Metastatic Hürthle Cell Carcinoma of the Thyroid to the Brain – Case Report and Review of the Literature

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Received 3 August 2012; Published online 10 November 2012

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Abstract

Hürthle cell carcinoma (HCC) is an uncommon form of thyroid cancer that has a high likelihood of metastasis; however, brain metastases from HCC are an uncommon occurrence. We report a 70-year-old woman who had a total thyroidectomy followed by radiotherapy for a Hürthle cell carcinoma of the thyroid with histologic evidence of capsular invasion. Routine imaging two months after thyroidectomy showed an intraventricular mass in the superolateral temporal horn that was treated with two rounds of gamma knife radiosurgery. More than seven years after her initial diagnosis, enlargement of the intracranial mass resulted in total gross resection. Histologic examination was consistent with metastatic Hürthle cell carcinoma with positive immunohistochemical staining for thyroid transcription factor-1 (TTF-1) and thyroglobulin. In spite of the rarity of this entity, improvements in clinical management have made it increasingly important to recognize the patterns of rare metastases from thyroid carcinomas.

Keywords: Brain; Hürthle cell carcinoma; Metastasis

1. Introduction

Metastases are the most common tumors found in the central nervous system (CNS), occurring in 20 to 30% of all cancer patients. (Sul & Posner, 2007) The most common tumors that metastasize to the brain include lung cancer, breast cancer, renal cell carcinoma, and melanoma. (Schouten et al., 2002) Thyroid cancers that metastasize to the brain are comparatively uncommon, with estimates that brain metastases occur in only 1% of all cases of thyroid carcinomas. (Parker et al., 1986) Of thyroid cancer subtypes that metastasize to the brain, papillary and follicular thyroid cancers are the most frequent types. (Biswal et al., 1994; Chiu et al., 1997; McWilliams et al., 2003) Hürthle cell carcinoma (HCC) accounts for a small percentage of all differentiated thyroid malignancies, and a brain metastasis of HCC of the thyroid is an unusual finding. (Bhattacharyya, 2003) As a result of
the rarity of HCC as a histologic subtype of thyroid carcinomas, particularly in the setting of brain metastases, management continues to be controversial.

We report a case of HCC with a brain metastasis identified by imaging two months after thyroidectomy in a 70-year-old woman and use the case as an opportunity to review the literature on thyroid cancer brain metastasis.

2. Case Report

The patient is a 70-year-old female with a history of hypertension and mixed hyperlipidemia, who initially presented with a neck mass. Fine needle aspiration of the mass resulted in a diagnosis of a Hürthle cell neoplasm. She underwent a partial thyroidectomy, followed by a complete thyroidectomy with excision of two lymph nodes. The final diagnosis was Hürthle cell carcinoma, Stage II (T3N0M0). Multiple foci of capsular invasion and intracapsular vascular invasion were noted.

Fig 1. There is a sharp demarcation of the tumor (left) and the gliotic brain parenchyma (right) typical of many metastatic tumors (hematoxylin and eosin, original magnification 200X)
Fig 2. The tumor showed areas with a follicular architecture, marked by cells with round to oval nuclei, prominent nucleoli and abundant granular eosinophilic cytoplasm, consistent with a Hürthle cell neoplasm. Focal hemosiderin deposition was also present (hematoxylin and eosin, original magnification 200X)

The patient subsequently underwent ablation with radioactive iodine-131. She was maintained on thyroid hormone replacement therapy and remained asymptomatic except for an infrequent, dull occipital headache that did not require intervention. She also described some blurring in the vision of her left eye, which she attributed to prior cataract surgery. Her neurological exam was intact with a Karnofsky Performance Status (KPS) of 90. A post-ablation whole body scan demonstrated abnormal uptake in the neck and left orbit; a subsequent whole body imaging study showed no abnormal uptake. Postablation thyroglobulin levels were persistently elevated.

Brain magnetic resonance imaging (MRI) was performed as routine workup two months after treatment and showed a left temporal intraventricular lesion. Subsequent serial scans showed increases in mass size. A whole body PET-CT (without examination of the head) was performed and showed moderate abnormal uptake in the left thyroid gland bed. No metastatic lesions were identified. A subsequent octreotide scan showed an abnormal area of uptake in the left neck as well as an area of uptake in the left intracranial region, confirming the presence of metastatic disease. Bone scans were not performed. Eighteen months after her initial diagnosis, the patient underwent left periventricular gamma knife stereotactic radiosurgery (GKRS). Her post-treatment course was complicated by a stroke unrelated to treatment. Subsequent regular interval imaging of the left temporal mass showed that it continued to be stable with dimensions of 1.9 x 0.8 x 1.3 cm. Twenty-five months after her initial thyroidectomy, progressive enlargement of left jugular lymph nodes led
to a modified left neck dissection for metastases involving left central and left jugular chain lymph nodes with gross invasion of the left internal jugular vein and adjacent soft tissues by tumor.

