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IDH1 mutations as molecular signature and predictive factor of secondary glioblastomas.

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PURPOSE: To establish the frequency of IDH1 mutations in glioblastomas at a population level, and to assess whether they allow reliable discrimination between primary (de novo) glioblastomas and secondary glioblastomas that progressed from low-grade or anaplastic astrocytoma. **EXPERIMENTAL DESIGN:** We screened glioblastomas from a population-based study for IDH1 mutations and correlated them with clinical data and other genetic alterations. **RESULTS:** IDH1 mutations were detected in 36 of 407 glioblastomas (8.8%). Glioblastoma patients with IDH1 mutations were younger (mean, 47.9 years) than those with EGFR amplification (60.9 years) and were associated with significantly longer survival (mean, 27.1 versus 11.3 months; $P < 0.0001$). IDH1 mutations were frequent in glioblastomas diagnosed as secondary (22 of 30; 73%), but rare in primary glioblastomas (14 of 377; 3.7%; $P < 0.0001$). IDH1 mutations as genetic marker of secondary glioblastoma corresponded to the respective clinical diagnosis in 95% of cases. Glioblastomas with IDH1 mutation diagnosed as primary had clinical and genetic profiles similar to those of secondary glioblastomas, suggesting that they may have rapidly progressed from a less malignant precursor lesion that escaped clinical diagnosis and were thus misclassified as primary. Conversely, glioblastomas without IDH1 mutations clinically diagnosed as secondary typically developed from anaplastic rather than low-grade gliomas, suggesting that at least some were actually primary glioblastomas, that may have been misclassified, possibly due to histologic sampling error. **CONCLUSION:** IDH1 mutations are a strong predictor of a more favorable prognosis and a highly selective molecular marker of secondary glioblastomas that complements clinical criteria for distinguishing them from primary glioblastomas.

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