suggested malignancy. Gonzalez et al (1992) reported that the presence of significant nuclear pleomorphism was a significant discriminator which favour tumour (47%). The reason for the wide variation in the literature regarding the significance of nuclear pleomorphism is not clear.

In present study large nucleoli were observed only in malignant conditions. The presence of cells with small nucleoli favour benign condition over neoplastic lesion on FNAC. Kini et al (1981) observed that presence of a single cherry red macronucleus was characteristic of Hurthle cell neoplasm & was infrequently seen in non-neoplastic nodules.

In present study it was observed that lymphocytes were present in 58.75% cases of total cases (141 cases out of 240 cases) and 57.88% of macrophage containing lesion (Table 21-22). The maximum cases were of Hashimoto's thyroiditis (65 cases out of 65 cases i.e. 100%). Ravinsky et.al (1998) found lymphoid cell in all 6 Hurthle cell tumour. However Gonzalez et al (1992) could detect more than few lymphocytes in 11% Hurthle cell tumour and 37% of non-neoplastic lesions. Jayaram et al (1989) in their study of cytomorphological features of 54 cases of Graves disease they found that lymphocytes were seen in 41% of cases and multinodular colloid goiter were observe in less than one fourth of the cases.

Presence of abundant colloid favoured the presence of non-neoplastic lesions (60%) cases in total thyroid FNAC and 58.88% in cases with macrophages containing lesions). While presence of abundant colloid exclude the possibility of neoplastic pathology in both total thyroid FNAC and macrophage containing lesions.. Kini et al (1981) commented on presence of scanty colloid in neoplastic lesion, However Gonzalez et al (1992) did not found the amount of colloid to be statistically significant contribution.

In present study 51 cases (i.e. 21.66%) had many macrophages, 38 cases (i.e. 15.84%) had occasional macrophages and 62.50% cases had non-macrophage. Macrophages were absent in all neoplastic condition. Jaffar et al (2009) studied the presence of macrophages to distinguish between a benign colloid nodule and a follicular neoplasm which remains a difficult problem. Published criteria have emphasized what amounts to be a single criteria – the interdependent features of the size of the follicles, the amount of colloid, and the cellularity. Additional criteria have been suggested in other publications, but quantification of the relative value of these criteria is lacking in the literature. Criteria that appear useful for excluding a follicular neoplasm include variation from follicular group to follicular group, in cytologic features. An extensive search revealed that these easily quantifiable features have not been validated. Also, they have not been given recent attention for distinguishing benign colloid nodules from follicular neoplasm. The results of this study illustrate that if PTC and Hurthle cell neoplasms are excluded, the presence of macrophages strongly supports the diagnosis of benign colloid nodule ($P < 0.0001$).

As we know the current criteria for distinguishing follicular neoplasm from benign colloid nodules have stressed microfollicular architecture, scant colloid and high cellularity relative to colloid content [Baloch et al 2008]. These three features are necessarily interdependent, because a microfollicular arrangement necessarily makes the amount of colloid low, relative to the number of follicular cells. Validation of additional diagnostic discriminators between colloid nodules and follicular neoplasm would, therefore, be useful. Presence of macrophages in FNA smears could be an additional evidence in favour of non-neoplastic lesions of thyroid compared to neoplastic lesions.

VI. Conclusions

Thyroid FNAC provided a more rapid, safe & accurate diagnosis of thyroid swelling. The presence of macrophages favoured a diagnosis of non- neoplastic lesion (i.e. 37.50%) over neoplastic (i.e. 02.91%) lesions. The presence of abundant colloid was found to favour the presence of a non-neoplastic lesion (i.e. 97.08 % cases total thyroid FNAC). The presence of significant nuclear pleomorphism, nucleoli, cellularity, marginal vacuoles were not helpful in distinguishing between neoplastic lesions and non-neoplastic lesions with macrophages.

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Table – I: Percentage of Various Lesions in Thyroid FNAC

S.No.	Diagnosis	No. of Patient	Percentage
1.	Colloid goiter	150	62.50
2.	Hashimoto's thyroiditis	65	27.08
3.	Follicular epithelial hyperplasia	15	6.25
4.	Granulomatous thyroiditis	3	1.25
5.	Follicular neoplasm	3	1.25
6.	Papillary carcinoma	2	0.8
7.	Medullary carcinoma	1	0.4
8.	Anaplastic carcinoma	1	0.4
	Total	240	100

Table - II: Percentage of Various macrophages Containing Lesions of Thyroid

S.No.	Diagnosis	Total Cases	No. of macrophages containing lesions	Percentage
1.	Colloid goiter	150	78	52.00
2.	Hashimoto thyroiditis	65	06	09.23
3.	Follicular epithelial hyperplasia	15	03	20.00
4.	Granulomatous thyroiditis	03	03	100
5.	Follicular neoplasm	03	00	00
6.	Papillary carcinoma	02	00	00
7.	Medullary carcinoma	01	00	00
8.	Anaplastic carcinoma	01	00	00
	Total	240	90	37.50

