Diffuse intrinsic pontine gliomas-current management and new biologic insights. Is there a glimmer of hope?

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Abstract
Diffuse intrinsic pontine glioma (DIPG) has proven to be one of the most challenging of all pediatric cancers. Owing to a historical reticence to obtain tumor tissue for study, and based on an erroneous assumption that the biology of DIPG would mirror that of supratentorial high-grade astrocytomas, innumerable studies have been undertaken—all of which have had a negligible impact on the natural history of this disease. More recently, improvements in neurosurgical techniques have allowed for the safe upfront biopsy of DIPG, which, together with a wider use of autopsy tissue, has led to an evolving understanding of the biology of this tumor. The discovery of a recurrent somatic gain-of-function mutation leading to lysine 27 to methionine (p.Lys27Met, K27M) substitution in histone 3 variants characterizes more than 85% of DIPG, suggesting for the first time the role of the epigenome and histones in the pathogenesis of this disease, and more unified diagnostic criteria. Along with further molecular insights into the pathogenesis of DIPG, rational targets are being identified and studied in the hopes of improving the otherwise dismal outcome for children with DIPG.

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