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Metabolic therapy: A new paradigm for managing malignant brain cancer.

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Abstract

Little progress has been made in the long-term management of glioblastoma multiforme (GBM), considered among the most lethal of brain cancers. Cytotoxic chemotherapy, steroids, and high-dose radiation are generally used as the standard of care for GBM. These procedures can create a tumor microenvironment rich in glucose and glutamine. Glucose and glutamine are suggested to facilitate tumor progression. Recent evidence suggests that many GBMs are infected with cytomegalovirus, which could further enhance glucose and glutamine metabolism in the tumor cells. