CLINICAL VIGNETTE

Metastatic Hurthle Cell Carcinoma: A Survivor's Journey

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Clinical History

A 70-year-old Caucasian male was found to have an enlarged left lobe of the thyroid more than twenty years ago. FNA revealed hemosiderin-laden macrophages, suggestive of degenerating colloid nodule and he underwent left thyroid lobectomy. Pathology demonstrated Hurthle cell carcinoma and he underwent total thyroidectomy with pathology again consistent with Hurthle cell carcinoma. After surgery he received radioactive iodine 100 microcuries over three years.

Two years after his last dose of radioactive iodine, two new left neck lymph nodes were noted. FNA confirmed Hurthle cell carcinoma. He underwent annual lymph node dissections and radioactive iodine for three years. His thyroglobulin levels remained elevated and chest CT scan six years after neck dissection showed a small right middle lobe lung nodule with scattered subpleural nodules. Repeat neck CT showed metastatic thyroid cancer. Patient underwent a redo left modified radical neck dissection with left cervical lymph node biopsy. Pathology revealed metastatic Hurthle cell carcinoma in the lymph nodes.

He continued to have elevated thyroglobulin levels and a new left submandibular mass was found two years later. He underwent another redo left modified radical neck dissection. A repeat chest PET CT then showed the right lung lesion to be unchanged and no intervention was recommended.

His condition remained stable for four years, when repeat PET CT showed interval development of solid bilateral pulmonary nodules with increased FDG uptake suspicious for pulmonary metastasis. His thyroid surgical bed did not suggest local recurrence. The lung nodules were biopsied and returned negative for malignancy. Patient remained asymptomatic.

One year later, repeat chest CT showed slight increase in the size of the multiple bilateral pulmonary nodules without any recurrent disease in the neck. His only complaint was fatigue. Right lower lobe CT directed lung biopsy showed metastatic Hurthle cell carcinoma and he underwent thermal ablation of two right middle lobe metastasis. After ablation he became dyspneic after traveling out of state to a high-altitude area. He was admitted with moderate multiloculated pneumothoraces and underwent chest tube placement and was prescribed levofloxacin which caused rash and joint pains. Dermatology ruled out drug induced vasculitis and another ablation therapy was completed. His breathing eventually improved.

Due to the onset of the COVID-19 pandemic, follow-up visits were limited to video visits. He underwent four additional lung ablations. He also developed abdominal zoster which responded to valacyclovir and gabapentin.

His most recent PET CT six months ago revealed an avid para-esophageal lymph node and subpleural nodules. Lymph node biopsy was consistent with metastatic lymph node cancer. He opted for ablation of the lymph node with follow up CT showing slight increase in size of the right para-esophageal lymph node, which was attributed to inflammation and which will be monitored with PET CT in two months.

He feels clinically well and continues to be followed by endocrinology and urology.

Discussion

Well-differentiated thyroid carcinomas are among the most common endocrine malignancies and also offer the most favorable prognosis. They include papillary, follicular, and medullary thyroid cancers. Pathologically, there is a debate as to whether Hurthle cell thyroid cancer is a variant of follicular thyroid cancer or a variant unto itself. It accounts for approximately 5% of well differentiated thyroid cancers and it's a relatively rare malignancy.[1] Because of this, clinical data and experiences with this cancer are lacking in the literature. Some researchers have reported a very favorable clinical course for this tumor, whereas others have considered Hurthle cell carcinoma to be a relatively aggressive thyroid gland malignancy.[2] There is no clear etiology for Hurthle cell cancers although radiation to the head, neck, and chest and family history are potentially known risks for thyroid cancers in general.

The surveillance, epidemiology, and end results (SEER) database for January 1 1973 to December 31 1998 was examined. The mean age of diagnosis was 55.9 years with a female preponderance of almost 68%. 2.7% of the patients had positive nodes at the time of diagnosis. Five- and ten-year survival for Hurthle cell carcinoma cohort was 85.1% and 71.1% respectively. Mean survival time was 109 months (95% CI, 105-114 months).[1]

There is some controversy in the clinical management of this cancer due to the difficulties and the interpretation of the pathology of Hurthle cell neoplasms. There have been varying

morphologic criteria to distinguish benign from malignant Hurthle cell tumors.[2,3] Molecular studies are increasingly being used to distinguish benign from malignant tumors to help avoid aggressive surgeries. These include identifying BRAF and RAS mutations, mRNA genomic sequencing classified testing and microRNA gene expression modalities.[4-6] These tumors may behave like follicular thyroid cancers and may be managed accordingly. There is consensus that they should be treated aggressively.

