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Surgical management of metastatic Hürthle cell carcinoma to the skull base, cortex, and spine: illustrative case

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BACKGROUND Hürthle cell carcinoma (HCC) is an unusual and aggressive variant of the follicular type of differentiated thyroid cancer (DTC), accounting for less than 3% of DTCs but posing the highest risk of metastasis. Brain metastases are uncommonly reported in the literature but pose a poor prognosis. The low rate of brain metastases from HCC coupled with ambiguous treatment protocols for the extracranial disease complicate successful disease management and definitive treatment strategy. The authors present the case of a patient with HCC metastasis to the skull base, cortex, and spine with recent tibial metastasis.

OBSERVATIONS Despite the presence of metastasis to the cortex, skull base, and spine, the patient responded very well to radiation therapy, sellar mass resection, and cervical spine decompression and fixation and has made a remarkable recovery.

LESSONS The authors' multidisciplinary approach to the patient's care, including a diverse team of specialists from oncology, neurosurgery, orthopedic surgery, radiology, endocrinology, and collaboration with clinical trial researchers, was fundamental to her successful outcome, demonstrating the utility of intersecting specialties in successful outcomes in neuro-oncological patient care.

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KEYWORDS metastatic Hürthle cell carcinoma; multidisciplinary management; neurosurgery

Hürthle cell carcinoma (HCC) is an unusual and generally aggressive variant of the follicular type of differentiated thyroid cancer (DTC). Hürthle cell carcinoma accounts for less than 3% of all DTCs but has the highest incidence of metastasis and the worst prognosis among all DTCs.[1] Hürthle cell carcinoma typically metastasizes to the lung and bones, with brain metastases (BMs) being uncommon.[2] However, rare cases of pituitary metastases,[3] skull metastases,[4] single choroid plexus metastasis,[5] and cerebral metastasis[6] of HCC have been reported in the literature. Patients with distal DTC metastasis have poor outcomes, and those with BM have a worse overall survival, ranging from 7.1 to 33 months.[7] Given the rarity of HCC, the clinical outcomes are unclear, and meticulous treatment guidelines are absent.

Hürthle cell carcinomas are relatively more prevalent in women and present as painless cervical nodules, often in combination with multinodular goiters. Hürthle cell carcinomas are oxyphilic and characterized by an abundance of dysfunctional mitochondria (> 75% of cell volume), unique chromosomal landscapes (responsible for their aggression), and DNA copy number alterations.[8–10] The prognosis of HCC is predicted via investigation of tumor size, degree of infection, extrathyroidal disease extension, and initial nodal or distant metastasis.[11] Fine-needle aspiration biopsy analysis is currently used to distinguish HCCs from benign Hürthle cell neoplasms/nodules. The final diagnosis of HCC metastasis requires histological confirmation of capsular and/or vascular infiltration.[12]

The unique molecular pathogenesis and unpredictable biological behavior of HCC are distinct challenges in outlining and applying a definitive treatment strategy. The low rate of BMs from HCC coupled with ambiguous treatment protocols for the extracranial disease

ABBREVIATIONS BM = brain metastasis; cEBRT = conventional external beam radiation therapy; CSF = cerebrospinal fluid; DTC = differentiated thyroid cancer; HCC = Hürthle cell carcinoma; ICU = intensive care unit; MDT = multidisciplinary team; MRI = magnetic resonance imaging; RAI = radioactive iodine; STS = stereotactic radiosurgery; WBRT = whole-brain radiation therapy.

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further complicate successful disease management. Present-day therapeutic modalities for HCC are diffuse and include radioactive iodine therapy (safe and frequently applied despite a lack of firm consensus), extracorporeal radiation therapy, and/or surgical intervention (resection).[13] For small, unifocal, intrathyroidal carcinomas or nodular goiters (tumor size < 4 cm), thyroid lobectomy alone is adequate; total thyroidectomy is recommended for tumors larger than 4 cm. A well-defined, full-fledged management protocol for HCC with BM, apart from local therapies, has yet to take shape. We present the case of a patient with HCC metastasis to the skull base, cortex, and spine with recent tibial metastasis.