Fig 3. The tumor demonstrated diffuse positive staining with antibody to thyroglobulin (thyroglobulin, original magnification 200X)

The patient continued to remain active and asymptomatic except for infrequent headaches and a decline in higher cognitive functions, particularly short-term memory (KPS 80). Five years after receiving GKRS, MRI studies indicated interval enlargement of the intraventricular mass in the superolateral temporal horn to dimensions of 2.2 x 1.5 x 1.5 cm, and she underwent a second round of GKRS. With continuing progressive enlargement of the intraventricular mass and vascularity, concerning for a high-grade malignancy, a persistently elevated thyroglobulin and no evidence of carcinoma recurrence in the neck, the patient underwent a craniotomy and gross total resection of the tumor 7 years and 5 months after her initial diagnosis.

Histologically, there was a sharp interface between brain parenchyma and metastatic tumor. (Fig. 1) The neoplasm had areas of follicular architecture and areas of solid nests.

(Fig. 2) Tumor nuclei were round to oval in shape with prominent nucleoli and finely granular chromatin. The neoplastic cells had abundant eosinophilic granular cytoplasm and mild pleomorphism. Nuclear features of papillary carcinoma were absent. The tumor was intermixed with areas of fibrosis with hemosiderin deposition and calcification. (Fig. 2) Focal necrosis and perivascular macrophages were also noted.

The adjacent brain parenchyma contained hemosiderin deposits, vascular sclerosis, and reactive astrocytes. Immunohistochemical staining of the tumor with antibodies to thyroid transcription
factor TTF-1 (1:40 dilution, DAKO, Carpenteria, CA, USA) and thyroglobulin (1:8000 dilution, DAKO, Carpenteria, CA, USA) was performed, and positive staining of the tumor with both antibodies was observed (Fig. 3).

3. Discussion

The incidence of brain metastases has been increasing over the past few decades, presumably a natural consequence of improved cancer monitoring and therapy that has resulted in a lengthened natural history of disease. Differentiated thyroid carcinomas, which usually demonstrate a more indolent disease course, have been no exception. Distant metastases of thyroid cancers have been observed at reported rates of 5%, most commonly to the lungs and bones. (Dinneen et al., 1995; Mazzaferri & Massoll, 2002; J. R. Clark et al., 2005) The prognosis in the context of distant metastasis is poor, decreasing the 10-year survival rate from 80-95% to only 50% of patients. (Schlumberger, 1998; Elisei et al., 2010)

Differentiated thyroid cancers with CNS metastasis occur with an incidence of only 1% and are rarely reported. (Parker et al., 1986) However, an estimated 10% of patients who succumb to thyroid cancer have evidence of at least one CNS metastasis at autopsy, raising concern that rare distant metastases are being overlooked. (Silverberg et al., 1970) The most common differentiated thyroid carcinomas, follicular and papillary thyroid cancers, have the highest number of reported cases of CNS metastasis, with observations that 15% of patients with distant metastases from differentiated thyroid cancer eventually develop brain metastases. (McConahey et al., 1986; Biswal et al., 1994; Chiu et al., 1997; McWilliams et al., 2003) Metastases to the cerebral hemispheres occur most frequently, similar to the reported CNS distributions of metastases from other primary sources. (Aguiar et al., 2001)

HCC comprises only 5% of all differentiated thyroid carcinomas. (Bhattacharyya, 2003) Its rarity, as well as difficulty in distinguishing benign from malignant types, has resulted in controversy over its pathologic and clinical significance. While some studies suggest that HCC is an aggressive form of thyroid carcinoma and that up to a third of patients with HCC develop metastatic disease, (Shaha et al., 1997; McDonald et al., 1996) others argue that it has a benign course that parallels the more indolent follicular carcinoma. (Yutan & O. H. Clark, 2001; Tallini et al., 1992; Barnabei et al., 2009) A series of 47 cases of brain metastases from thyroid cancer identified at the University of Texas M.D. Anderson Cancer Center over a 51 year period includes only three cases of HCC metastasis. (Chiu et al., 1997) Because the authors from the M.D. Anderson Cancer Center series opted to categorize the histologic subtypes as differentiated and anaplastic carcinomas, patient details regarding these cases of HCC are unavailable. Of the 16 pathologically confirmed cases of thyroid cancer CNS metastases identified over 25 years at the Mayo Clinic, only one case had a histologic type of HCC. (McWilliams et al., 2003) This patient was a 65-year-old male with HCC who was diagnosed with a brain metastasis nearly three years after initial diagnosis (T4N1M0); the patient was treated with GKRS, external beam radiation therapy (EBRT), and gross total resection. Similar to our patient, that patient was an older individual with a high tumor stage and evidence of capsular invasion at initial diagnosis. Given the rarity of this histologic type, it is difficult to generalize about the characteristics of the natural history of HCC brain metastases. Clinical management of brain metastases from thyroid cancer in general is usually aggressive, and consists of a consideration of surgical resection because of increased survival benefit. (Chiu et al., 1997; Krammer et al., 2011)
The histologic differential diagnosis of the CNS mass in this case is limited, given the history of the patient and the histology of the tumor. This patient had a known history of Hürthle cell carcinoma, and the follicular architecture of the resected brain tumor was indicative of a thyroid carcinoma. In this case, immunohistochemical staining with TTF-1 and thyroglobulin was sufficient to confirm that the primary source was the thyroid gland. In cases where a solid growth pattern may predominate or a history is unknown or unavailable, immunostaining may be useful in identifying a thyroid origin. Care should be taken in such situations not to rely on TTF-1 alone, as it is well recognized that tumors from other organ sites, most notably lung adenocarcinomas, may be positive as well.

References


