Glioblastomas with IDH1/2 mutations have a short clinical history and have a favorable clinical outcome.


Abstract

OBJECTIVE: Glioblastomas with isocitrate dehydrogenase 1/2 mutations comprise a biologically distinct subgroup of glioblastomas. We studied isocitrate dehydrogenase 1/2 mutant glioblastomas at the clinical, molecular and radiological levels to define their clinical features, including the prognostic value of isocitrate dehydrogenase 1/2 mutations compared with isocitrate dehydrogenase 1/2 wild-type glioblastomas.

METHODS: We investigated 128 newly diagnosed glioblastoma patients who were treated at our institute between January 2005 and May 2013. Isocitrate dehydrogenase 1/2 mutation status was determined using pyrosequencing. O-6-methylguanine deoxyribonucleic acid methyltransferase promoter methylation and 1p/19q co-deletions were also analyzed using pyrosequencing and multiplex ligation-dependent probe amplification, respectively.

RESULTS: Isocitrate dehydrogenase 1/2 mutations were detected in 10 of 128 patients (7.8%). Isocitrate dehydrogenase 1/2 mutations were correlated with a younger age, the presence of an oligodendroglial component and 1p/19q co-deletions and a longer survival time. The interval from initial symptom to initial operation did not differ according to isocitrate dehydrogenase 1/2 mutation status (median interval: 2.3 versus 1.2 months; P = 0.13). Two of three isocitrate dehydrogenase 1/2 mutant glioblastomas harboring 1p/19q co-deletions had an oligodendroglial component and were associated with a prolonged survival time. Multivariate analysis of 90 patients treated with temozolomide-based chemoradiotherapy indicated that age, extent of resection, postoperative Karnofsky performance score and O-6-methylguanine deoxyribonucleic acid methyltransferase promoter methylation were correlated with better survival. Isocitrate dehydrogenase 1/2 mutations showed a trend for improved survival (P = 0.068).

CONCLUSIONS: Most isocitrate dehydrogenase 1/2 mutant glioblastomas have a short clinical history, and some isocitrate dehydrogenase 1/2 mutant glioblastomas harboring 1p/19q co-deletions behave like oligodendrogial tumors. Isocitrate dehydrogenase 1/2 mutations may have a positive prognostic impact on the Japanese population.

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KEYWORDS: IDH1/2; MGMT; glioblastoma; prognostic factor; temozolomide

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