Table - III : Correlation of cellularity in various lesion of thyroid

Diagnosis	No.	%	Cellularity					
			<20 follicular cell (Scanty)		20-100 cell (Moderate)		>100 follicular cell (High)	
			No.	%	No.	%	No.	%
Colloid goiter	150	62.5	05	3.3	107	71.33	38	25.33
Hashimoto's thyroiditis	65	27.0	00	00	09	13.84	56	86.15
Follicular epithelial hyperplasia	15	6.25	00	00	00	00	15	100
Granulomatous thyroiditis	03	1.25	00	00	01	33.34	02	66.67
Follicular neoplasm	03	1.25	00	00	00	00	02	100
Papillary carcinoma	02	0.8	00	00	00	00	01	100
Medullary carcinoma	01	0.4	00	00	00	100	00	00
Anaplastic carcinoma	01	0.4	00	00	01	00	01	100
Total	240	100	05	2.08	118	49.2	117	48.75

Table – IV: Correlation of lymphocytes in various lesions of Thyroid

Diagnosis	No.	%	Present		Absent	
			No.	%	No.	%
Colloid goiter	150	62.5	64	45.31	86	57.33
Hashimoto's thyroiditis	65	27.0	65	100	00	00
Follicular epithelial hyperplasia	15	6.25	09	60.00	06	40
Granulomatous thyroiditis	03	1.25	03	100	00	00
Follicular neoplasm	03	1.25	00	00	03	100
Papillary carcinoma	02	0.83	00	00	02	100
Medullary carcinoma	01	0.4	00	00	01	00
Anaplastic carcinoma	01	0.4	00	00	01	00
Total	240	100	141	58.75	99	41.25

Table – V : Correlation of giant cells in lesions of thyroid containing Macrophages

Diagnosis	No.	%	Giant Cells	
			No.	%
Colloid goiter	78	86.67	06	7.69
Hashimoto's thyroiditis	06	06.66	05	83.33
Follicular epithelial hyperplasia	03	3.33	00	00
Granulomatous thyroiditis	03	03.33	03	100
Total	90	100	14	15.55

Table – VI : Correlation of Plasma Cells in various lesions of thyroid

Diagnosis	No.	%	Present		Absent	
			No.	%	No.	%
Colloid goiter	150	62.5	00	00	150	100
Hashimoto's thyroiditis	65	27.0	33	50.60	32	49.40
Follicular epithelial hyperplasia	15	6.25	00	00	15	100
Granulomatous thyroiditis	03	1.25	03	100	00	00
Follicular neoplasm	03	1.25	00	00	03	100
Papillary carcinoma	02	0.83	00	00	02	100
Medullary carcinoma	01	0.4	00	00	01	100
Anaplastic carcinoma	01	0.4	01	100	00	00
Total	240	100	37	15.40	203	84.60

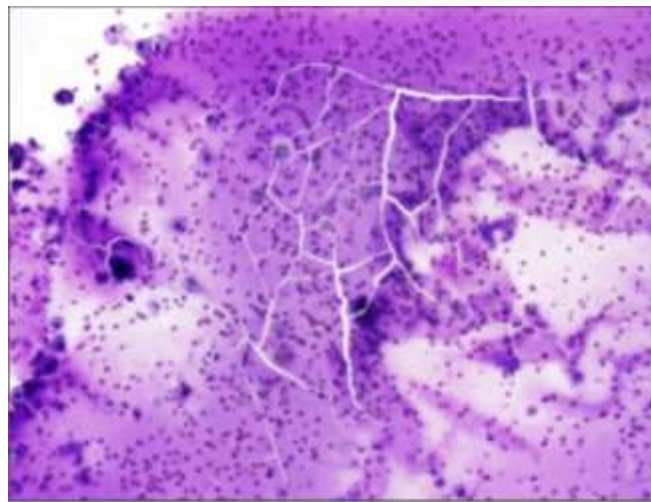
Table – VII : Correlation of Colloid in various lesions of thyroid

Diagnosis	No.	%	None Scanty to		Moderate		Abundant	
			No.	%	No.	%	No.	%
Colloid goiter	150	62.5	00	00	30	20	120	80
Hashimoto's thyroiditis	65	27.0	15	23.07	35	53.84	15	53.33
Follicular epithelial hyperplasia	15	6.25	00	00	07	46.64	08	33.34
Granulomatous thyroiditis	03	1.25	00	00	02	66.67	01	33.33
Follicular neoplasm	03	1.25	3	100	00	00	00	00
Papillary carcinoma	02	0.83	00	00	02	100	00	00
Medullary carcinoma	01	0.4	00	00	01	100	00	00
Anaplastic carcinoma	01	0.4	00	00	01	100	00	00
Total	240	100	18	7.50	78	32.50	144	60

