Hurthle cell tumor of the thyroid: A case series
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Abstract

The purpose of this paper is to report a series of cases of Hurthle Cell Carcinoma of the thyroid. A review of the literature addressing the incidence, management, recurrence and survival rates is discussed. These tumors may be considered as variants of follicular thyroid neoplasms. They can be potentially lethal and are considered as the most aggressive well-differentiated neoplasm of the thyroid. Treatment should consist of thyroidectomy with post-surgical management.

Introduction

Hurthle cells, also known as oncocyes or oxyphilis, are large, polygonal, intra-follicular cells found in the thyroid gland. [1,2] Hurthle cell tumors are an aggressive variant of thyroid follicular neoplasms that have a >75% composition of Hurthle cells. [3] They present as well-differentiated, encapsulated benign or malignant tumors. The main differentiating factors between adenoma and carcinoma are capsular or vascular invasion determine, while others like tumor size, male sex and older age are also associated with increased chances of malignancy. [4,5,6] Patients develop HCC anywhere from 20-85 years of age, but mean age of occurrence is between the 5th and 6th decades. Risk factors for developing Hurthle cell carcinoma include history of radiation, iodide deficiency and a family history. [7]

Pre-operative diagnosis with Fine Needle Aspiration (FNA) is able to identify Hurthle cell neoplasms, but cytology is unable to differentiate benign from malignant. [7,8] Surgical excision and histology must be done to confirm suspicion of malignancy. A multidisciplinary treatment approach with partial lobectomy or total thyroidectomy is currently used in treating the carcinoma. We present a series of cases of HCC of uncertain malignant potential in a 30-year-old female, recurrent HCC in a 51-year-old female, and HCC in a 00-year-old female. We will discuss the diagnostic and treatment plan for this relatively rare neoplasm with a brief review of literature.

Case Series

Case # 1
A 51 year old female presented to the emergency room with a history of increasing anterior neck swelling at the site of a previous thyroid incision. She denied dysphagia, odynophagia or respiratory distress. She had surgery for a thyroid mass approximately two years prior. Fine needle aspiration was non-diagnostic. Computerized axial tomography revealed a solid mass with necrosis, cervical lymphadenopathy, and a thyroid mass. Thyroid function tests including T3, T4, and TSH were normal. Initial biopsy revealed a recurrent Hurthle cell carcinoma. A wide local excision of the lesion with involved neck skin and strap muscles in conjunction with a modified neck dissection. The patient has done well with no evidence of recurrent disease over the past six years.

Case # 2
A 30-year-old female with a history of thyroid goiter was evaluated. She complained of compressive symptoms including coughing, occasional respiratory distress and sensation of choking. Head and neck exam showed mobile vocal cords on indirect laryngoscopy and a palpable thyroid mass in the neck. She had a fine needle aspiration, and ultrasound that showed tracheal compression. A CAT scan prior to surgery showed tracheal compression by the thyroid mass. She was then scheduled for a subtotal thyroidectomy. A total thyroidectomy was performed with preservation of the parathyroid and recurrent laryngeal nerve. Complete removal of the gland was done because the thyroid mass, measuring 5 x 6 cm, extended into both lobes.

Pathologic evaluation illustrated a thyroid measuring 6.8 x 6.5 x 4.3 cm with a vast majority representing a cystic nodule. The large thyroid mass showed histologic evidence of an encapsulated Hurthle cell tumor of uncertain malignant potential.

Case # 3
A 70-year-old female presented with a history of thyroid mass. She complained of palpitations and feeling the thyroid mass when swallowing. She also complained of occasionally struggling with oropharyngeal secretions. She denied compressive symptoms and heat or cold intolerance. A fine needle aspiration showed atypical follicular cells and she was scheduled for thyroidectomy. Histologic evidence of an encapsulated Hurthle cell tumor of uncertain malignant potential.

