



Pitfalls in the Diagnosis of Oncocytic Thyroid Lesions-A Retrospective Study

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ABSTRACT

Thyroid oncocytic follicular cells are found in a variety of non-neoplastic & neoplastic conditions. Evaluation of oncocytic thyroid lesions is challenging and laden with diagnostic pitfalls. The purpose of this study was to evaluate the cytological and histopathological findings in oncocytic thyroid lesions. FNAC was performed on 460 cases of thyroid swellings and correlated with histopathological examination. In cytology, 148 cases were found to be associated with oncocytic changes of which 110(74.32%) were non-neoplastic and 38(25.68%) neoplastic. On follow up with histopathology, 10 cases among 110 cytologically non-neoplastic cases, were proved neoplastic. False negative result was observed in 9.1% of cases. This study concludes that false negative results may be obtained in cytological diagnosis of oncocytic thyroid lesions. This may be due to obscuring of small foci of neoplasm on FNAC. Therefore, histopathological examination with thorough sectioning and adequate tissue submission are of utmost importance to correctly diagnose oncocytic thyroid lesions.

KEYWORDS : Thyroid, Oncocytic, Hurthle cell, Diagnostic pitfalls

INTRODUCTION

Oncocytes, also known as Hurthle cells, Oxyphilic cells, or Askanazy cells are derived from thyroid follicular cells.^[1] Microscopically they are characterized by abundant eosinophilic, granular cytoplasm, distinct cell borders, and large hyperchromatic nuclei with prominent nucleoli.^{[1][2][3][4]} They are formed due to aberrant accumulation of mitochondria.^[3] Oncocytic follicular cells are found in a variety of non-neoplastic and neoplastic pathologic conditions like Hashimoto's thyroiditis, long standing Graves' disease, multinodular goitre, Hurthle cell variant of papillary carcinoma, Hurthle cell variant of follicular neoplasm etc.^[5] Non-neoplastic thyroid lesion characterised by oncocytic metaplasia and/or hyperplasia may present in cytology as population of monotonous cells, leading to a misdiagnosis of an oncocytic neoplasm.^{[6][7][8]} Cytopathologists have diagnostic challenge to differentiate between oncocytic metaplasia or hyperplasia in a benign nodule versus oncocytic neoplasm.^{[9][10]} The present study has been undertaken to concentrate on the pitfalls in the diagnosis of thyroid lesions with oncocytic changes.

MATERIALS AND METHODS:

Materials

1. Syringe with needle(10 ml syringe)
2. Glass slides
3. Leishman- Giemsa's stain and H & E stain
4. Knife for tissue cutting
5. Formalin for fixation
6. Alcohol, Xylene & wax for tissue processing
7. Paraffin wax for blocking
8. Microtome for section cutting
9. Light microscope

Method

A 2 years retrospective study of cytological and histopathological examination of thyroid was carried out on 460 cases.

All the patients from outpatient department during this study period with different clinical symptoms such as thyroid swelling, pain in the thyroid etc, were included in the study after informed consent. FNAC

samples were collected by 10 ml syringe, stained by Leishman- Giemsa's stain after air dry. Cytopathological evaluation was performed in each cases. Cases with oncocytic changes in cytology were considered for histopathological examination. Final histopathology reports (considered gold standard used for the diagnosis of the lesions) were based solely on the findings of formalin fixed paraffin embedded tissue and H & E staining.

RESULT & ANALYSIS

Out of 460 cases studied, 148 cases were associated with oncocytic changes in FNAC.

Out of 148 cases 110 (74.32%) cases were diagnosed as non-neoplastic and 38(25.68%) as neoplastic.

Table 1: RESULTS ON CYTOLOGY

| Non-neoplastic conditions | Neoplastic conditions |
|--|--|
| Adenomatoid goitre with oncocytic changes-40(27.03%) | Papillary carcinoma with Oncocytic changes-22(14.86%) |
| Cystic nodule-24(16.22%) | Follicular neoplasm with Oncocytic changes-12(8.11%) |
| Hashimoto's thyroiditis-19(12.84%) | Hurthle cell neoplasm-2(1.35%) |
| Lymphocytic thyroiditis-15 (10.13%) | Medullary carcinoma of thyroid with oncocytic changes-1(0.68%) |
| Graves disease with oncocytic changes-12(8.11%) | Non-Hodgkin lymphoma-1(0.68%) |
| Total -110 cases | Total-38 |

All the cases which were reported neoplastic (38 cases) in FNAC underwent surgery.

Among the FNAC reported non-neoplastic lesions 38 out of 40 cases of adenomatoid goitre and all 24 cystic lesions underwent surgery.

