"The definition of primary and secondary glioblastoma" – Letter

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We read with great interest the article by Kleihues and Ohgaki (1) in which the molecular genetetic concept of primary and secondary glioblastoma (GBM) was reviewed. In response to this most interesting article we want to present the first case in which the occurrence of an IDH1-negative GBM was monitored over time by combined \[^{11}C\]methionine (MET) amino acid transport PET/MRI (Figure 1).

This case underlines that the uncertainty in differential diagnosis between primary and secondary GBM, despite the clinical definition and advanced imaging, can be overcome with molecular genetics: Although in this case there was evidence of a less malignant precursor lesion in PET, a secondary glioblastoma could be ruled out on the basis of the IDH1 profile.

Kleihues and Ohgaki outline the high clinical importance of predicting malignant transformation in primary brain tumors. We would like to expand the molecular genetic perspective of their article by that of molecular imaging. In the present case, the 47% increase in amino acid transport observed over 6 weeks allowed ruling out a low grade tumor. This is in keeping with other literature reporting high accuracy of amino acid brain tumor imaging for grading astrocytomas and evaluating their malignant transformation (2,3). For the future, an incremental diagnostic value in the assessment of astrocytomas can even be expected from multi-parametric analyses of different imaging informations as they are now for the first time obtainable within one session by combined PET/MRI (4,5).
Figure 1 – Case example of a 72-year-old man with sudden onset of aphasia and use of neologisms who showed an unspecific left temporal swelling on initial MRI. On baseline $[^{11}\text{C}]\text{MET PET/MRI}$ (A), high amino acid transport was observed. Due to absence of contrast enhancement in MRI and unremarkable NMR spectroscopy, the finding was diagnosed as a low-grade astrocytoma. In the absence of symptoms under
anticonvulsants a “wait and see” strategy was chosen over stereotactic biopsy. On follow-up $[^{11}C]$MET PET/MRI 6 weeks later (B), the initial PET finding was confirmed by a typical contrast-enhancing mass on MRI with further increase in amino acid transport (increase in target-to-background uptake ratio: 47%). Resection and histopathological workup revealed a GBM. High expression of EGFR was found. Molecular cytogenetic analysis revealed no IDH1 mutation but trisomy 7, monosomy 10 and a hemizygous deletion of PTEN in 50% of the analyzed interphase cells.


