Hurthle Cell Carcinoma

63

Elgin Özkan and Çiğdem Soydal

Abstract

Hurthle cell carcinoma (HCC) is a histopathologic variant of follicular thyroid carcinoma. HCC is more aggressive than follicular tumors. It causes more nodal metastases than follicular cancer, and it has the highest metastatic frequency among the differentiated thyroid cancers. In this report, we describe a 50-year-old female patient who presented with an enlarging palpable mass in the left thyroid lobe for 3 years. Neck ultrasonography (USG) demonstrated a 4 × 2.5 × 4 cm heterogeneous isoechoic nodule in the left thyroid lobe. There was no pathologic lymph node on USG. The patient underwent a left hemithyroidectomy, and histopathological examination of the surgical specimen revealed a Hurthle cell carcinoma with a maximum diameter of 4.2 cm. Radioiodine ablation treatment (RAT) with 3700 MBq (100 mCi) iodine-131 (^{131}I) was applied approximately 2 months after the operation. Six months after the RAT, diagnostic whole-body scintigraphy with 185 MBq (5 mCi) ^{131}I was performed. The serum-stimulated Tg level and the ^{131}I whole-body scintigraphy were entirely normal. There has been no evidence of disease, on the 8-year follow-up period. Despite of good response to therapy, due to high risk of HCC, the patient is still under close follow-up.

63.1 Case Presentation

In this report, we describe a 50-year-old female patient who presented with an enlarging palpable mass in the left thyroid lobe for 3 years. A 4.5 × 4.5 cm mobile mass was palpated in the left thyroid lobe upon physical examination. Neck ultrasonography (USG) demonstrated a 4 × 2.5 × 4 cm heterogeneous isoechoic nodule in the left thyroid lobe. Additionally, a 0.7 cm isoechoic nodule with a hypoechoic outer halo was observed in the right thyroid lobe. There was no pathologic lymph node on USG. Serum thyroid function tests were compatible with euthyroidism. Thyroid fine needle aspiration biopsy (FNAB) revealed a Hurthle cell neoplasm. The patient underwent a left hemithyroidectomy, and histopathological examination of the surgical specimen revealed a Hurthle cell carcinoma (HCC) in the left thyroid lobe with a maximum diameter of 4.2 cm. Additionally, capsular and vascular invasion was detected during the

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histopathological examination. Following lobectomy, a completion thyroidectomy was performed. Histopathological analysis revealed no tumor in the right thyroid lobe. Radioiodine ablation treatment (RAT) with 3700 MBq (100 mCi) iodine-131 (^{131}I) was applied approximately 2 months after the operation. The serum thyroid-stimulating hormone (TSH) and thyroglobulin (Tg) levels were measured as 32 IU/ml and <0.5 ng/ml, respectively. Radioiodine uptake limited to the thyroid bed was observed on postablative whole-body scintigraphy. Six months after RAT, a diagnostic whole-body scintigraphy with 185 MBq (5 mCi) ^{131}I was performed to evaluate the success of the ablation. The serum-stimulated Tg level and the ^{131}I whole-body scintigraphy were normal. There has been no evidence of disease over an 8-year follow-up period.

63.2 Evaluation and Diagnosis

Hurthle cell carcinoma of the thyroid gland accounts for approximately 2–10% of all differentiated thyroid cancers [1, 2]. HCC, which is also known as oncocytic or oxyphilic carcinoma, is classified as a variant of follicular thyroid carcinoma [3]. HCC contains at least 75% Hurthle cells, or oxyphilic cells, which have abundant granular cytoplasm because of an extreme number of mitochondria and a large nucleus [4]. Hurthle cells are also observed in nonneoplastic conditions of the thyroid gland, such as thyroiditis and nodular and toxic goiters. The cytological features of Hurthle cell neoplasms are hypercellularity of the Hurthle cells (usually >75%), few or no lymphocytes, and insufficient or absent colloid. A benign neoplasm cannot be distinguished from a malignant neoplasm based on cytological analysis of FNAB samples. The definitive differentiation of Hurthle cell carcinoma from Hurthle cell adenoma is based on histopathological analysis and the presence of capsular and/or vascular invasion [5]. The incidence of malignancy in Hurthle cell neoplasms varies between 13% and 67%. Hurthle cell tumors are more aggressive than follicular tumors. HCC has the potential to cause more nodal metastases than follicular cancer, although not as many as papillary cancer. Additionally, HCC has the highest metastatic frequency among the differentiated thyroid cancers [6–8].

A palpable mass in the thyroid is the most common clinical sign of Hurthle cell neoplasms. In certain cases, pressure symptoms, such as dysphagia, dyspnea, and coughing, can accompany HCC. If the mass rapidly enlarges, pain and other compressive symptoms may be more obvious. In our case, the patient had a growing palpable mass for the last 3 years, and she did not have local pressure symptoms.

Hurthle cell carcinoma can be multifocal and bilateral, and regional lymph node metastasis may occasionally also be felt in the neck. Careful collection of the patient's history and an attentive neck examination can provide clues regarding Hurthle cell carcinomas. In particular, the presence of a family history of thyroid cancer and the history of head and neck external beam irradiation should be questioned. Vocal cord paralysis may also indicate a carcinoma. The presence of pathological bone fractures and physical findings of metastases are essential for the diagnosis of a carcinoma.

In most cases, thyroid function test results are concordant with euthyroidism. Accordingly, in our case, the thyroid function tests were normal. However, in rare instances, thyrotoxicosis due to functional metastases may be observed.

