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A case of glioblastoma harboring non-amplified epidermal growth factor receptor variant III: Critical molecular detection using RNA-based panel analysis

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Abstract

Amplification of the epidermal growth factor receptor gene (EGFR) and its variants are the most commonly detected pathogenic gene alterations in glioblastoma. Herein, we report a case of molecularly defined glioblastoma harboring an EGFR variant III (EGFRvIII) without EGFR amplification. The initial histological diagnosis was isocitrate dehydrogenase (IDH)-wildtype low-grade glioma, due to an absence of anaplasia, necrosis, and microvascular proliferation, and a low Ki-67 labeling index. DNA-based next-generation sequencing (NGS) panel analysis revealed a TERTp promoter mutation but no EGFR mutation or amplification, supporting the diagnosis of "molecular glioblastoma." However, RNA-based NGS panel analysis revealed mRNA expression of EGFRvIII. Therefore, the final integrative diagnosis was glioblastoma with non-amplified EGFRvIII. Our report suggests that non-amplified EGFRvIII might be an early molecular event in glioblastoma tumorigenesis. In addition to the usual DNA-based analysis, RNA-based analysis is required to identify exon-skipping EGFR variants without EGFR amplification.

Keywords: Bimodal DNA- and RNA-based NGS; Glioblastoma; Non-amplified EGFR variant III.