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High-grade glioma in infants and young children is histologically, molecularly, and clinically diverse-Results from the SJYC07 trial and institutional experience

Jason Chiang [1], Aditi Bagchi [2], Xiaoyu Li [1], Sandeep K Dhanda [2], Jie Huang [3], Soniya N Pinto [4], Edgar Sioson [5], James Dalton [1], Ruth G Tatevossian [6], Sujuan Jia [6 7], Sonia Partap [8], Paul G Fisher [8], Daniel C Bowers [9], Tim Hassall [10], Congyu Lu [5], Airen Zaldivar-Peraza [5], Karen D Wright [11], Alberto Broniscer [12], Ibrahim Qaddoumi [2], Santhosh A Upadhyaya [2], Anna Vinitsky [2], Noah D Sabin [4], Brent A Orr [1], Paul Klimo [13 14], Frederick A Boop [13 14], Jason M Ashford [15], Heather M Conklin [15], Arzu Onar-Thomas [3], Xin Zhou [5], David W Ellison [1], Amar Gajjar [2], Giles W Robinson [2]

Affiliations

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Abstract

Background: High-grade gliomas (HGG) in young children pose a challenge due to favorable but unpredictable outcomes. While retrospective studies broadened our understanding of tumor biology, prospective data is lacking.

Methods: A cohort of children with histologically diagnosed HGG from the SJYC07 trial was augmented with non-protocol patients with HGG treated at St. Jude Children's Research Hospital from November 2007 to December 2020. DNA methylome profiling and whole genome, whole exome, and RNA sequencing were performed. These data were integrated with histopathology to yield an integrated diagnosis. Clinical characteristics and pre-operative imaging were analyzed.

Results: Fifty-six children (0.0-4.4 years) were identified. Integrated analysis split the cohort into four categories: infant-type hemispheric glioma (IHG), HGG, low-grade glioma (LGG), and other-central nervous system (CNS) tumors. IHG was the most prevalent (n=22), occurred in the youngest patients (median age=0.4 years), and commonly harbored receptor tyrosine kinase gene fusions (7 ALK, 2 ROS1, 3 NTRK1/2/3, 4 MET). The 5-year event-free (EFS) and overall survival (OS) for IHG was 53.13% (95%CI:35.52 -79.47) and 90.91% (95%CI:79.66-100.00) vs. 0.0% and 16.67% (95%CI:2.78-99.74%) for HGG (p=0.0043, p=0.00013). EFS and OS were not different between IHG and LGG (p=0.95, p=0.43). Imaging review showed IHGs are associated with circumscribed margins (p=0.0047), hemispheric location (p=0.0010), and intratumoral hemorrhage (p=0.0149).

Conclusions: HGG in young children is heterogeneous and best defined by integrating histopathological and molecular features. Patients with IHG have relatively good outcomes, yet they endure significant deficits, making them good candidates for therapy de-escalation and trials of molecular targeted therapy.

Keywords: Infant-type hemispheric glioma; high-grade glioma; outcomes; prospective; young children.