ABSTRACT

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The early infiltrative phase of GBM hypothesis: are molecular glioblastomas histological glioblastomas in the making? A preliminary multicenter study.

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PURPOSE: The presence of necrosis or microvascular proliferation was previously the hallmark for glioblastoma (GBM) diagnosis. The 2021 WHO classification now considers IDH-wildtype diffuse astrocytic tumors without the histological features of glioblastoma (that would have otherwise been classified as grade 2 or 3) as molecular GBM (molGBM) if they harbor any of the following molecular abnormalities: TERT promoter mutation, EGFR amplification, or chromosomal + 7/-10 copy changes. We hypothesize that these tumors are early histological GBM and will eventually develop the classic histological features.

METHODS: Medical records from 65 consecutive patients diagnosed with molGBM at three tertiary-care centers from our institution were retrospectively reviewed from November 2017-October 2021. Only patients who underwent reoperation for tumor recurrence and whose tissue at initial diagnosis and recurrence was available were included in this study. The detailed clinical, histopathological, and radiographic scenarios are presented.

RESULTS: Five patients were included in our final cohort. Three (60%) patients underwent reoperation for recurrence in the primary site and 2 (40%) underwent reoperation for distal recurrence. Microvascular proliferation and pseudopalisading necrosis were absent at initial diagnosis but present at recurrence in 4 (80%) patients. Radiographically, all tumors showed contrast enhancement, however none of them showed the classic radiographic features of GBM at initial diagnosis.

CONCLUSIONS: In this manuscript we present preliminary data for a hypothesis that molGBMs are early histological GBMs diagnosed early in their natural history of disease and will eventually develop necrosis and microvascular proliferation. Further correlative studies are needed in support of this hypothesis.

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