Illustrative Case

History and Examination

A 58-year-old right-handed female had skull base, left frontal cortex, and cervical spine metastasis. She had been diagnosed with ovarian cancer in October 2015 and had undergone a hysterectomy and bilateral salpingo-oophorectomy. One year later, she was diagnosed with metastatic Hürthle cell thyroid cancer and underwent a thyroidectomy and radioiodine therapy. In September 2018, she had both a right lower lobe wedge resection and mediastinal lymph node sampling. The results of this biopsy revealed Hürthle cell thyroid cancer, thereby confirming metastatic disease. Given the unique nature of her asymptomatic presentation, systemic therapy was deferred, and she was followed for observation. In February 2020, she started experiencing tunnel vision and severe neck and upper back pain. On examination, the patient showed upper-extremity weakness, presenting predominantly with left-hand weakness and left-wrist extension weakness. She was also severely myelopathic with clear hyperreflexia. Magnetic resonance imaging (MRI) scans revealed a large, bilobed, 23-mm sellar/suprasellar mass consistent with a metastatic lesion rather than a pituitary macroadenoma (Fig. 1). A 28-mm left frontal calvarial metastasis with deep extension into the extra-axial space was also seen. Cervical spine MRI showed lesions in the lower cervical spine with significant narrowing at the C6–7 level. A left frontal metastasis was also detected. Of note, the patient also had compensated diabetes insipidus, manifested by polyuria and polydipsia.

Sellar Mass Resection

The patient was first taken for an urgent endoscopic endonasal decompression of her optic apparatus given her rapidly progressive visual deterioration. A preinduction arterial line was placed, and the patient was maintained in a rigid cervical collar with mean arterial pressures above 80 mm Hg throughout induction, positioning, and pinning. Motor evoked potentials and somatosensory evoked potentials were also continuously monitored throughout this process without any changes. The ear, nose, and throat (ENT) surgeons first raised a reverse, right-sided nasal septal flap given considerable scarring from a prior septoplasty. Bilateral sphenoidotomies and a posterior ethmoidectomy were then performed with all septations reduced and the rostrum partially removed to expose the sella and cavernous sinus. The middle clinoids and medial opticocarotid recesses were also removed to ensure adequate exposure of the tumor. After confirmation with stereotactic navigation, the dura was opened in a cruciate fashion and the tumor was immediately encountered. The tumor was quite firm, with intraoperative biopsy confirming the diagnosis of metastatic carcinoma. The gland was displaced to the right and inferiorly rather than superiorly, as would typically be expected from an adenoma. The tumor was meticulously resected while paying close attention to a small area of infiltration of the diaphragma superiorly. A point of low-flow egress of cerebrospinal fluid (CSF) was noted, and the decision was made to leave a small residual of tumor along the diaphragma to prevent a high-flow CSF leak given the patient's need for eventual adjuvant radiation therapy. Once maximal safe resection was achieved, complete hemostasis was obtained and the nasoseptal flap was placed over the defect.

The following day, the patient underwent awake Embosphere (Merit Medical) particle embolization of the bilateral costocervical and right thyrocervical trunk that was then occluded proximally with Gelfoam (J&J Medtech). Postembolization angiography confirmed near-complete angiographic obliteration of the tumor blush. The patient was monitored in the intensive care unit (ICU), and the following day she returned for the next stage of her procedure.

