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RESEARCH ARTICLE

Marginal vacuoles in thyroid lesions: A cytomorphological Study on Fine needle aspiration.

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Abstract

Introduction: Fine needle aspiration of thyroid nodule is an important, sensitive and widely accepted method for diagnosing the thyroid lesions. The cytological features like cell pattern, cell morphology, intracytoplasmic vacuoles and background are important features in reaching the diagnosis. Marginal vacuoles are magenta coloured irregular cytoplasmic vacuoles seen at the periphery of follicular epithelial cells with unstained central areas on MGG stain. The present study was aimed to find out the significance of marginal vacuoles in FNAC of various thyroid lesions presenting as single thyroid nodule.

Patients and Methods: This study was done on 46 patients presented with solitary thyroid nodule. The various cytomorphological features along with presence of marginal vacuoles were studied.

Results: Significant marginal vacuoles were seen in thyrotoxic goiter patients (100%) followed by patients with hyperplastic nodule (75%). Autoimmune thyroiditis (50%) and Follicular Neoplasm (31.5%) cases also showed presence of grade II and grade-III marginal vacuoles in significant number of cases. None of the colloid goiter case had grade-II + grade-III marginal vacuoles.

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INTRODUCTION

Solitary thyroid nodules are very common and usually benign.¹ Fine needle aspiration (FNAC) of thyroid is first line of diagnostic modality in cases presenting as solitary thyroid nodule.² FNAC provides information which is helpful in management of such patients by identifying and segregating the patients who require surgical intervention.³ The cytomorphological features including cell pattern, cell morphology, intracytoplasmic vacuoles and background are important features in making the diagnosis. Marginal vacuoles/fire flare are described as

magenta coloured irregular cytoplasmic vacuoles 1-7 micron in diameter seen at the periphery of follicular epithelial cells. They are deeply eosinophilic at the periphery with large unstained areas in the center. Because of resemblance to rising fire, the term fire flare has been coined. They are not well appreciated on wet fixed haematoxylin-eosin and PAP stained smears.

Ultrastructurally marginal vacuoles (MV's) are the dilated cisternae of endoplasmic reticulum formed by their hyperactivity and vacuolar content as dilated phagolysosomes.^{4,5} Marginal vacuoles were first diagnosed in the smears of toxic goiter patients.⁶ Marginal vacuoles were thought to be specific for thyrotoxicosis. But many subsequent studies have shown that MV's although are suggestive of thyroid hyperfunction in thyrotoxicosis cases, are non-specific as these are significantly present in other cases like hyperplastic nodule, autoimmune thyroiditis and Follicular Neoplasm. Papillary carcinoma cases don't show significant MV's except in follicular variant cases.⁷ So marginal vacuoles represents the diffusion of the thyroid hormones from the basal aspect of follicular epithelial cells into the inter-follicular capillaries.⁸ The present study was aimed to find out the significance of marginal vacuoles in FNAC of various thyroid lesion.

Patients and Method:

The present study was done on 46 patients presenting with solitary thyroid nodule. The various cytomorphological features along with the presence of marginal vacuoles were noted on MGG stained air dried smears. The marginal vacuoles were noted and graded based upon the criteria given by Nilsson G.et.al.⁹

Grade I: Distinct MV's >2micron in diameter seen in <10% of the cells.

Grade II: MV's seen in 10-50% of the cells.

Grade III: MV's demonstrated >50% of the cells.

Grade II and grade III were taken significant.

Results:

Detailed cytomorphological features were studied on the FNAC smears of 46 cases presenting with solitary thyroid nodule. Special emphasis was given on the presence of marginal vacuoles and its grading.

Female patients outnumbered male patients with F:M ratio of 4.8:1. 38/46 patients were female and 8/46 were males.

The age group varied from 13-80 years with the maximum number of cases in third and fourth decade.

Majority of the cases 30/46 (65%) had neoplastic pathology. The rest 16/46 (35%) were of non-neoplastic etiology.

Follicular Neoplasm constituted 19/46 (41.3%) cases followed by papillary carcinoma cases 11/46 (24%). Among non-neoplastic lesions presenting as solitary thyroid nodule, colloid goiter cases were maximum accounting for 8 out of 46 cases (17.3%) followed by hyperplastic nodule (4/46-8.7%). Thyrotoxic goiter and autoimmune thyroiditis accounted for 2/46 (4.4% each).

