

AB014. The accurate classification of high-grade glioma, *IDH*-wildtype, is based on methylation profiling: a case report

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Background: The 2021 World Health Organization (WHO) classification has significantly enhanced the molecular diagnostics of diffuse gliomas, emphasizing the role of molecular features alongside histology. However, accurate classification remains challenging, particularly for high-grade gliomas, *IDH*-wildtype. DNA methylation profiling provides an unbiased diagnostic approach, offering valuable insights into tumor classification. Here, we present a case of a high-grade glioma, initially diagnosed as glioblastoma, *IDH*-wildtype based on histological and genetic analysis, but later reclassified as a diffuse pediatric-type high-grade glioma, *H3*-wildtype and *IDH*-wildtype (*RTK2* subtype) through methylation profiling.

Case Description: A 7-year-old boy presenting with seizures was admitted to our hospital, where brain magnetic resonance imaging revealed a tumor in the right temporal lobe. Intraoperative histology indicated a high-grade glioma, prompting maximal resection. Diagnosis according to the 2021 WHO classification involved histological analysis, immunohistochemistry, testing for specific genetic alterations, and DNA methylation profiling. Histological and immunohistochemical assessment initially identified the tumor as a high-grade astrocytoma, *IDH*-wildtype. Specific genetic testing revealed *IDH1*-wildtype, *IDH2*-wildtype,

and *TERT* promoter mutation, consistent with a diagnosis of glioblastoma, *IDH*-wildtype. However, methylation profiling yielded a classifier score of 0.99 for a diffuse pediatric-type high-grade glioma, *H3*-wildtype and *IDH*-wildtype (*RTK2* subtype).

Conclusions: Our case illustrated that conventional histological and genetic analysis classification can be reclassified according to the DNA methylation analysis, demonstrating that methylation profiling is useful to accurately classify high-grade gliomas, particularly those of the *IDH*-wildtype subtype.

Keywords: High-grade glioma; *IDH*-wildtype; methylation profiling; case report

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committees and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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