Cervical Spine Decompression and Fixation

The patient's imaging showed severe spinal cord compression and left-sided C7–T1 nerve root compression. The surgical plan was to debulk the epidural tumor to achieve spinal cord decompression and separation and to perform spinal fixation across the cervico-thoracic junction. After fixation and exposure, a large, friable, and hemorrhagic mass was noted to be dorsally located on C6–T1 and protruding from between the transverse processes at T1–2. The transverse processes and pedicles of T2 and T3 had been fully eroded on the left side. Next, right-sided T1–4 screws were placed under fluoroscopic guidance, and a temporary rod was placed on the right side to stabilize the spine during the decompression and tumor removal. A laminectomy from C6 to T1 was then performed to remove the dorsally located tumor largely en bloc. Ultrasound was used to confirm adequate spinal cord decompression. Generous foraminotomies were performed to fully expose the left C7–T2 nerve roots, and the surrounding tumor was carefully stripped from the nerve roots. The tumor was then carefully separated from the thecal sac. The left-side T1, T4, and T5 screws were placed, skipping the right T5 screw as the tumor had obliterated this pedicle. Prior to rod placement, decortication was performed and tapered rods were placed on both sides. Anteroposterior and lateral radiographs were obtained to confirm hardware positioning. Joints and laminae, where still present, were drilled out along the construct. Despite preoperative tumor embolization, substantial bleeding arose from the metastatic disease, for which the patient was transfused with a total of 6 units of packed red blood cells. The patient's wound was closed, with 2 Hemovac drains left in place, and transferred to the ICU in stable condition. One week later, she had stereotactic surgery for her left frontal metastasis. During her latest follow-up in May 2023, she remained stable with no acute intracranial findings and showed no evidence of developing intracranial or spinal metastases.

Patient Informed Consent

The necessary patient informed consent was obtained in this study.

Discussion

Observations

Despite the presence of metastasis to the cortex, skull base, and spine, our patient responded very well to treatment and has