Grade-II + Grade-III marginal vacuoles were noted in twelve cases 12/46 (26%). Two cases of (2/2-100%) thyrotoxic goiter included in the study had moderate to abundant MV's followed by hyperplastic nodule 3/4 (75%) and autoimmune thyroiditis-one out of total two cases (50%)(Fig 1, Fig 2, Fig 3). Out of nineteen total follicular neoplasm cases, significant grade-II and grade-III MV's were seen in six cases (31.5%) (Fig 4) These were not observed in other cases of neoplastic etiology-papillary carcinoma case. Though grade-I MV's were noted in one case of papillary carcinoma thyroid. None of the total eight cases of colloid goiter showed moderate to abundant MV's through grade-I MV's were seen in two cases. (Table 1)

Table 1

| Correlation of MVs with cytological diagnosis | | | |
|-----------------------------------------------|-----------------|----------------------------------------|------------|
| Thyroid Lesions | Number of cases | Grade-II + Grade-III Marginal Vacuoles | Percentage |
| Follicular Neoplasm | 19 | 06 | 31.5% |
| Papillary Carcinoma | 11 | 00 | - |
| Colloid goitre | 08 | 00 | - |
| Autoimmune Thyroiditis | 02 | 01 | 50% |
| Hyperplastic Nodule | 04 | 03 | 75% |

| | | | |
|-------------------|----------|----------|------|
| Thyrotoxic goitre | 02 | 02 | 100% |
| | Total=46 | Total=12 | |

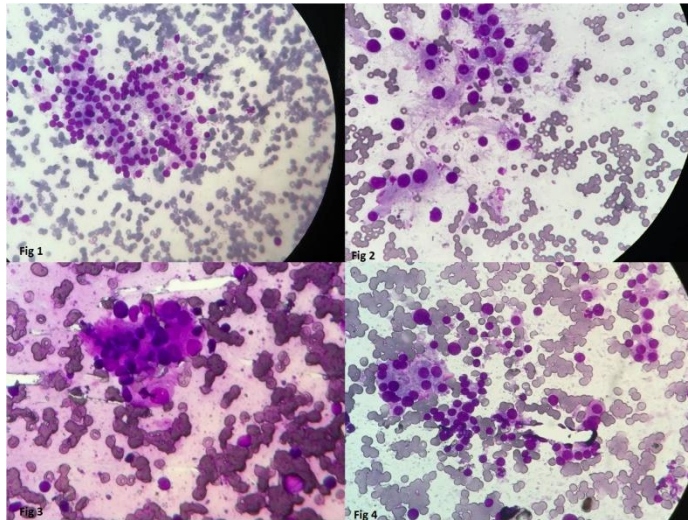


Figure Legends:

1. Fig 1: Marginal vacuoles in cytological smears of thyrotoxic goiter (MGG 100x)
2. Fig 2: Marginal vacuoles in smears of hyperplastic nodule (MGG 100x)
3. Fig 3: Marginal vacuoles in hashimotos thyroiditis (MGG 400x)
4. Fig 4: Marginal vacuoles in follicular neoplasm (MGG 100x)

Discussion:

Detailed cytomorphological study of 46 cases submitted was done. Presence of marginal vacuoles/fire flares seen at the periphery of the follicular epithelial cells was given special attention besides other cytological features. Grading of these MV's was done. Significant MV's presence is considered a specific sign of thyroid hyperfunction in thyrotoxicosis patients but these are also present significantly in other cases like hyperplastic nodule, autoimmune (Hashimoto's) thyroiditis and Follicular neoplasm.^{6,7} Marginal vacuoles represent the diffusion of the thyroid hormones from the basal aspect of follicular epithelial cells into the follicular capillaries.⁸ In the present study significant grade-II and grade-III MV's were noted in 26% of the cases (12/46). In other studies this percentage varied from 14.7% to 22.5%.^{7,10} All the cases of thyrotoxic goiter had moderate to abundant MV's (100%) correlating the findings of study conducted by Das et al.⁷ One out of two (50%) cases of Hashimoto's thyroiditis had significant marginal vacuoles/fire flares. Similar findings were observed in previous studies.^{8,10}