2 cases reported as Hashimoto's thyroiditis in FNAC underwent sur-

gery as they were not responding to the medical treatment and radiologically there was multinodularity.

Total cases that underwent surgery were 102 (64 non-neoplastic cases and 38 neoplastic cases)

Table 2: RESULTS OF HISTOPATHOLOGICAL EXAMINATION

| Non-neoplastic conditions | Neoplastic conditions |
|--|---|
| Adenomatoid goitre with oncocytic changes- 35(34.31%) | Papillary carcinoma with Oncocytic changes-30(29.41%) |
| Benign cystic lesion-18(17.65%) (Colloid goitre with cystic change-11 ; Adenomatoid goitre with cystic change-7) | Follicular adenoma with Oncocytic changes-13(12.75%) |
| Hashimoto's thyroiditis-1(0.98%) | Hurthle cell adenoma-2(1.96%) |
| | Lymphoma (non- Hodgkin)-2(1.96%) |
| | Medullary carcinoma with oncocytic changes-1(0.98%) |
| Total-54 | Total-48 |

Figure 1.

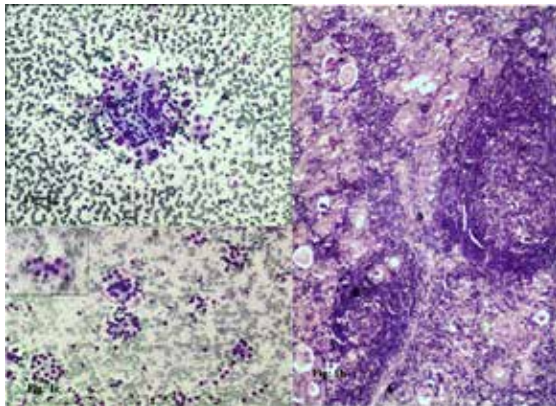


Figure 1: 1a. Cytological features of Hashimoto's thyroiditis (MGG, 40X) ; 1b. Histopathology of Hashimoto's thyroiditis (H&E, 40X) ; 1c. Cytology of Grave's disease with oncocytic changes

Figure 2:

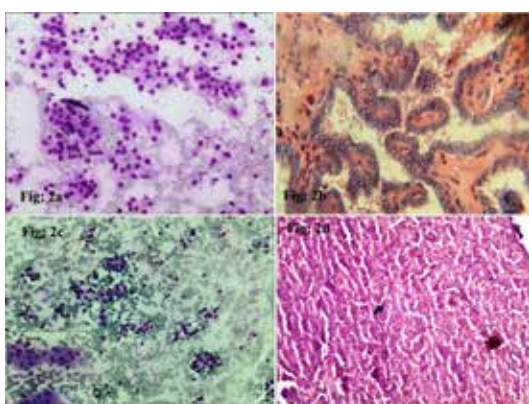


Figure 2: 2a. Cytological features of papillary carcinoma of thyroid with intranuclear inclusions (MGG, 40X) ; 2b. Histopathology of papillary carcinoma thyroid (H&E, 40X) ; 2c. Cytological features of follicular neoplasm of thyroid with oncocytic changes (MGG, 10X) ; 2d. Histopathology of follicular adenoma with oncocytic changes (H&E, 40X)

Figure 3:

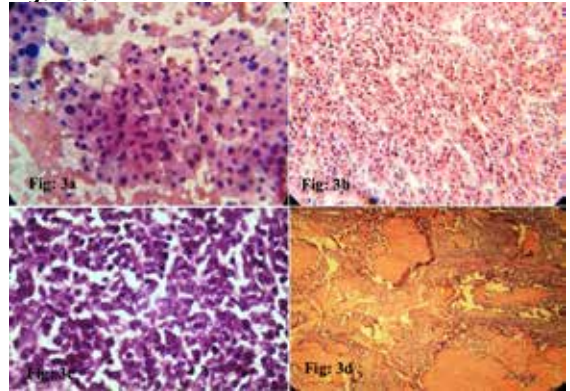


Figure 3: 3a. Cytological features of Hurthle cell neoplasm (PAP, 40X) ; 3b. Histopathology of Hurthle cell adenoma (H&E, 40X) ; 3c. Histopathology of Non-hodgkin lymphoma of thyroid (H&E, 40X) ; 3d. Histopathology of medullary carcinoma of thyroid (H&E, 10X)

