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Case Report | RADIOLOGY-PATHOLOGY CORRELATION

Molecular GBM versus Histopathological GBM: Radiology-Pathology-Genetic Correlation and the New WHO 2021 Definition of Glioblastoma

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ABSTRACT

Given the recent advances in molecular pathogenesis of tumors, with better correlation with tumor behavior and prognosis, major changes were made to the new 2021 WHO (CNS5) classification of CNS tumors, including updated criteria for diagnosis of glioblastoma. Diagnosis of GBM now requires absence of isocitrate dehydrogenase and histone 3 mutations (IDH-wildtype and H3-wildtype) as the basic cornerstone, with elimination of the IDH-mutated category. The requirements for diagnosis were conventionally histopathological, based on the presence of pathognomonic features such as microvascular proliferation and necrosis. However, even if these histological features are absent, many lower grade (WHO grade 2/3) diffuse astrocytic gliomas behave clinically similar to GBM (grade 4). The 2021 WHO classification introduced new molecular criteria that can be used to upgrade the diagnosis of such histologically lower-grade, IDH-wildtype, astrocytomas to GBM. The three molecular criteria include: concurrent gain of whole chromosome 7 and loss of whole chromosome 10 (+7/-10); TERT promoter mutation; epidermal growth factor receptor (EGFR) amplification. Given these changes, it is now strongly recommended to have molecular analysis of WHO grade 2/3 diffuse astrocytic, IDH-wildtype, gliomas in adult patients, as identification of any of the above mutations allows for upgrading the tumor to WHO grade 4 (“molecular GBM”) with important prognostic implications. Despite at an early stage, there is active ongoing research on the unique MRI features of molecular GBM. This paper highlights the differences between “molecular” and “histopathological” GBM, with the aim of providing a basic understanding about these changes.

ABBREVIATIONS: GBM=Glioblastoma; TERT=telomerase reverse transcriptase; EGFR=epidermal growth factor receptor; MGMT= methylguanine-DNA methyltransferase; NGS= next-generation sequencing; IDH= isocitrate dehydrogenase

Footnotes

- Conflict of interests: None for all authors.