Neck USG is a vital imaging modality for the evaluation of the nature of thyroid nodules and the neck lymph nodes. Computed tomography (CT) and magnetic resonance imaging (MRI) also provide more detailed information regarding the tumor and adjacent neck structures.

According to the 2015 ATA guideline, diagnostic FNAB is recommended, especially in the presence of a nodule ≥1 cm in the greatest dimension with a sonographic pattern of high or intermediate suspicion and in the presence of a nodule ≥1.5 cm in the greatest dimension with a sonographic pattern of low suspicion [9]. However, FNAB cannot differentiate an adenoma from a carcinoma in Hurthle cell lesions. Definitive differentiation is based on histopathological analysis and the presence of capsular and/or vascular invasion.

63.3 Management

The surgical approach is the primary treatment modality for patients with Hurthle cell carcinomas. According to the 2015 ATA guideline, all patients with differentiated thyroid carcinomas should undergo total or near-total thyroidectomy [9]. The ATA recommendation 35 states that, in the presence of a thyroid tumor >1 and <4 cm without extrathyroidal extension and without the clinical manifestations of any lymph node metastases, a unilateral procedure can be selected. In our case, a histopathological examination of the surgical specimen revealed a Hurthle cell carcinoma, i.e., a high-risk tumor, with a diameter of 4.2 cm in the left thyroid lobe. Additionally, the patient was older than 45 years. Completion thyroidectomy was applied to enable RAI therapy. No tumor was detected in the surgical specimen. Approximately 2 months after the last operation, a treatment dose of ^{131}I (3700 MBq) was administered, and a total body scan was obtained 6 days later. Radioiodine uptake limited to the thyroid bed was observed on the postablative whole-body scintigraphy. Postoperative ^{131}I or ^{123}I scanning can also be performed 4–6 weeks after surgery. In our department, we do not use routine postoperative iodine scintigraphy because of stunning effect of ^{131}I. Low-dose (37–111 MBq) ^{131}I or alternative isotopes, such as ^{123}I, can be used to avoid or prevent this effect.

Because the ^{131}I avidity of Hurthle cell carcinomas is lower than those of other well-differentiated thyroid carcinomas, the efficacy of radioiodine treatment is limited. Therefore, therapy for recurrent or metastatic Hurthle cell carcinoma may be difficult. However, radioiodine treatment is used as a first-choice treatment for most patients with HCC after thyroidectomy and in the treatment of recurrent and metastatic HCC patients. In a recent study involving 1909 cases, the authors reported that radioactive iodine therapy improved the survival of patients with HCC [10]. According to the findings of this study, the 5- and 10-year survival rates of patients who received ^{131}I and those who did not were statistically significant (88.9% vs. 83.1% and 74.4% vs. 65%, respectively, $p < 0.001$).

63.4 Follow-Up and Outcome

Although HCC is a histopathologic variant of follicular carcinoma, it exhibits differences in biological behavior compared to the conventional type of follicular carcinoma. Because of the ability of HCC to metastasize to the lymph nodes and possibly higher rates of recurrence and tumor-related mortality, close follow-up is most critical for HCC patients. Specifically, neck USG can identify small-volume metastatic cervical lymph nodes. In cases of suspected lymph nodes, serum Tg measurements in the washout of fine needle aspirates and/or cytological evaluations may be applied. The surgical approach is the first choice for the management of recurrent HCC. However, in cases of metastatic disease, due to low avidity for ^{131}I, other methods, such as tyrosine kinase inhibitors, can be selected for multiple progressive metastatic diseases [11]. Chemotherapy is generally ineffective for metastatic thyroid carcinomas. The 2015 ATA guideline indicates a weak recommendation for the use of cytotoxic chemotherapy. Cytotoxic chemotherapy may provide a selective benefit to patients who do not respond to kinase inhibitors and, perhaps, to patients with poorly differentiated thyroid cancers [12]. External radiotherapy may be applicable to symptomatic metastatic disease and iodine-negative tumors and can also be used to control recurrent tumors [13].

Although HCC is more aggressive than follicular carcinoma, our patient's clinical course was excellent. The good clinical outcome may be associated with the absence of local recurrence and/or metastatic disease in the follow-up.

63.5 Future

Hurthle cell carcinomas have low avidity for ^{131}I. Non-radioiodine avid metastatic thyroid carcinomas create a particularly challenging patient group. Surgical resection can be performed in cases with a limited number of metastases. In addition to tyrosine kinase inhibitors, new targeted treatments should be developed. Regarding radionuclides, Lu-177 DOTA-peptide treatment has

been reported to be an alternative option for somatostatin receptor-expressing tumors. However, large prospective studies with large numbers of patients should be designed to reveal the effectiveness of Lu-177 DOTA-peptide treatment.

What Can We Learn from This Case?

- Hurthle—oncocytic or oxyphilic—cell carcinoma is a histopathologic variant of follicular thyroid carcinoma.
- It contains hypercellularity of Hurthle cells (usually >75%).
- Definitive diagnosis is based on histopathological analysis, with a presence of capsular and/or vascular invasion.
- Hurthle cell carcinoma is more aggressive than follicular tumors. It causes more nodal metastases than follicular cancer, and it has the highest metastatic frequency among the differentiated thyroid cancers.
- Hurthle cell carcinoma has lower ^{131}I avidity than the other well-differentiated thyroid carcinomas.

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