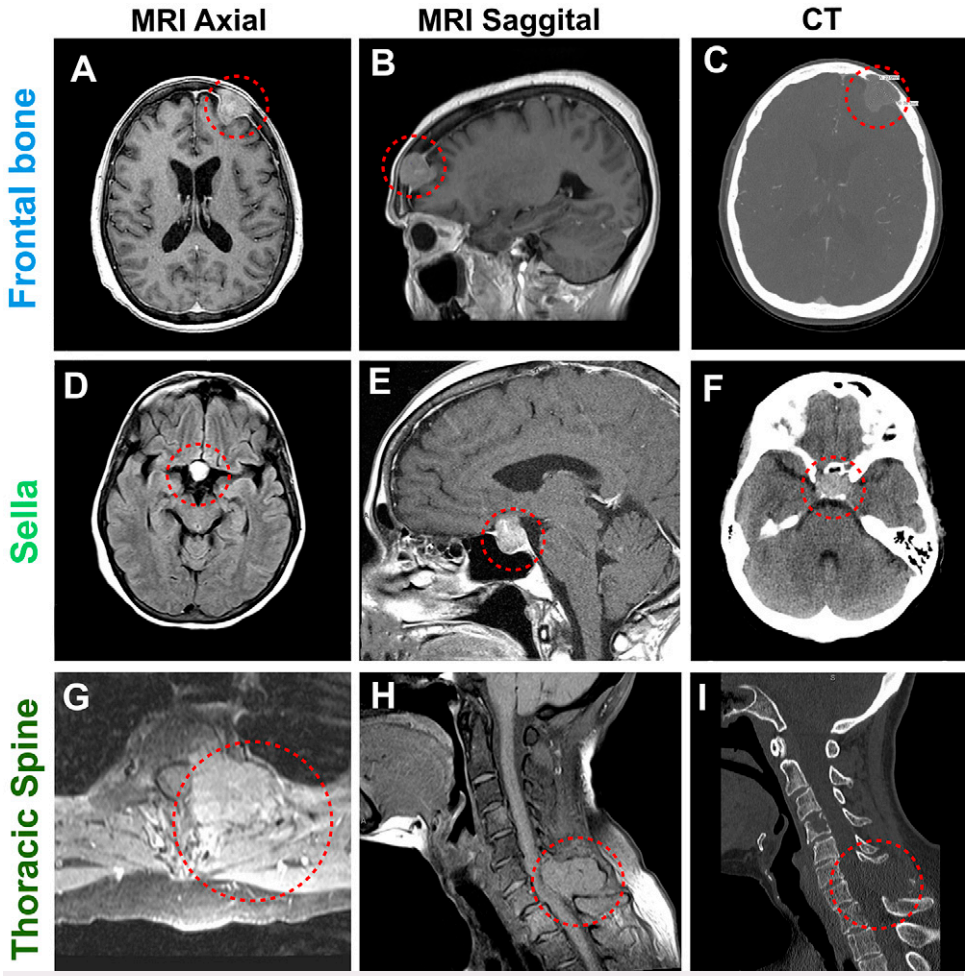

FIG. 1. Preoperative imaging. **A–C:** Left frontal calvaria lesion (*red circles*, 28 × 24 mm) consistent with an osseous metastasis, demonstrating clear deep extension into the left frontal extra-axial space and superficial extension into the left frontal scalp. Mild mass effect on the adjacent left frontal lobe also appears. **D–F:** Enhancing sellar/suprasellar mass (*red circles*, 19 × 16 × 23 mm) showing considerable suprasellar extension with secondary superior displacement of the adjacent optic chiasm and posterior aspects of both optic nerves. No definite cavernous sinus invasion can be detected. **G–I:** Mass involving the posterior elements at the C7, T3, and C4 levels. At C6–7, there is bulging of the posterior elements of C6 and C7 with a large metastasis resulting in severe compromise of the cord and signal change in the cord suggestive of myelomalacia at the C6–7 level, particularly at C7. Compromise at T1–2 can also be noted. CT = computed tomography; MRI = magnetic resonance imaging.

made a remarkable recovery (Fig. 2). The presence of distant metastasis in HCC is a significant predictor of poor prognosis; Chindris et al.[14] found that 5-year survival dropped from 91% to 24% when comparing patients diagnosed with M0 and M1 stage disease, respectively. Moreover, multiple metastases often indicate reduced survival compared with single metastatic lesions, with brain metastasis predicting the poorest outcomes.[15,16] Metastasis to the brain is very rare in all subtypes of metastatic thyroid carcinoma; to our knowledge, only 3 cases of HCC metastasis to the central nervous system have been reported.[3] McWilliams et al.[15] found that median survival for patients with metastatic thyroid carcinoma to the brain was 20.8 months for patients who had undergone partial or gross-total resection, but this was further reduced to only 8.3 months when evaluating patients with carcinomas of follicular cell origin. Patients who did not undergo any resection had a median survival of 2.7 months.[15] Given these established survival metrics, our patient had outcomes consistent with, if not better than, other patients diagnosed with metastatic thyroid carcinoma with the involvement of multiple organ systems. Our multidisciplinary approach to her care, including a diverse team of specialists from oncology, neurosurgery, orthopedic surgery, radiology, and endocrinology and collaboration with clinical trial researchers, was fundamental to her successful outcome.

Lessons

Hürthle cell carcinoma is a rare and more aggressive type of cancer that originates from follicular cells of the thyroid gland. It is more likely to metastasize to distant sites (27%), recur (14%–44%), or result in death.[14,17,18] Five-year survival ranges from 74% to 93.9%; however, survival drops to about 42% when distant metastases are present.[14,17,18] Often, these lesions do not respond well to curative treatment, and palliative care is pursued. In the past 35 years, survival

