Radiofrequency ablation of isolated liver metastasis from facial Merkel cell carcinoma

Arnes Huskic, MD, and Robert Goldstein, MD

Department of General Surgery, Baylor University Medical Center, Dallas, Texas

ABSTRACT

Merkel cell carcinoma is a highly aggressive skin neuroendocrine tumor with early malignant potential. Metastasis was previously considered a sign of unresectability and short life expectancy. This report describes an isolated metastasis to the liver from Merkel cell carcinoma of the left frontotemporal area and an effective treatment that may meaningfully prolong life.

KEYWORDS Liver metastasis; Merkel cell carcinoma; radiofrequency ablation

Numerous isolated neuroendocrine tumor metastases have been described in the literature, but to our knowledge, no other article has been published describing minimally invasive treatment of metastatic liver Merkel cell carcinoma (MCC). This case report emphasizes the rarity of such a lesion and the effectiveness of radiofrequency ablation (RFA) for isolated liver metastasis.

CASE DESCRIPTION

A 57-year-old man with a history of MCC on the left frontotemporal scalp—diagnosed and removed with Mohs surgery—complained of a painful and enlarging left preauricular mass 3 months later. Studies showed that the mass was in-transit MCC with no signs of disease elsewhere. Left superficial parotidectomy and selective node dissection yielded positive nodes. Thereafter, the patient had 34 sessions of radiation therapy to the left neck. After a disease-free period, the patient developed a tender mass near the site of the neck incision 20 months after the initial diagnosis. Imaging studies suggested that this was a neuroma, but an incidental 5.5×4 cm mass was found in the liver. Though biopsy yielded an inadequate tissue specimen, it was definitive for malignant cells. The decision was made to take the patient for a diagnostic laparoscopy with subsequent intervention. The patient's medical history was normal with the exception of >20 excisions for basal cell carcinoma. Given the history, RFA was elected as the modality of treatment.

Intraoperatively, anesthesia, gaining of pneumoperitoneum via Optiview technique, and laparoscopic core needle biopsy on a frozen specimen were all performed without complications. There was no evidence of further malignant dissemination. Using a needle introducer, the electrode was inserted deep and posterior into the liver mass spanning segments 2 and 3. Two doses of ablation were used; the first was a 10-minute segment, and the second was a 5-minute segment that was more superficial and was anterior to the previous. Pneumoperitoneum was evacuated, and the patient was extubated and taken to the postanesthesia care unit in stable condition. The patient was discharged the same day with minimal pain medications. Follow-up imaging 1 month later showed no residual disease.

DISCUSSION

Merkel cells are mechanoreceptors for light touch located in the epidermis, specifically in the stratum basalis or rete ridges (epidermal extensions into the dermis). They were previously thought to be of neuroendocrine origin (cells that sense neurotransmitters and release hormonal molecules), but recent studies suggest that they are of epithelial origin.¹

Most MCC development is thought to be related to an infection by Merkel cell polyomavirus,² one of seven known oncoviruses that promotes T antigen proliferation.³ Diagnosis of MCC is based on histological findings on hematoxylin and eosin staining (typically showing small blue cells) and cytology findings, which typically show positive results

Corresponding author: Arnes Huskic, MD, Department of General Surgery, Baylor University Medical Center, 3500 Gaston Avenue, Dallas, TX 75246 (e-mail: Arnes.huskic@bswhealth.org)

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for CK20, chromogranin A, synaptophysin, neurofilament protein, neuron-specific enolase, and CD56.⁴ Due to similar histological findings, small cell carcinoma needs to be excluded, so imaging modalities are recommended (magnetic resonance imaging, computed tomography, and/or positron emission tomography).

Standard surgical technique is to excise the mass with margins of 1 to 2 cm to the investing fascia and with sentinel lymph node biopsy or Mohs surgery for cosmetically sensitive areas. Positive biopsy results or palpable lymph nodes require lymphadenectomy. Radiation is recommended unless the primary lesion is <1 cm, wide excisions are obtained, no evidence of lymphovascular invasion is observed, sentinel lymph node biopsy is negative, and no immunosuppression can be identified. Chemotherapy is debatable and typically not indicated, because the disease process is thought to originate from viral proliferation and retrospective studies have shown no survival benefits⁴; however, immunotherapy such as avelumab, pembrolizumab, and nivolumab has shown benefit.⁴

