Expansion of CD133-positive glioma cells in recurrent de novo glioblastomas after radiotherapy and chemotherapy.

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Abstract
Object Recent evidence suggests that a glioma stem cell subpopulation may determine the biological behavior of tumors, including resistance to therapy. To investigate this hypothesis, the authors examined varying grades of gliomas for stem cell marker expressions and histopathological changes between primary and recurrent tumors. Methods Tumor samples were collected during surgery from 70 patients with varying grades of gliomas (Grade II in 12 patients, Grade III in 16, and Grade IV in 42) prior to any adjuvant treatment. The samples were subjected to immunohistochemistry for MIB-1, factor VIII, GFAP, and stem cell markers (CD133 and nestin). Histopathological changes were compared between primary and recurrent tumors in 31 patients after radiation treatment and chemotherapy, including high-dose irradiation with additional stereotactic radiosurgery. Results CD133 expression on glioma cells was confined to de novo glioblastomas but was not observed in lower-grade gliomas. In de novo glioblastomas, the mean percentage of CD133-positive glioma cells in sections obtained at recurrence was 12.2% ± 10.3%, which was significantly higher than that obtained at the primary surgery (1.08% ± 1.78%). CD133 and Ki 67 dual-positive glioma cells were significantly increased in recurrent de novo glioblastomas as compared with those in primary tumors (14.5% ± 6.67% vs 2.16% ± 2.60%, respectively). In contrast, secondary glioblastomas rarely expressed CD133 antigen even after malignant progression following radiotherapy and chemotherapy. Conclusions The authors' results indicate that CD133-positive glioma stem cells could survive, change to a proliferative cancer stem cell phenotype, and cause recurrence in cases with de novo glioblastomas after radiotherapy and chemotherapy.

PMID: 23991844 [PubMed - as supplied by publisher]