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CASE REPORT
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ONCOCYTIC VARIANT OF THYROID

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ABSTRACT

INTRODUCTION

Hürthle cell carcinoma (HCC) is a rare subtype of thyroid cancer, accounting for approximately 3–4% of all thyroid malignancies. It is considered more aggressive than other oncocytic thyroid neoplasms. Due to its rarity, its biological behavior and pathological features remain incompletely understood. HCC predominantly affects women and is most commonly diagnosed in individuals in their fifth and sixth decades of life.

METHODS

This study reviews the clinical, cytological, and pathological characteristics of HCC, with emphasis on diagnostic challenges, imaging findings, surgical management, and cellular morphology. Data were synthesized from existing literature and cytological observations, including ultrasonographic and histo-pathological features.

RESULTS

Preoperative diagnosis of HCC is challenging. Indicators of malignancy include male sex, older age, tumor size greater than 4 cm, solid nodules with irregular margins, and psammoma calcifications on ultrasonography. Surgical management varies: thyroid lobectomy is adequate for small, unifocal, intrathyroidal tumors or cases with clinically evident cervical lymph-node metastasis, whereas tumors larger than 4 cm require total thyroidectomy. The benefit of radioactive iodine therapy remains controversial. Cytologically, Hürthle cells are large with abundant eosinophilic, granular cytoplasm due to mitochondrial accumulation, and possess large hyperchromatic nuclei with prominent nucleoli. Distinguishing true Hürthle cells from oncocytic metaplasia is difficult; ultrastructural examination shows that true Hürthle cells have densely packed mitochondria and loss of cell polarity, unlike metaplastic cells.

DISCUSSION

HCC presents significant diagnostic and therapeutic challenges due to overlapping features with benign oncocytic lesions and lack of definitive biomarkers. Accurate differentiation between neoplastic and metaplastic oncocytic cells relies on ultrastructural characteristics rather than immunohistochemical quantification. Further research is required to clarify its pathogenesis and optimize management strategies.

KEYWORDS

Hürthle cell carcinoma, Oncocytic thyroid lesions, Mitochondrial pathology

INTRODUCTION

Approximately 3-4 percent of all thyroid cancer is the hurthle cell carcinoma (HCC), which is said to be more aggressive than oncocytic thyroid cancer. The biological functioning and the

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pathological characteristics of this disease have not been well understood due to its relative rarity. HCC is more prevalent in women and in the majority of cases, it manifests itself in 50s and 60s. Preoperative diagnosis is not that simple; but the signs of malignancy include those of male sex, advanced age, size of the tumour to be greater than 4 cm, solid nodule with irregular margins, and the presence of psammoma calcifications on the ultrasonographic image. In small, unifocal, intrathyroidal tumours, or in those cases where there are clinical apparent cervical lymph-node metastases, thyroid lobectomy is usually adequate. Nevertheless, tumours that are bigger than 4 cm are advised to be removed completely in the form of total thyroidectomy. The advantage of radioactive iodine therapy on HCC is still debatable. [2,3]

On cytology of Hurthle cells, they appear large cells with an abundance of eosinophilic and finely granulocytic cytoplasm with large and hyperchromatic denominated nucleus with a prominent nucleolus. This granular cytoplasmic build up is a property of mitochondrial build up, which also accounts for the swollen appearance of the cytoplasm. Because mitochondrial proteins have a strong affinity for eosin, Hürthle cells are often referred to as oxyphilic cells.

Thyroid lesions composed of cells with these classic oncocytic features are considered Hürthle cell lesions; however, not all oncocytic cells of thyroid are necessarily Hürthle cells. In some thyroid diseases, including autoimmune thyroiditis, nodular goitre, aging factors and after irradiation, focally, cells with a less intensive, or incomplete, eosinophilic, granular cytoplasm may be found depending upon the disease. These metaplastic changes are non-neoplastic oncocytic variants. [2,3]

Even though by immunohistochemical staining using anti-mitochondrial markers, it is possible to determine the regions of oncocytic metaplasia, no quantitative markers can reliably be used to differentiate between oncocytic metaplasia and actual Hurthle cells. On ultrastructural examination, true Hürthle cells exhibit cytoplasm densely packed with mitochondria and demonstrate complete loss of cell polarity, whereas metaplastic oncocytic cells retain partial polarity and contain fewer mitochondria.

CASE PRESENTATIONS

CASE 1 :

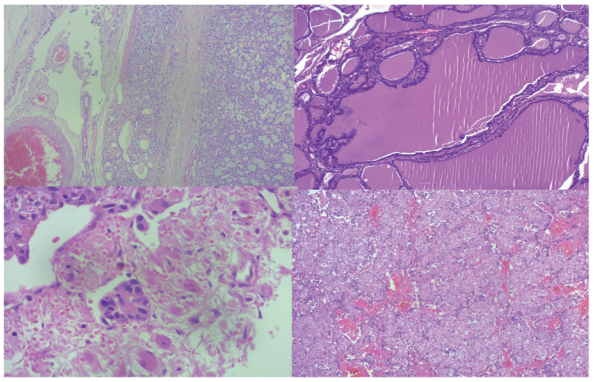
A 28-year-old male from Mangalore presented with a 20-day history of a midline neck swelling. The swelling had an insidious onset, was non-progressive, and was not associated with any aggravating or relieving factors. Comprehensive evaluation—including general physical examination, local examination, laboratory investigations, radiological imaging, and cytological analysis—suggested a Hurthle cell neoplasm. Following the diagnosis, the patient was admitted and underwent a total thyroidectomy.

