ABSTRACT

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Genetic predisposition to central nervous system tumors in children - what the neurosurgeon should know.

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BACKGROUND: Historically, few pediatric central nervous system (CNS) tumors were thought to result from genetic predisposition. However, within the last decade, new DNA sequencing methods have led to an increased recognition of high-risk cancer predisposition syndromes in children with CNS tumors. Thus, genetic predisposition is increasingly impacting clinical pediatric neuro-oncology.

METHODS: In this narrative review, we discuss the current understanding of genetic predisposition to childhood CNS tumors and provide a general overview of involved research methodologies and terminology. Moreover, we consider how germline genetics may influence neurosurgical practice.

RESULTS: Introduction of next-generation DNA sequencing has greatly increased our understanding of genetic predisposition to pediatric CNS tumors by enabling whole-exome/-genome sequencing of large cohorts. To date, the scientific literature has reported germline sequencing findings for more than 2000 children with CNS tumors. Although varying between tumor types, at least 10% of childhood CNS tumors can currently be explained by rare pathogenic germline variants in known cancer-related genes. Novel methodologies continue to uncover new mechanisms, suggesting that a much higher proportion of children with CNS tumors have underlying genetic causes. Understanding how genetic predisposition influences tumor biology and the clinical course in a given patient may mandate adjustments to neurosurgical treatment.

CONCLUSION: Germline genetics is becoming increasingly important to clinicians, including neurosurgeons. This review provides an updated overview of genetic predisposition to childhood CNS tumors with focus on aspects relevant to pediatric neurosurgeons.

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