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Antiangiogenic therapy and mechanisms of tumor resistance in malignant glioma.

Rahman R, Smith S, Rahman C, Grundy R.

Children's Brain Tumour Research Centre, Medical School, Queens Medical Centre, University of Nottingham, Nottingham NG7 2UH, UK.

Abstract

Despite advances in surgery, radiation therapy, and chemotherapeutics, patients with malignant glioma have a dismal prognosis. The formations of aberrant tumour vasculature and glioma cell invasion are major obstacles for effective treatment. Angiogenesis is a key event in the progression of malignant gliomas, a process involving endothelial cell proliferation, migration, reorganization of extracellular matrix and tube formation. Such processes are regulated by the homeostatic balance between proangiogenic and antiangiogenic factors, most notably vascular endothelial growth factors (VEGFs) produced by glioma cells. Current strategies targeting VEGF-VEGF receptor signal transduction pathways, though effective in normalizing abnormal tumor vasculature, eventually result in tumor resistance whereby a highly infiltrative and invasive phenotype may be adopted. Here we review recent anti-angiogenic therapy for malignant glioma and highlight implantable devices and nano/microparticles as next-generation methods for chemotherapeutic delivery. Intrinsic and adaptive modes of glioma resistance to anti-angiogenic therapy will be discussed with particular focus on the glioma stem cell paradigm.

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