Table 3: CORRELATION BETWEEN CYTOLOGY AND HISTOPATHOLOGICAL EXAMINATION (102 CASES)

| Cytological diagnosis | Histological concordance | Histological discordance |
|--|---|--|
| Hashimoto's thyroiditis-2 | Hashimoto's thyroiditis -1 | 1 case (confirmed as non-Hodgkin lymphoma) |
| Adenomatoid goitre with oncocytic changes-38 | Adenomatoid goitre with oncocytic changes-35 | 3 cases (1 case confirmed as Follicular adenoma & 2 cases confirmed as Papillary carcinoma of thyroid) |
| Cystic lesions-24 | Cystic lesion-18 | 6 cases (confirmed as papillary carcinoma thyroid) |
| Neoplastic lesions-38 | All neoplastic lesions confirmed histopathologically-38 cases | Nil |

DISCUSSION

Hurthle cells can be encountered in FNAC specimens of both non-neoplastic and neoplastic lesions of the thyroid. [6][9][11] It is well known that the oncocytic cells are commonly encountered in thyroid affected by chronic lymphocytic thyroiditis and Hashimoto's thyroiditis. [5] Thus, it is likely that FNAC of these lesions will pose problems in differentiating between a oncocytic hyperplastic nodule versus Hurthle cell neoplasms. [9] In lymphocytic and Hashimoto's thyroiditis the oncocytes are large, atypical, and pleomorphic, with lymphocytic infiltration whereas Hurthle cell tumors usually show monotonous cells and absence of lymphocytes. [3][4][5][9] The presence of nuclear atypia in a thyroid tumor is not necessarily associated with malignancy. [2][3][4] In fact, atypical hyperchromatic nuclei in a thyroid lesion are more often a reflection of hyperstimulation rather than being indicative of malignant potential. [2] Atypical Hurthle cells with scanty or no lymphoid population ('Burnt out Hashimoto thyroiditis'), can be easily mistaken for neoplasia. [10][11] In early stages of Hashimoto's thyroiditis needling of proliferating Hurthle cell nodules may lead to a smear dominated by Hurthle cells, with nuclear pleomorphism which may mimic malignancy. [3] Also, the follicular epithelium adjacent to the lymphoid aggregate can show atypical nuclear changes that can simulate Papillary carcinoma of thyroid. [3] Blood mixed aspirate and extensively necrotic aspirate may also obscure the proper view. [4]

As is widely known, thyroid FNAC cannot distinguish between benign and malignant oncocytic thyroid neoplasia, that is Hurthle cell adenoma or carcinoma. [12][13][14] This distinction can only be accomplished by histopathologic examination to demonstrate capsular invasion and/or vascular invasion. [12][18][19] Histologic presentation of chronic lymphocytic thyroiditis can range from focal involvement of the gland to diffuse. [9][12]

The most widely practiced cytologic criteria to render a diagnosis of oncocytic follicular neoplasm in FNAC includes cellular smear showing a monotonous population of oncocytes (75% or more). Other criteria include prominent nucleoli, transgressing vessels and minimal background colloid^{[15][16][17][18]}

There can be various pitfalls in proper cytological diagnosis of lesions containing oncocytes. False negative results in cytology can occur in cystic lesions harboring a malignancy most commonly papillary carcinoma^{[2][3][4]}. In our study 6 cases reported as cystic lesion of thyroid on FNAC were confirmed histologically as papillary carcinoma. False negative results in cytology are also common in cases where a dominant non-neoplastic lesion overlies or obscures a small carcinoma^[3] as was seen in 3 of our cases. High-grade non-Hodgkin lymphoma is easily identified in FNAC but low-grade and MALT lymphomas are often difficult to distinguish from reactive lymphoid population seen in thyroiditis.^{[3][4]}One case in our study reported cytologically as Hashimoto's thyroiditis was proved to be non-Hodgkin lymphoma on histology.

The malignant tumors seen in our study included papillary thyroid carcinoma (30 cases), medullary carcinoma (1 case) and Non-Hodgkin lymphoma (1 case). Similar results have been reported by Pu *et al*, Giorgadze *et al*, Roh *et al* and Canberk *et al*.^{[6][7][9][20]} These results from various studies point to the fact that oncocytic cytoplasm can also be seen in cytology of papillary carcinoma and other malignant tumors of the thyroid and thus should be interpreted with utmost care.^{[5][9][10]}

Our study concludes that evaluation of oncocytic thyroid lesions is challenging and laden with diagnostic pitfalls. False negative results may be obtained in cytological diagnosis of oncocytic thyroid lesions. Presence of oncocytic cells in FNAC smears especially in cystic lesions should be reported very cautiously as they often obscure the actual diagnosis. Therefore, histopathological examination with thorough sectioning and adequate tissue submission are of utmost importance to correctly diagnose oncocytic thyroid lesions.

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