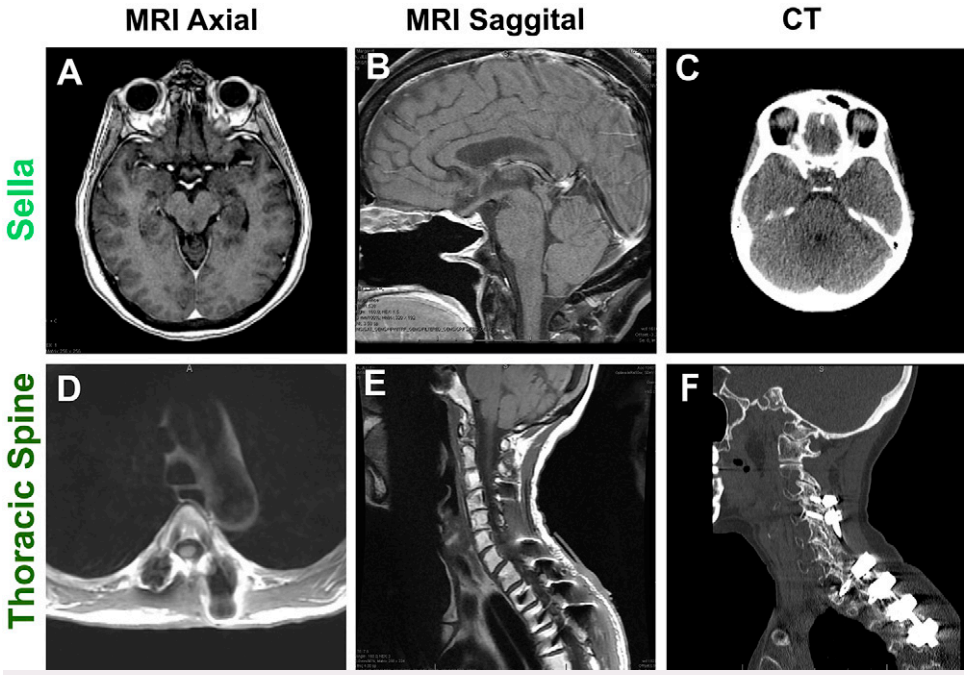

FIG. 2. Postoperative imaging. **A–C:** Postsurgical changes from an endonasal resection of the sellar/suprasellar mass. The bulk of the tumor has been removed along the sellar component. Mild residual tumor along the suprasellar component abutting the optic chiasm with associated mild deviation of the optic chiasm superiorly can be seen. **D–F:** Status postcervical spinal fusion. No new lesions are noted, and no enhancing masses are identified.

has increased in patients with HCC with an increased age ($>$ 45 years), larger tumors ($>$ 4 cm), or local disease. Conversely, survival rates have not changed for patients with smaller tumors ($<$ 4 cm) or distant metastases.[18] Given the poor survival rates and stagnant nature of disease management for HCC, there is an urgent need to develop new therapeutic approaches for the improved management of distant HCC metastases.

There is no consensus on the most effective treatment for metastatic brain disease.[19] Current management aims to treat systemic disease, control disease in the brain to prevent death, and provide the best possible quality of life to patients.[19] Treatments such as tumor resection, whole-brain radiation therapy (WBRT), or stereotactic radiosurgery (SRS) can be used alone or in combination to treat metastatic brain tumors. Surgery is suggested for large, accessible, and radioresistant tumors causing significant edema or mass effect. Whole-brain radiation therapy is suitable for patients with a poor prognosis because of the disease's diffuse activity, but it has adverse effects such as increased fatigue, decreased quality of life, and cognitive impairment. Advances in radiation technology have led to a shift toward SRS, which involves a high-dose radiation treatment focused on the tumor border, protecting healthy tissue and minimizing side effects. Stereotactic radiosurgery is an alternative to surgery for tumors in inaccessible or eloquent regions and serves as an adjuvant to surgery to reduce local recurrence rates. Studies have shown that SRS does not have significant disadvantages compared with WBRT+SRS in terms of overall survival.[19,20]

Assessment of clinical and tumor-related risk factors is integrated into individual spinal metastases treatment plans with the primary goals of controlling pain, preserving or restoring function, maintaining spinal stability, and ensuring a reasonable quality of life.[21] Presently, conventional external beam radiation therapy (cEBRT) is the recommended radiation approach and significantly reduces pain in 50%–80% of patients with spinal metastases.[21,22] However, the effectiveness of cEBRT is limited by the tolerance of surrounding healthy tissues to radiation.[21] Stereotactic radiosurgery and other focal therapies are indicated for patients with radioresistant tumors or for those with tumor progression after cEBRT.[22] Resection is indicated upfront for patients presenting with spinal instability or radioresistant tumors or as a second-line therapy for patients with declining neurological function or spinal progression after primary treatment with radiation and chemotherapy. Recently, minimally invasive surgical techniques like vertebroplasty, kyphoplasty, and ablative therapy have gained popularity in their effectiveness in pain control, stabilization of vertebral bodies, and local control of tumors.[21,22]

