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Hurthle Cell Lesion of the Thyroid – A Case Report and Review of Literature

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Abstract

Hurthle cell tumors constitute rare tumors comprising < 5% of all the thyroid neoplasms.
We present a 43 yr female who presented with swelling in the neck which on FNAC was diagnosed as Atypia of Undetermined Significance (Bethesda III) not ruling out Hurthle cell neoplasm. To differentiate between Hurthle cell adenoma and carcinoma a pathologist have to rely on the presence or absence of capsular and vascular invasion of the adjacent thyroid parenchyma. These findings are easy to detect on widely invasive disease and somewhat subjective for the diagnosis of minimally invasive or borderline invasive disease. Preoperative and intraoperative differentiation too is difficult with no specific imaging characteristics. Final histopathological evaluation is the corner stone in the differentiation of these lesions.

Keywords: NIL

Introduction

Hurthle cell tumors constitute rare tumors comprising < 5% of all the thyroid neoplasms.[1] Hurthle cell tumors have also been named as Askanazy cell tumors [2] , Oncocytomas, and Mitochondriomas or Oxyphil tumors. Hurthle cell is properly used only to describe cells of thyroid follicular origin.[3 , 4]

The Hurthle cell is characterized cytologically as a large cell with abundant eosinophilic, granular cytoplasm and a large hyperchromatic nucleus with a prominent nucleolus.[5] Many nonneoplastic conditions of the thyroid show Hurthle cells and are not specific for any disease.[6,7]

Thyroid nodules containing Hurthle cells in cytologic evaluation may be seen in a wide variety of thyroid lesions, ranging from nonneoplastic (most commonly multinodular goiter, nodular hyperplasia and lymphocytic thyroiditis but also in Grave's disease or in patients treated with radiotherapy or systemic chemotherapy) and in all types of benign or malignant thyroid neoplasms (including follicular adenoma, follicular carcinoma, papillary thyroid carcinoma, and even medullary thyroid carcinoma).[8]

Hurthle cell lesions have been a diagnostic conundrum in pathology since they were recognised. To differentiate between Hurthle cell adenoma and carcinoma pathologist have to rely on the presence or absence of capsular and/or vascular invasion of the adjacent thyroid parenchyma. These findings are easy to detect on widely invasive disease and somewhat subjective for the diagnosis of minimally invasive or borderline invasive disease.[9] Preoperative and intraoperative differentiation too is difficult [9] with no specific imaging characteristics.[10]

Case Report

43-year female presented with right sided neck swelling of eight months duration. Patient had no

associated pain or pressure symptoms. She had no hoarseness of voice and she was euthyroid at the time of presentation. Patient had no family history of neck swelling. Patient had no history of loss of appetite. Alsoshe had no bowel and bladder involvement. Ultrasound of the lesion on OPD basis revealed that the right lobe of thyroid was Bulky with smooth margins measuring 3.5 x 3.5 x2.5 cm. Few small cystic areas were seen with in it. Thin peripheral hypoechoic halo was seen around it. Left lobe of the thyroid measured 1.1 x 1.1cm with small hypoechoic nodule measuring 2.7 x 2.2mm. Isthmus was normal in shape & size and no obvious focal lesion seen. Mild peripheral vascularity was seen on color doppler likely follicular adenoma (Thyroid Imaging Reporting and Data System, TIRADS 3[11]).

Initially she presented to another hospital where Fine Needle Aspiration Cytology(FNAC) was done which revealed follicular epithelial cells arranged in monolayered sheets and small clumps showing bland nuclei in the background of thin colloid. Suggestive of Bethesda II - Benign follicular nodule (Colloid Goitre). After 5 months she underwent another FNAC at another institute which was reported as FNAC from midline thyroid swelling which yielded in Haemorrhagic cellular aspirate smears which showed Hurthle cells in monolayered sheets, trabeculae and a few micro-follicles. These cells exhibit mild anisokaryosis with prominent nucleoli and granular cytoplasm . Focal lymphocytic impingement seen in a few clusters. Occasional ? fire flares were seen. Background showed scant colloid and a few cystic macrophages. No intranuclear inclusions / grooves were seen in smears examined. FNAC was Suggestive of Atypia of Undetermined Significance (Bethesda III) with diagnostic possibility of Hyperplastic Hurthle cell nodule in the background of lymphocytic thyroiditis. However, Hurthle cell neoplasm cannot be excluded.

