Intellectual Outcome in Molecular Subgroups of Medulloblastoma.


Abstract

PURPOSE: To evaluate intellectual functioning and the implications of limiting radiation exposure in the four biologically distinct subgroups of medulloblastoma: wingless (WNT), sonic hedgehog (SHH), Group 3, and Group 4.

PATIENTS AND METHODS: A total of 121 patients with medulloblastoma (n = 51, Group 4; n = 25, Group 3; n = 28, SHH; and n = 17, WNT), who were treated between 1991 and 2013 at the Hospital for Sick Children (Toronto, Ontario, Canada), Children's National Health System (Washington, DC), or the Lucile Packard Children's Hospital (Palo Alto, CA), had intellectual assessments. First, we compared intellectual trajectories between subgroups. Next, we evaluated the effect of treatment with reduced-dose craniospinal irradiation (CSI) plus a tumor bed boost versus treatments that deliver higher CSI doses and/or larger boost volumes to the brain (all other treatments) within subgroups. Linear mixed modeling was used to determine the stability or change in intelligence scores over time.

RESULTS: Intellectual outcomes declined comparably in each subgroup except for processing speed; SHH declined less than Group 3 (P = .04). SHH had the lowest incidence of cerebellar mutism and motor deficits. Treatment with reduced-dose CSI plus a tumor bed boost was associated with preserved intellectual functioning in WNT and Group 4 patients considered together (ie, subgroups containing patients who are candidates for therapy de-escalation), and not in Group 3 or SHH. Across all subgroups, patients in the all other treatments group declined over time (all P < .05).

CONCLUSION: SHH patients appear to have the most distinct functional (ie, motor deficits and mutism) outcomes and a unique processing speed trajectory. Only WNT and Group 4 patients seem to benefit from limiting radiation exposure. Our findings highlight the value of conducting subgroup-specific analyses, and can be used to inform novel biologically based treatment protocols for patients with medulloblastoma.

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