

Expression of angiogenesis related factors in glioblastoma and peritumor tissue

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Glioblastoma (GBM) is a lethal brain glial tumor characterized by extensive angiogenesis that is mostly triggered by tumor hypoxia. We previously reported that in GBM and in peritumor areas, endothelial cells expressed CD105, which probably marks newly formed vessels with a quite similar morphology. In this study, with the aim of better understanding the involvement of angiogenesis in tumor progression, we analyzed, by immunohistochemistry, the expression of Hypoxia-inducible factor (HIF) 1 α and 2 α , VEGF and its receptors (VEGFR-1 and -2) in GBM and in peritumor tissue. Twenty two patients were enrolled in this study. Tissue specimens were derived from enhanced lesion (first area) and white matter at a distance ≤ 1 mm from the tumor edge (second area). Immunoreactivity for all markers was detected not only in the tumor but also in the peritumor tissue and it was present in neoplastic cells, in endothelium and in apparently normal glial cells. HIF1 α and 2 α expression was mainly confined in the nuclei. VEGF, localized in the cytoplasm, showed diffuse expression with an intense staining in GBM. VEGFR-1 and 2 immunopositivity was localized especially to the cell membrane and also to the cytoplasm, as expected.

All molecule staining was evident in a heterogeneous manner and there was no significant difference in the expression marker levels between the first and second area also in relation to the presence or absence of tumor cells in the second area.

No significant correlation was found between the above molecule expression and survival time.

In conclusion, we demonstrated that HIF1 α , HIF2 α , VEGF and VEGFR-1 and -2 are present in peritumor area, probably reflecting perturbations of oxygenation emanating from the tumor microenvironment. Since, unfortunately, the response to anti-VEGF therapy is transient and the majority of patients eventually relapse, the gain of a deeper knowledge of the above molecule role, in the peritumor tissue, may lead to consider them as the target for new treatment regimens to counteract angiogenesis.

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Key words

Glioblastoma, peritumor tissue, angiogenesis, HIF1 α , HIF2 α , VEGF and VEGFR-1 and-2.