After this, she underwent Right Hemithyroidectomy at Onco-surgery unit at our hospital .

The Gross of the specimen described thyroidectomy specimen labelled as right thyroid nodule with isthmus measuring 6.5 x 3.5 x 2.5 cm. Outer surface well encapsulated. On cut, a greyish brown firm to hard nodule noted along with small cystic cavities. Nodule was measuring 3.2 x 2.0 x 2.0 cm. The isthmus appears unremarkable. Microscopic examination showed variable sized colloid filled follicles separated by sheets of Hurthle cells having eosinophilic cytoplasm and round uniform nuclei. At an occasional place mitotic activity was noted. The tumour was richly vascular however, no definite tumour emboli noted. No capsular invasion was seen. Right sided thyroid nodule with Isthmus for HPE showed features suggestive of Hurthle cell adenoma.(Figure 1) Immunohistochemistry (IHC) for thyroglobulin and CK14 were advised. But were not done due to financial reasons.

Patient's one year follow up was uneventful. Her ultrasonography eleven months after surgery of the remaining left lobe of thyroid showed normal size , outline and echotexture. No mass lesion /cyst / calcification seen.

Discussion

The Hurthle Cell (HC), a misnomer, is used to describe follicular-derived epithelial cells with oncocytic cytology. An epithelial cell with an acidophilic cytoplasm is called as Oncocytic change, containing a vast number of mitochondria. Apart from the thyroid gland these cells are found throughout the body, including kidney, salivary glands, and para-thyroids.[12]

More specifically, the HC is a large (10–15 micron, Figure 2), polygonal cell with distinct cell borders, abundant eosinophilic finely granular cytoplasm, a large hyperchromatic round to oval nucleus, and a prominent nucleolus. There are numerous mitochondria in the cytoplasm contributing to the cell's size and staining characteristics. Although the actual amount of cytoplasm in HCs may vary, it is generally sufficient to produce a low nuclear–cytoplasm ratio.[12,13] Ultrastructurally, when viewed via electron microscopy, the mitochondria often appear to fill the cytoplasm, to the near exclusion of other organelles. HCs contain up to 5,000 mitochondria, whereas a typical eosinophil may contain approximately thirty. The mitochondria often show filamentous inclusions, as well as dense core granules. The accumulation of mitochondria has been reported to be a result of alterations in the mitochondrial DNA encoding for mitochondrial enzymes, leading to proliferation through stimulation of transcription factors encoded by the nucleus .[13, 14]

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Thyroid nodules are exceedingly common, occurring in 5%– 8% of the clinical population, increasing to 15%-67% when high-frequency ultrasound is employed. There is 50% prevalence in autopsy series.[15, 16] Nodules may be discovered on routine physical exam, when they begin to cause symptoms of compression, or increasingly, as incidental findings on imaging studies performed for other reasons.[12] In our case also, patient presented with nodular swelling in the neck region without any secondary symptoms. Patient was euthyroid at the time of presentation. FNAC has become an invaluable tool and the gold standard in the evaluation of thyroid nodules.[12]

In our case FNAC was done twice at two different institutions 5 months apart. Second FNAC was found to be Hurthle Cell Predominant (HCP).

FNAs consisting exclusively or almost exclusively of HCs, pose a diagnostic challenge for any pathologist, as it is often difficult to distinguish Neoplastic from Non Neoplastic nodules on basis of cytology. HCP FNAs often fall into one of two indeterminate TBSRTC (The Bethesda System for Reporting Thyroid Cytopathology) categories: Atypia / follicular lesion of undetermined significance (AUS/FLUS) and Follicular neoplasm / suspicious for follicular neoplasm (FN/SFN).[17,18]

In our case too second FNAC was labelled as Atypia of Undetermined significance with diagnostic possibility of Hyperplastic Hurthle cell nodule in the background of lymphocytic thyroiditis. However, Hurthle cell neoplasm cannot be excluded.