Hurthle cell carcinoma is almost always treated initially with surgery. Total thyroidectomy preferably done by a thyroid cancer surgeon is highly recommended. Thyroid hormone replacement therapy to keep the TSH in the low range can lower recurrence and mortality; Hurthle cell cancer responds to TSH. Radioactive iodine can be used for iodine-avid tumors.[7] However, only up to 53% of metastatic tumors are iodine avid.[8] Radiation therapy has been used to treat metastatic symptoms of pain and nausea, and to control and prevent recurrent tumors.[9] Clinical trials may be sought if other treatment modalities have been ineffective.

Conclusion

Our patient illustrates a greater than 30-year battle with his thyroid cancer. Hurthle cell cancer, a well-differentiated thyroid cancer, can be responsive to conventional approaches of aggressive surgery, with serial chemical and radiologic follow-up, with or without radioactive iodine therapy. Distant metastases do not preclude radiation therapy as evidenced by our patient's response to thermal ablation of his lung metastases. He has had good long-term follow-up and coordination with his treatment team. This may be a model for other patents with metastatic Hurthle cell carcinoma.

REFERENCES

1. **Bhattacharyya N**. Survival and prognosis in Hürthle cell carcinoma of the thyroid gland. *Arch Otolaryngol Head Neck Surg*. 2003 Feb;129(2):207-10. doi: 10.1001/archotol.129.2.207. PMID: 12578450.
2. **Nishiyama RH**. Overview of surgical pathology of the thyroid gland. *World J Surg*. 2000 Aug;24(8):898-906. doi: 10.1007/s002680010157. PMID: 10865033.
3. **Carcangiu ML, Bianchi S, Savino D, Voynick IM, Rosai J**. Follicular Hurthle cell tumors of the thyroid gland. *Cancer*. 1991 Nov 1;68(9):1944-53. doi: 10.1002/1097-0142(19911101)68:9<1944::aid-cncr2820680917>3.0.co;2-i. PMID: 1913544.
4. **Yip L, Wharry LI, Armstrong MJ, Silbermann A, McCoy KL, Stang MT, Ohori NP, LeBeau SO, Coyne C, Nikiforova MN, Bauman JE, Johnson JT, Tublin ME, Hodak SP, Nikiforov YE, Carty SE**. A clinical algorithm for fine-needle aspiration molecular testing effectively guides the appropriate extent of initial thyroidectomy. *Ann Surg*. 2014 Jul;260(1):163-8. doi: 10.1097/SLA.0000000000000215. PMID: 24901361.
5. **Xing M, Haugen BR, Schlumberger M**. Progress in molecular-based management of differentiated thyroid cancer. *Lancet*. 2013 Mar 23;381(9871):1058-69. doi: 10.1016/S0140-6736(13)60109-9. Epub 2013 Mar 22. PMID: 23668556; PMCID: PMC3931461.
6. **Hodak SP, Rosenthal DS; American Thyroid Association Clinical Affairs Committee**. Information for clinicians: commercially available molecular diagnosis testing in the evaluation of thyroid nodule fine-needle aspiration specimens. *Thyroid*. 2013 Feb;23(2):131-4. doi: 10.1089/thy.2012.0320. Epub 2012 Nov 27. PMID: 22984796.
7. **Jillard CL, Youngwirth L, Scheri RP, Roman S, Sosa JA**. Radioactive Iodine Treatment Is Associated with Improved Survival for Patients with Hürthle Cell Carcinoma. *Thyroid*. 2016 Jul;26(7):959-64. doi: 10.1089/thy.2016.0246. Epub 2016 Jun 6. PMID: 27150319.
8. **Besic N, Schwarzbartl-Pevec A, Vidergar-Kralj B, Crnic T, Gazic B, Marolt Music M**. Treatment and outcome of 32 patients with distant metastases of Hürthle cell thyroid carcinoma: a single-institution experience. *BMC Cancer*. 2016 Feb 26;16:162. doi: 10.1186/s12885-016-2179-3. PMID: 26921186; PMCID: PMC4768323.
9. Oncolink Penn Medicine. Hurthle Cell Carcinoma: Staging and Treatment. [Internet] Available at: https://www.oncolink.org/cancers/thyroid/huerthle-cell-carcinoma-staging-and-treatment.