CASE 2:

A 26 year old female hailing from Karwar, complaints of midline neck swelling since 3.5 years, started insidiously, gradually progressed to its current size, no aggravating or relieving factors. Patient also gives history of weight loss and hair loss since the past 3 years and had also undergone myomectomy 8 months back for an anterior uterine wall fibroid diagnosed on ultrasound. Her ultrasound neck revealed a right lobe measuring 13mmx14mmx41mm classified as TIRADS IV and left lobe measuring 17mmx15mmx37mm category of TIRADS III lesion. Appropriate investigations were done and patient managed with total thyroidectomy.

CASE 3:

A 36-year-old male from Mangalore presented with a nodular swelling on the right side of the midline neck, present for 1.5 months. The swelling had an insidious onset, was non-progressive, and was not associated with any aggravating or relieving factors. Relevant laboratory and radiological investigations were performed, and the patient subsequently underwent a right hemithyroidectomy.



DISCUSSION

HCC is an infrequent thyroid malignancy that is only 1 percent in nature that is characterized by the presence of either Hurthle cell or oxyphilic cell which is a derivation of follicular epithelium of the thyroid. Hurthle cell neoplasm is common in women despite the fact that the malignant form is more intense in men. The benign ones are benign histopathologically, where there is no invading vascular and capsular phenomenon and malignant where they occur. Oncocytic lesions that could be categorized with a definitive ruling in cases of fine needle aspiration is hardly achievable as there are enormous numbers of circumstances wherein oncocytic change may be noted like non-neoplastic and neoplastic lesions of the thyroid. The non-neoplastic ones are the lymphocytic thyroiditis (Hashimoto thyroiditis), and oncocytic metaplasia. Oncocytic carcinoma (H4 -cell carcinoma), oncocytic adenoma (H4 -cell adenoma) papillary thyroid carcinoma (PTC) and medullary thyroid carcinoma are examples of neoplastic Tumors. Oncocytic metaplasia is a normal reaction of body organs on various stresses by the cells. Oncocytic metaplasia is seen in benign adenomatous nodule, Hashimoto thyroiditis, PTC, medullary and poorly differentiated thyroid carcinoma. Oncocytic follicular cell-derived thyroid carcinomas occur in a great number, i.e. oncocytic PTC, oncocytic encapsulated follicular subtype of PTC, oncocytic poorly differentiated carcinoma and oncocytic medullary thyroid carcinoma. Immuno-stains are not available that can differentiate OCA and oncocytic adenoma.

Cytomorphologic evaluation on fine-needle aspiration (FNA) can assist in distinguishing non neoplastic thyroid lesions from oncocytic thyroid neoplasms. The presence of chronic inflammatory changes is indicative of lymphocytic thyroiditis, whereas abundant colloid with admixed bland follicular cells is characteristic of hyperplastic (nodular) goiter.

Oncocytic neoplasms (ON), similar to their non-oncocytic counterparts, typically demonstrate high cellularity, scant or absent colloid, and a non-macrofollicular architectural pattern. This architectural profile includes a predominantly microfollicular arrangement, the presence of dis-cohesive single cells, and three-dimensional clusters. Transgressing blood vessels (TBV)—identified as capillaries traversing loosely cohesive groups of oncocytic cells—may also be seen in association with ON; however, their diagnostic utility has been debated, likely due to variability in the cytologic criteria used to define TBV.

Also, two types of cytologic dysplasia are described in oncocytic carcinoma as small cell dysplasia, oncocytic cells characterized by high nuclear-to-cytoplasmic ratio and cytoplasmic diameters below a factor of two relative to the nuclear size, and large cell dysplasia, in which nuclear enlargement more than a twofold change in size has been observed, due to the presence of large nucleoli and irregular nuclear contours.

Oncocytic thyroid carcinoma can be categorised as minimally invasive, encapsulated vascular invasion and widely invasive". Minimal invasion is only used to describe tumours which showed invasion on the tumour capsule. Tumours with vascular invasion which is encapsulated is further stratified according to the invasion extent: in limited vascular invasion, there are less than four vessels, whereas in extensive vascular invasion, there are four or more vessels.[4]

Tumour necrosis, hyper-mitotic activity (more than three mitoses per mm 2), abnormal mitoses, and areas of small cell change with an evidence of cytoplasmic loss are histopathologic features that are associated with aggressive behaviour. The tumours with such characteristics tend to be resistant to the radioactive treatment with iodine. Mutations frequently observed in thyroid cancers such as RAS, TSHR, EIF1AX, TP53, PTEN, BRAF, PAX8 PPAR -g and MEN1 are uncommon in oncocytic thyroid carcinoma.[1]

CONCLUSION

Hürthle cells represent enlarged follicular epithelial cells characterized by abundant, finely granular, eosinophilic cytoplasm. Malignant transformation is suggested by features such as marked cellular pleomorphism, increased cellularity, and evidence of invasion into adjacent tissues. Oncocytic (Hürthle cell) carcinoma is considered a variant of follicular thyroid carcinoma (FTC), and therefore follows the same risk-stratification principles, with diagnostic lobectomy typically recommended. Fine-needle aspiration (FNA) and intraoperative frozen-section evaluation generally cannot reliably distinguish benign from malignant oncocytic neoplasms; however, Tumors larger than 4 cm carry a higher likelihood of malignancy.

Patients with oncocytic thyroid carcinoma (OTC) who did not undergo surgical management have been shown to experience significantly reduced survival compared with those who received surgery, underscoring the central role of thyroidectomy in treatment. OTC exhibits relatively poor radioactive iodine (RAI) avidity compared with other differentiated thyroid cancers (DTCs). Even when metastatic lesions demonstrate apparent RAI uptake, clinical responses to therapeutic RAI are typically limited. Despite the scarcity of robust data, current management strategies for OTC commonly include total thyroidectomy followed by RAI therapy when appropriate.

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