Figure 1: Initial thyroid mass

Figure 2: Pathology of initial thyroid mass – low power

Figure 3: Histopathology of Hurthle cell carcinoma from radical neck specimen

Figure 4: Pathology of Hurthle Cell Tumors Adapted from Maxim et al [4]

Discussion

Hurthle cells were first described by Askanazy in 1898. [2] Refered to also as oxyphilic and oncocytic, they are large polygonal cells with abundant, finely granular, eosinophilic cytoplasm. They present with large cytoplasm-nuclear ratios and numerous mitochondria that can number up to 5000. The large number of mitochondria are thought to slowly accumulate due to mutations in mtDNA that cause an imbalance in mitochondrial proliferation and destruction. [2,4] These cells are present not only in several thyroidal conditions such as Hashimoto thyroiditis, nodular goiters and Graves’ disease, most thyroid neoplasms have a Hurthle cell variant. [8] HCC is a more aggressive variant that represents 3-7% of differentiated thyroid cancers. It has low 131I avidity, greater likelihood of lymph node or distant metastasis at 33% (compared to 10-22% for other differentiated cancers) and increased chances of late recurrence. [1,10]

Hurthle cell neoplasms are grossly solitary lesions with partial or complete capsules with a characteristic brown color due to abundant mitochondrial cytochromes. Hemorrhage and necrosis may be present, especially following FNA. [3] On microscopic exam, the tumors show a greater than 75% population of Hurthle cells with several patterns of possible growth, including follicular, solid, trabecular and pseudopapillary. There may also be calcified deposits found in the colloid of the tumor. [3,4] Prognostic factors like large tumor size, older age and male gender can predict poor tumor behaviour, but differentiating between benign and malignant lesions depends on capsular/vascular invasion. [3,10]

Initial evaluation of a thyroid nodule is done with ultrasound. Work-up also includes thyroid function tests (TSH, T4, Free T4), antiperoxidase antibodies and antithyroglobulin antibodies. Pre-operative FNA and cytology of nodules can identify Hurthle cell neoplasms, but it is not effective in differentiating benign from malignant. Histology of a surgically resected sample is essential for definitive diagnosis of suspected malignancy. [2] Radiological imaging with Computed Tomography (CT) scan and magnetic resonance imaging (MRI) have value in evaluating the tumor structure, location, identification and metastatic disease. Octreotide scintigraphy, 99Tc- sestamibi scan and novel 18F-FDG PET, are sensitive in detecting metastatic HCC. [2]

Thyroid lobectomy is essential following a diagnosis of Hurthle cell tumor. Repeat surgery with complete thyroidectomy following lobectomy might be necessary in cases where histological evaluation confirms malignancy. [9] Initial total thyroidectomy is preferred when there is prior history of head or neck irradiation, large tumors (>4cm), severe atypia seen on biopsy or to avoid future surgeries. [2,9]

Post-surgical management of HCC is with radiodine therapy when active 131I uptake is seen on scanning. This has limited scope, however, because HCC has low avidity for 131I and only 5-10% of malignant tumors take up 131I. [9,11] Suppressive therapy of thyroid stimulating hormone using levothyroxine (T4) and external beam radiation therapy (EBRT) have also been employed in post-surgical management. Fode et al. studied the use of EBRT in a small cohort of patients and concluded that if may be useful as an adjuvant to conventional therapy especially in preventing tumor recurrence and providing palliative care in advanced metastatic or unresectable disease. [11] Chemotherapy is a last resort in management and has been shown to have significant morbidity with limited improvement. [12] Post-procedure monitoring with thyroglobulin tracks residual thyroid activity. Long-term 20-year survival rates have been reported to be 65%, significantly decreased from 87% for classic papillary thyroid cancer and 81% with follicular thyroid cancer. [10] Local recurrence may occur in up to 30% of patients with HCC. [12]

Conclusions

Hurthle cell carcinoma is an unusual and rare type of thyroid cancer. Predictors for the outcome of HCCs are the extent of invasion, extrathyroidal extension, tumor size and invasiveness. Metastasis can occur in up to one third of cases and long-term 20-year survival is significantly lower compared to papillary and follicular thyroid carcinomas. Thyroidectomy is the cornerstone of management in HCC. Initial management is lobectomy and further surgery is determined by diagnosis of malignancy by histology. Adjunct therapy is limited but may still be prudent to consider for locally advanced cancers.

References

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