ABSTRACT

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Omission of upfront craniospinal irradiation in patients with low-risk WNT-pathway medulloblastoma is associated with unacceptably high risk of neuraxial failure.

Gupta T(1), Pervez S(2), Dasgupta A(1), Chatterjee A(2), Epari S(3), Chinnaswamy G(2), Jalali R(4).

Author information:
(1)Advanced Centre for Treatment, Research & Education in Cancer, Navi Mumbai, Maharashtra, India.
(2)Tata Memorial Hospital, Mumbai, Maharashtra, India.
(3)Advanced Centre for Treatment, Research & Education in Cancer and Tata Memorial Hospital, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, Maharashtra, India.
(4)Apollo Proton Cancer Centre, Chennai, India.

BACKGROUND: Medulloblastoma is a heterogenous disease comprising four molecular subgroups - wingless (WNT), sonic hedgehog (SHH), Group 3, and Group 4 respectively. Excellent long term outcomes have prompted de-intensification of therapy in WNT-pathway medulloblastoma. We assessed safety of avoiding upfront craniospinal irradiation (CSI) in children with low-risk WNT-pathway medulloblastoma.

METHODS: Children with low-risk WNT-pathway medulloblastoma were treated with post-operative focal conformal radiotherapy avoiding upfront CSI followed by 6 cycles of adjuvant systemic chemotherapy. A group-sequential design (triangular test) with pre-defined stopping rules if the rate of relapse exceeded 15% at 2 years was incorporated to ensure safety of study participants.

RESULTS: Seven children with low-risk WNT-pathway medulloblastoma were accrued after written informed consent/assent and treated as per protocol. One child succumbed to neutropenic sepsis and multi-organ dysfunction during chemotherapy. Three children were detected with neuraxial failure (supratentorial brain and/or spine) on surveillance neuro-imaging within 2 years from index diagnosis leading to premature study termination. At relapse, children were treated with salvage CSI plus boost irradiation of metastatic deposits followed by second line chemotherapy. Two of them continue to be in remission (32 and 26 months after first relapse) while one child developed second relapse necessitating further systemic chemotherapy and craniospinal re-irradiation resulting in excellent clinico-radiological response. At a median follow-up of 42 months, the 2 year Kaplan-Meier estimates of event-free survival, recurrence-free survival and overall survival were 42.9%, 50% and 85.7% respectively.

CONCLUSION: Omission of upfront CSI in low-risk WNT-pathway medulloblastoma is associated with unacceptably high risk of neuraxial failure.

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