Follow-up studies, however, have shown that risks of malignancy (ROM) associated with HCP are appreciably lower than those of non-HCP, which could potentially lead to increased number of unnecessary surgeries.[19] Molecular studies have been utilized in recent years with intended purpose of increasing the predictive power of indeterminate cytologies, but HCP indeterminate lesions have not been extensively studied.[20] Reported negative predictive values (NPV) and positive predictive values (PPV) are 94–96% and 40–46%, respectively.[21]

The major strength of molecular testing is identifying nodules that have a high likelihood of being benign, but a major limitation is their low specificity which results in significant false-positive rates. In addition, reflex molecular testing is not performed at many institutions, and an indeterminate cytologic diagnosis may either lead to a repeat FNA with triage for molecular testing or lobectomy following a repeat indeterminate diagnosis.[21]

In our case also following the FNAC, patient was subjected to thyroid lobectomy along with part of isthmus. On Histopathology the lesion was labelled as Hurthle cell adenoma as vascular and capsular infiltration was not seen. Nuclear atypia, which is the hallmark of the Hurthle cell, multinucleation, and mitotic activity were not considered useful for predicting prognosis [22] as in our case also biopsy showed mitotic activity at occasional places. Patient was from lower socioeconomic back ground hence immunohistochemistry for hurtle cells was not possible. However, there remained a group of Hurthle cell lesions that were not invasive and were considered to be Hurthle cell adenomas, yet they gave rise to lymph node metastases.[22]

Conclusion

Thyroid nodules containing Hurthle cells are comprises of wide range of pathologic entities. The Cytologic evaluation in such cases is difficult because of predominance of Hurthle cells seen in thyroid FNACs of all of these pathologic entities. Molecular techniques have proven to be ineffective in distinguishing Hurthle Cell neoplasm from benign hurthle cell lesions. Final histopathological evaluation, cytomorphological features, vascular and capsular invasion guides the clinicians in diagnosing these patients.

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Figure 1: Left side showing sheets of Hurthle cells with fibrous capsule and thyroid follicles filled with colloid on the right side. (H&E 10X)

