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A Stereotactic Solution for Glioblastoma in the Setting of Prior Craniospinal Irradiation for Adult Medulloblastoma

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Abstract

Objectives:

Management of multicentric malignant glioma in the setting of prior craniospinal irradiation is a challenging clinical scenario. We report a case of short-interval development of multicentric malignant glioma with MET mutation in a patient in a patient previously treated with craniospinal radiation for adult medulloblastoma. In this patient, gamma knife stereotactic radiosurgery to minimize the integral dose exposure of normal tissues surrounding the target volume proved to be particularly advantageous in the setting of prior craniospinal irradiation.

Methods:

The patient was, at the time of initial diagnosis of glioblastoma, a 51-year-old male, with minimal medical comorbidities and a history notable for medulloblastoma of the cerebellum diagnosed and treated 7 years prior. The medulloblastoma was of the sonic hedgehog (SHH) molecular subtype and was treated with surgical resection, craniospinal radiotherapy and adjuvant chemotherapy (without concurrent chemotherapy). He was initially prescribed craniospinal irradiation (CSI) to a dose of 3600 cGy in 18 fractions, but after a second opinion at an outside institution, he ultimately opted for reduced dose CSI (described in some recent reports) due to concerns regarding cogntive effects. He received CSI to a dose of 2340 cGy in 13 fractions followed by a posterior fossa boost of 3060 cGy in 17 fractions, for a total dose of 5400 cGy to the posterior fossa. He subsequently received adjuvant temozolomide, etoposide, vincristine, cyclophosphamide, and carboplatin chemotherapy. The patient then had a short-interval development of multicentric malignant glioma with MET mutation necessitating the use of stereotactic radio surgery. On surveillance imaging, a new (since MRI 10 months prior) 2.5 cm x 1.5 cm, contrast-enhancing, centrally necrotic, right superior cerebellar vermis lesion was seen, and attributed to either tumor progression vs. radiation necrosis. He received 6 cycles of bevacizumab after which the lesion markedly regressed. Subsequent MR neuroimaging demonstrated a non-enhancing left cerebellar peduncular lesion. A lumbar puncture revealed rare, small malignant cells and recurrent medulloblastoma was suspected. The patient underwent a stereotactic biopsy performed and pathology demonstrated low-grade glioma of astrocyte origin with a somatic MET mutation and no IDH mutation. No germline mutation was identified in this patient's glioma. He was then treated with temozolomide (5 total cycles), irinotecan, crizotinib and lomustine.
Six months after the non-enhancing left cerebellar lesion was identified, and 11 months after the enhancing right cerebellar lesion was seen, surveillance brain MR showed regression of the non-enhancing left cerebellar peduncle lesion and stability of the right cerebellar vermian lesion. In the interval, however, a new right temporal lobe contrast-enhancing mass had developed. Given his recent diagnosis of astrocytoma, and aggressive appearance and behavior of this new lesion, he opted for definitive radiotherapy without a biopsy or resection. The new tumor was treated with linear accelerator (LINAC) based fractionated stereotactic/IMRT to a dose of 30 Gy in 5 fractions, with concurrent temozolomide chemotherapy and 2 cycles of bevacizumab.

Results:

Subsequent imaging showed interval decrease in size of the right temporal lesion with improved mass effect, but development of a new left cerebellar hemispheric lesion which was resected. Pathology revealed IDH

wildtype, high-grade cerebellar glioma. He then underwent subsequent gamma knife SRS targeting the surgical cavity (Figure 6) to a dose of 27 Gy in 3 fractions to the margin. GKRS dosimetry parameters are summarized in Table 1. Brainstem composite dose of 84.2 Gy and composite D0.035cc of 82.2 Gy. The patient was noted to be awake, alert, and oriented to person, place, and time on subsequent patient visits following completion of GKRS. At the time of last follow-up, one year after completion of GKRS, the patient had not developed any symptomatic radiation necrosis or neuroimgaing changes reflective of treatment toxicity.

Conclusion(s):

This case highlights multiple considerations in the management of secondary glioma following prior craniospinal irradiation for medulloblastoma which poses treatment challenges. Stereotactic radiosurgery is an effective treatment modality, particularly in reducing the integral dose of radiation in patients who have undergone prior craniospinal irradiation. Radiation oncologists must be cognizant of the implications of a glial tumor's molecular profile, particularly the MET mutation, which may have contributed to this patient's short interval secondary glioma following prior definitive treatment of adult medulloblastoma.