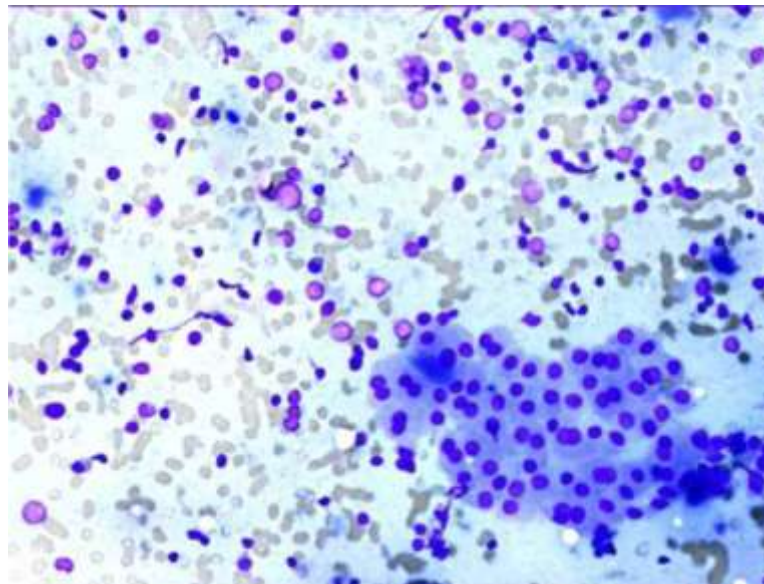
Table – VIII : Correlation of Colloid in various lesions of thyroid containing Macrophages

Diagnosis	No.	%	None to Scanty		Moderate		Abundant	
			No.	%	No.	%	No.	%
Colloid goiter	78	86.67	18	23.07	12	15.38	48	61.53
Hashimoto's thyroiditis	06	6.67	00	00	02	33.33	04	66.67
Follicular epithelial hyperplasia	03	3.33	00	00	02	66.67	01	33.33
Granulomatous thyroiditis	03	3.33	00	00	03	100	00	00
Total	90	100	18	20	19	21.11	53	58.88

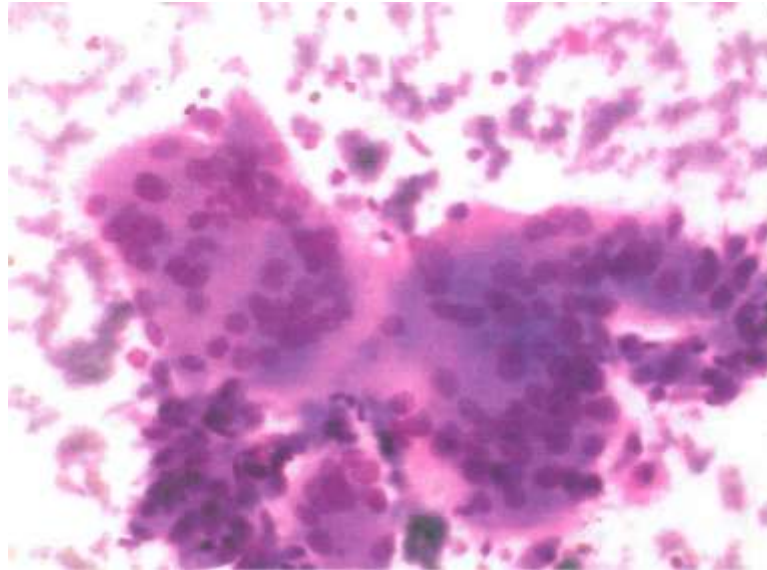
PHOTOGRAPHS



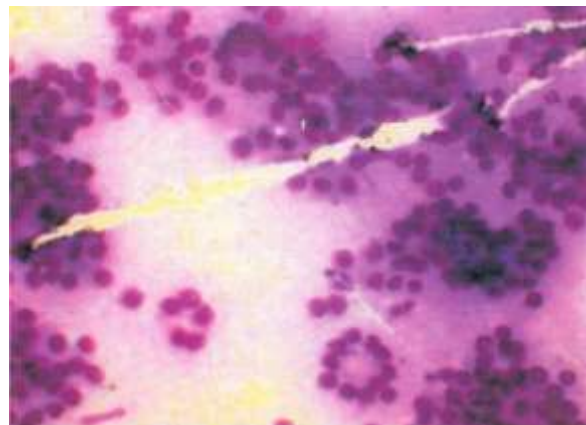
Smear from a case of Colloid Goiter showing colloid with cracked appearance and macrophages (Giemsa x 400)



Smear from a case of Hashimoto's thyroiditis microphotograph showing infiltration by lymphocytes & macrophages (Giemsa x 400)



Smear from a case of Granulomatous thyroiditis microphotograph showing large multinucleated giant cells & macrophages along with thick colloid (Giemsa \times 400)



Smear from a case of follicular neoplasm thyroid photomicrograph showing microfollicles or rosettes and absence of macrophages (Giemsa \times 400)



Smear from a case of papillary carcinoma photomicrograph showing nuclear groove & absence of macrophages (Arrow) (Giemsa \times 400)