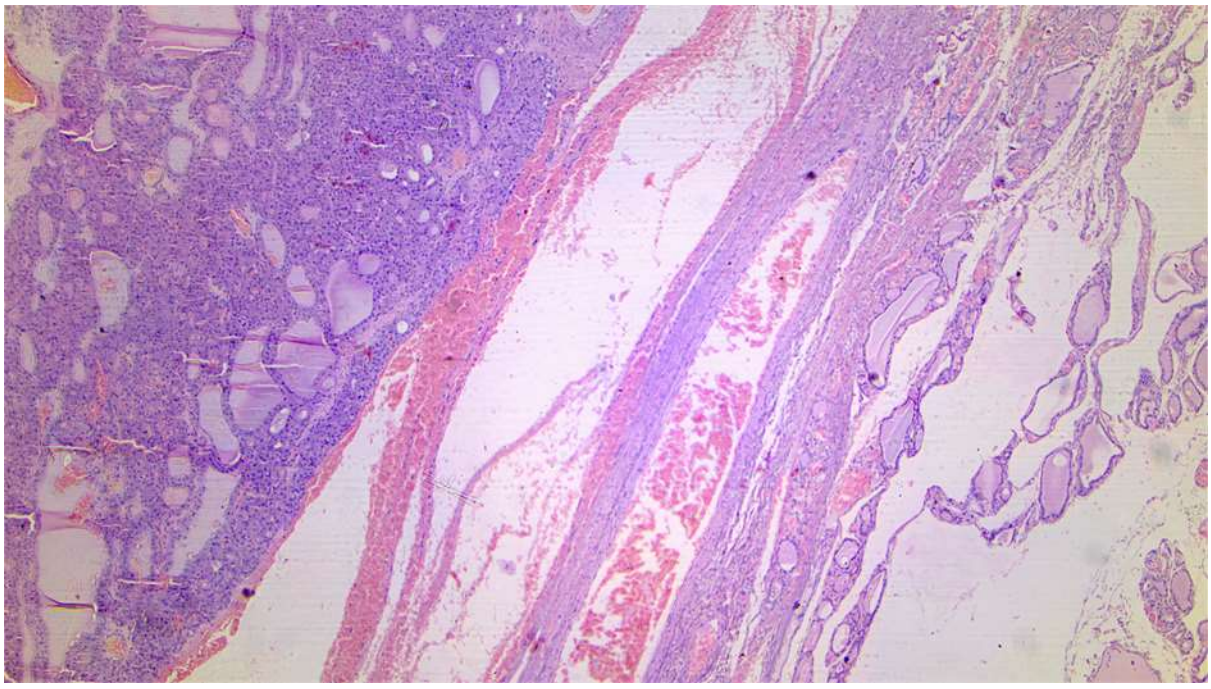
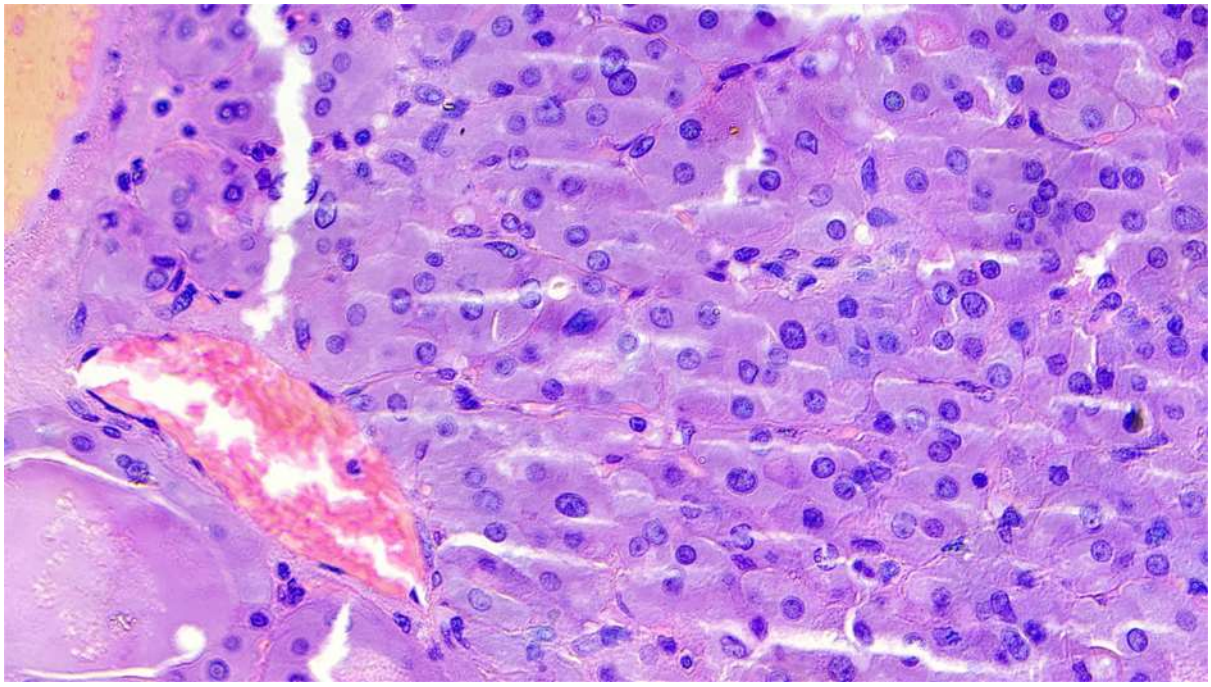


Figure 2: Hurthle cells in sheets (H&E 40X)



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