Because of its rare incidence, metastatic HCC lacks a standardized treatment protocol.[15,23] Management is based on results from case series and retrospective analyses. Given low sample sizes, HCC cases are typically included with other DTC cases, minimizing the HCC-specific conclusions that can be drawn from these studies.[15,23,24] Presently, the best strategy typically includes combined radioactive iodine (RAI) therapy and surgery.[15,23,24] Radioactive iodine therapy has been used to improve survival and reduce pain in brain and spinal metastases; however, there is a risk of cerebral edema, and cranial lesions typically have low uptake, limiting overall effectiveness.[15] Some studies have highlighted the use of recombinant human thyroid-stimulating hormone (TSH) stimulation to increase ^{131}I uptake, which may help increase treatment efficacy

when other options are not available. In both brain and spinal metastases, aggressive resection is also associated with better outcomes than those with palliative resection.[15,24] When resection is not feasible, radiotherapy via SRS or WBRT in the brain or cEBRT in the spine are effective options.[15,23,24] In spinal HCC lesions, alternative treatments such as selective embolization therapy and bisphosphonates can reduce bone pain and improve quality of life, but there is no evidence to suggest improved survival.[25,26] While there are no systemic therapies specifically for metastatic HCC, the U.S. Food and Drug Administration has approved 2 multikinase inhibitors, sorafenib and Lenvatinib, for the treatment of RAI-refractory differentiated thyroid cancer.[16,27] These studies also report a positive response rate for HCC.[27]

The multidisciplinary management of oncological cases is an established paradigm for effective coordination of care in cancer patients across specialties. When properly utilized, multidisciplinary teams (MDTs) can improve team dynamics, patient satisfaction, and clinical outcomes while preventing unnecessary harm. One study demonstrated that multidisciplinary tumor boards provide a valuable second opinion that leads to a change in management strategy in 58.5% of neuro-oncology cases, allowed for shorter referral times, and enhanced recruitment into clinical trials.[28] Advances in radiology, including the growing field of radiomics, allow for more nuanced imaging approaches and an increased role of radiologists for diagnosis, preoperative planning, and evaluation of response.[29] As developments in surgery and radiotherapy such as intraoperative ultrasound and SRS increase the safety of more aggressive treatments, there is a growing role for both surgical and radiation oncological contributions to MDTs managing primary and metastatic brain and spine lesions.[19] Moreover, our expanding understanding of tumor biology has allowed for the development of more targeted and personalized therapies through teamwork among pathologists and geneticists. Taken together, the power of recent medical advances is amplified by a multidisciplinary approach. Among patients with thyroid carcinoma, McWilliams et al.[15] reported that 85% died of systemic disease and its complications. Understanding that focal treatment of metastatic lesions in the brain or spine is only effective when the primary tumor(s) is also adequately addressed, there is a demonstrated need for improved control of local disease and an MDT approach to treating all patients with metastatic disease. Longitudinal communication and partnership between primary oncologists and neurosurgeons are therefore critical to improve prognosis.

In conclusion, HCC is an unusual and generally aggressive variant of the follicular type of DTC. The presence of distant metastasis is a particularly poor prognostic factor for patients with HCC. Given the low incidence of distant metastasis, there is no standardized treatment protocol. In this case report, we describe a multidisciplinary approach to treating a patient with HCC metastasis to the skull base and suprasellar region, demonstrating the utility of intersecting specialties in successful outcomes in neuro-oncological patient care.

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Author Contributions

Conception and design: Zinn, Hameed, Zenonos. Acquisition of data: Zinn, Hameed, Narayanan, Zenonos. Analysis and interpretation of data: all authors. Drafting of the article: Zinn, Hameed, Hoppe, Head, Narayanan. Critically revising the article: Zinn, Hameed, Hoppe, Head, Shanahan, Gross, Narayanan, Zenonos. Reviewed submitted version of the manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Zinn. Statistical analysis: Zinn. Administrative/technical/material support: Zinn. Study supervision: Zinn, Zenonos.

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