Staging is based on pathological or clinical tumor node metastasis classification (a 2- to 5-cm-diameter tumor is considered T2). Per stage, MCC mortality exceeds that of melanoma, with 5-year survival rates of 15% to 80%,^{5,6} underscoring MCC's aggressiveness. Risk factors include sun exposure, history of immunosuppression, and history of lymphoproliferative malignancies.⁴ Recurrence typically occurs within 8 months. Antibody titers to Merkel cell polyomavirus are being investigated and have been shown to correlate with disease recurrence, with low levels being associated with remission.⁵ Preferred metastatic sites include (in descending order) lymph nodes, liver/lung, subcutaneous tissue, pancreas, and bones.⁷ Of note, any time there is positive lymph node or metastatic disease, multidisciplinary tumor board consultation is strongly recommended.⁴

RFA is a medical procedure that allows for the conduction of electricity to the surrounding area through a directed probe and is becoming a prominent treatment modality for liver metastasis. Thus far, RFA has been effective in treating a multitude of problems, from chronic pain to cardiology. When neuroendocrine liver metastases were symptomatic, 92% of patients reported symptom improvement following ablation, with symptom relief lasting 2 to 3 years. Given the history of metastasis, recurrence was common within a 3-year period (50%–67%), and mortality and morbidity rates in this subgroup were 0.7% and 10%, respectively.⁸ Complications from RFA include bleeding, abscess, perforations, bile leak, transaminitis, pneumothorax, grounding

burns, pneumonia, pleural effusion, postablation syndrome (due to release of cytokines from necrotic tissue), and anesthetic complications.⁹

Different RFA modalities and systems have various ablation zones specific to the product, so company representatives should be readily available. Heat sink effect, which leads to inadequate ablation margin due to surrounding cooling effect from rapid blood flow,¹⁰ should be avoided by intraoperative ultrasound evaluation, preoperative imaging modalities, or additional doses of RFA. Large meta-analyses continue to support RFA in metastatic cancers localized to the liver, because its complication rates and lengths of hospital stay are more favorable than those of formal hepatic resections.¹¹ RFA techniques can be an effective treatment option in select patients with metastatic MCC.

1. Morrison KM, Miesegaes GR, Lumpkin EA, Maricich SM. Mammalian Merkel cells are descended from the epidermal lineage. *Dev Biol*. 2009;336(1):76–83. doi:10.1016/j.ydbio.2009.09.032.
2. Narisawa Y, Koba S, Nagase K, Inoue T, Misago N, Hashimoto K. Ultrastructural studies of perichromatin granules with special references to Merkel cell carcinoma. *Arch Dermatol Res*. 2014;306(6):571–576. doi:10.1007/s00403-014-1468-4.
3. Shuda M, Feng H, Kwun HJ, et al. T antigen mutations are a human tumor-specific signature for Merkel cell polyomavirus. *Proc Natl Acad Sci USA*. 2008;105(42):16272–16277. doi:10.1073/pnas.0806526105.
4. National Comprehensive Cancer Network. Merkel Cell Carcinoma (Version 1.2018). Available at https://www.nccn.org/professionals/physician_gls/pdf/mcc.pdf. Accessed February 1, 2018.
5. Cogshall K, Tello TL, North JP, Yu SS. Merkel cell carcinoma: an update and review: Pathogenesis, diagnosis, and staging. *J Am Acad Dermatol*. 2018;78(3):433–442. doi:10.1016/j.jaad.2017.12.001.
6. American Cancer Society. Survival rates for Merkel cell carcinoma, by stage. Available at <https://www.cancer.org/cancer/merkel-cell-skin-cancer/detection-diagnosis-staging/survival-rates.html>. Accessed May 8, 2018.
7. Kouzmina M, Koljonen V, Leikola J, Bohling T, Lantto E. Frequency and locations of systemic metastases in Merkel cell carcinoma by imaging. *Acta Radiol Open*. 2017;6(3):2058460117700449. doi:10.1177/2058460117700449.
8. Mohan H, Nicholson P, Winter DC, et al. Radiofrequency ablation for neuroendocrine liver metastases: a systematic review. *J Vasc Interv Radiol*. 2015;26(7):935–942.e1. doi:10.1016/j.jvir.2014.12.009.
9. Leung A, Bilchik A. Radiofrequency ablation of hepatic metastasis from colorectal cancer. *Curr Surg Ther*. 2013;11:337–338.
10. Pillai K, Akhter J, Chua TC, et al. Heat sink effect on tumor ablation characteristics as observed in monopolar radiofrequency, bipolar radiofrequency, and microwave, using ex vivo calf liver model. *Medicine*. 2015;94(9):e580. doi:10.1097/MD.0000000000000580.
11. Xu Q, Kobayashi S, Ye X, Meng X. Comparison of hepatic resection and radiofrequency ablation for small hepatocellular carcinoma: a meta-analysis of 16,103 patients. *Sci Rep*. 2015;4(1):7252. doi:10.1038/srep07252.