MV's were revealed in three out of four (75%) hyperplastic nodules, while in the previous study by Das et al it was seen 2.6% of hyperplastic nodules.⁷ None of the colloid goiter case presenting as solitary thyroid nodule had grade-II + grade-III MV's. Though grade-I MV's were seen in two cases. Similar findings were observed in a study in the past by Gupta A.¹⁰ A low of 5.2% was noted in the another study conducted.⁷

MV's were limited to neoplasm with follicular component only as six out of nineteen cases 6/19-31.5% of follicular neoplasm had prominent marginal vacuoles. This percentage varied from 26.7 to 57% in other studies.^{7,10,11} Significant marginal vacuoles were not observed in all eleven cases of papillary carcinoma though grade-I marginal vacuoles noted in one of the case. This observation correlates with the results of previous studies.^{10,12,13} No case of follicular variant of papillary carcinoma was encountered during the study though studies observed significant MV's presence in such cases.^{12,13}

In the above study of 46% cases of solitary thyroid nodule, it was concluded that marginal vacuoles/fireflares are not only seen in the patients of thyrotoxic goiter. Other conditions like hyperplastic nodule, autoimmune thyroiditis and follicular neoplasm also reveals their presence. This signifies that MV's are marker of follicular differentiation. MV's were infrequent in papillary carcinoma thyroid cases further emphasizing their relation with follicular differentiation. Further studies are recommended to corroborate the above conclusions because of limited sampling

size of the present study. These studies should include more of the papillary carcinoma, follicular variant of papillary carcinoma and other thyroid malignancy cases.

Bibliography:

1. Cooper DS, Doherty GM, Haugen BR, Hauger BR, Kloos RT, Lee SL, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2009;19:1167-1214.
2. Hamberger B, Gharib H, Melton Lj. Fine-needle aspiration biopsy of thyroid nodules: impact on thyroid practice and cost of care. *Am J Med*. 1982;73:381-4.
3. Jo Vy, Stelow EB, Dustin SM, Hanley KZ. Malignancy Risk for Fine-Needle Aspiration of Thyroid Lesions According to The Bethesda System for Reporting Thyroid Cytopathology. *Am J ClinPathol*. 2010;134:450-6.
4. Ramzy S, editor. *Clinical cytopathology and aspiration biopsy*. New York: Appelton and Lange;1990.p.273-93.
5. Davidson HG. Diagnostic problem in thyroid FNA. *DiagnCytopathol*. 1997;17:422-701.
6. Soderstrom N, Nilsson G. Cytologic diagnosis of thyrotoxicosis. *Acta Med Scand*. 1972;205:263-5.
7. Das DK, Jain S, Tripathi RP, Parkash S, Khan IU, Rajwanshi, et al. Marginal vacuoles in thyroid aspiration *ActaCytol*. 1998;42:1121-8.
8. Das DK. Marginal vacuoles (fire-flare appearances) in fine needle aspiration smears of thyroid lesions. Does it represent diffusing out of thyroid hormones at the base of follicular cells. *DiagnCytopathol*. 2006;34:277-83.
9. Nilsson G. Marginal Vacuoles in FNAB smears of toxic goiters. *ActaPatholMicrobiol Scand*. 1972;80:289-93.
10. Gupta A, Sharma S, Kalhan S, Gupta A, Dudani S, Devra A. The Diagnostic Role of the Marginal Vacuoles in FNAC of Solitary Thyroid Nodule. *J ClinDiagn Res*. Feb 2013;7(2):284-6.
11. Agarwal SK, Jayaram G, Prakash R, Pant CS. Fine needle aspiration cytologic diagnosis of the solitary cold thyroid nodule, comparison with ultrasonography, radionucleotide perfusion study and xeroradiography. *ActaCytol*. 1989;33:41-7.
12. Gallagher J, Oertel YC, Oertel JE. Follicular variant of papillary carcinoma of thyroid. *Diagn. CytoPathol*. 1997;16:207-13.
13. Olson MT, Boonyaarunnate T, Atlinboga AA, Ali SZ. 'Suspicious for Papillary Carcinoma' before and after The Bethesda System for Reporting Thyroid Cytopathology: Impact of Standardized Terminology. *ActaCytologica*. 2014;58:15-22.