Valproic Acid inhibits angiogenesis in vitro and glioma angiogenesis in vivo in the brain.

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Abstract

Antiangiogenic strategy is promising for malignant glioma. Histone deacetylase inhibitors (HDACIs) are unique anticancer agents that exhibit antiangiogenic effects. The in vitro and in vivo antiangiogenic effects of HDACIs, valproic acid (VPA), were investigated in malignant glioma in the brain. In vitro, VPA preferentially inhibited endothelial cell proliferation compared to glioma cell proliferation at the optimum concentration in a dose-dependent manner. VPA reduced vascular endothelial growth factor (VEGF) secretion of glioma cells in a dose-dependent manner under both normoxic and hypoxic conditions. VPA was also found to inhibit tube formation in the angiogenesis assay. In vivo, treatment with VPA combined with irinotecan reduced the number of vessels expressing factor VIII in the brain tumor model. VPA inhibits glioma angiogenesis by direct (inhibition of endothelial cell proliferation and tube formation) and indirect (decreased secretion of VEGF by glioma cells) mechanisms. These data suggest a potential role for VPA as an adjuvant therapy for patients with malignant glioma.


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