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Molecular characterization of long-term survivors of metastatic medulloblastoma treated with reduced-dose craniospinal irradiation

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Abstract

Background and aims: Current standard treatment for metastatic medulloblastoma consists of 36 Gray (Gy) of craniospinal irradiation (CSI) supplemented with local irradiation and adjuvant chemotherapy after surgery. Although contemporary protocols have been designed to limit a radiation dose using risk-adapted CSI dosing to reduce neurocognitive morbidity, high-dose CSI remains the standard of care. Recently, the molecular classification of medulloblastoma has been emerging but its clinical significance has not been established particularly in patients with metastatic medulloblastoma treated with lower dose of CSI.

Methods: We molecularly analyzed three cases of metastatic medulloblastoma treated with 24.0 Gy of CSI by DNA methylation analysis using the Illumina EPIC array.

Results: All three patients had spinal metastases at the time of diagnosis. Postoperative treatment included multiple courses of chemotherapy, 24 Gy of CSI with focal boost to primary and metastatic sites, and high-dose chemotherapy. There was no disease progression observed during the 9.0, 7.7, and 5.7 years post-diagnosis follow-up. The molecular diagnosis was Group 3/4 in all three cases. Cases 1 and 2 belonged to Subtypes 7 and 4, both of which were reported to be good prognostic subtypes among the group. Case 3 belonged to Subtype 5 with MYC amplification.

Conclusions: The present cases suggest that the novel subtype classification in Group 3/4 medulloblastoma may be useful for risk stratification of patients with metastatic medulloblastoma who received lower dose of CSI than standard treatment.

Keywords: Craniospinal irradiation; DNA methylation analysis; Medulloblastoma; Metastasis; Molecular classification.