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Optimizing reirradiation for relapsed medulloblastoma: identifying the ideal patient and tumor profiles

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Abstract

Background: First-line therapies for medulloblastoma(MBL) are obtaining higher survival-rates while decreasing late-effects, but treatment at relapse is not standardized. We report here the experience with MBL re-irradiation(re-RT), its timing and outcome in different clinical settings and tumor groups.

Methods: Patient's staging/treatment at diagnosis, histotypes/molecular subgroups, relapse site/s, re-treatments outcome are reported.

Results: 25 patients were included, with a median age of 11.4 years; 8 had metastases. According to 2016-2021 WHO-classification, 14 had SHH subgroup tumors(six TP53 mutated,one + MYC,one + NMYC amplification), 11 non-WNT/non-SHH (two with MYC/MYCN amplification).Thirteen had received HART-CSI, 11 standard-CSI, one HFRT; all post-radiation chemotherapy(CT), 16 also pre-RT. Median time to relapse (local-LR in nine, distant-DR in 14, LR + DR in two) was 26 months. Fourteen patients were re-operated, in five cases excising single DR-sites, thereafter three received CT, two after re-RT; out of 11 patients not re-operated, four had re-RT as first treatment and seven after CT. Re-RT was administered at median 32 months after first RT: focally in 20 cases, craniospinal-CSI in five. Median post-relapse-PFS/after re-RT was 16.7/8.2 months, while overall survival-OS was 35.1/23.9 months, respectively. Metastatic status both at diagnosis/relapse negatively affected outcome and resurgery was prognostically favorable. PD after re-RT was however significantly more frequent in SHH (with a suggestive association with TP53 mutation, p = 0.050). We did not observe any influence of biological subgroups on PFS from recurrence while SHH showed apparently worse OS compared to non-WNT/non-SHH group.

Conclusions: Re-surgery + reRT can prolong survival; a substantial fraction of patients with worse outcome belongs to the SHH-subgroup.

Keywords: Medulloblastoma relapse; Medulloblastoma subgroups; Reirradiation; SHH prognosis.

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