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Renal Cell Carcinoma Brain Metastasis Pseudoprogression with Nivolumab after Previous Treatment with Stereotactic Radiosurgery (SRS)

Gary D. Lewis [1] , Eric Jonasch [2] , Bin Teh [3]

1. Radiation Oncology, University of Texas Medical Branch at Galveston 2. Department of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center 3. Department of Radiation Oncology, Houston Methodist Hospital, Houston, USA

Corresponding author: Gary D. Lewis, gdlewis@utmb.edu

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Objectives: As immunotherapy gains more prominence in cancer treatment, the effects of these immunotherapy agents in combination with established therapies need to be assessed. For example, for brain metastases, these agents can cross the blood brain barrier, permitting therapy that was not possible with traditional systemic therapy. This ability also allows for treatment interaction with radiotherapy, possibly creating the opportunity for not only greater therapeutic effects but also increased toxicity.

Methods: We present a case of metastatic renal cell carcinoma of the brain treated with stereotactic radiosurgery that demonstrated pseudoprogression after treatment with the PD-1 inhibitor nivolumab. A retrospective chart review was performed, including review of the patient's clinical status, imaging studies, and pathology findings.

Results: The patient is a 36-year-old female with a history of metastatic renal cell carcinoma. MRI brain showed a 11mm right temporal lobe metastasis and a 5mm left frontal lobe metastasis. She was treated with stereotactic radiosurgery to a dose of 20Gy via a linear accelerator based system. Imaging 2 months later showed a good therapeutic response; the right temporal lobe metastasis decreased to 6mm in size and the left frontal lobe metastasis was stable. Repeat imaging in 2 months showed the temporal lobe metastasis remained stable, with residual associated edema and blood breakdown products. The other lesion had resolved. During this time, patient's only systemic therapy was axitinib, an oral tyrosine kinase inhibitor. However, with axitinib, she developed cardiomyopathy, so her therapy was switched to nivolumab. Imaging 2 months after this switch revealed that the area of enhancement in the right temporal lobe measured 17mm and had evidence of necrotic/cystic changes with associated edema. This was consistent with progression by Response Assessment in Neuro-Oncology (RANO) criteria. Nivolumab was continued and repeat imaging 1 month later showed enhancing area measured 28mm with a few areas of blooming, consistent with progressive disease by immunotherapy RANO (iRANO) criteria. The patient clinically noted only headaches and nausea after nivolumab infusion that resolved with steroids. She denied any new neurologic deficits. She was offered observation, laser interstitial thermal therapy (LITT), or surgical resection of the enhancing area. She chose surgical resection which showed inflammatory cells without any cancer cells, consistent with pathologic complete response.

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Conclusions: This case is one of the first to document pseudoprogression of a brain metastasis with nivolumab after successful treatment with SRS. This case also highlights the need for the continued study of the effects of immunotherapy combined with radiotherapy as well as the development of imaging techniques to distinguish pseudoprogression from disease progression. In regards to therapy, conservative management with steroids or change in immunotherapy may be reasonable alternatives to surgery or LITT.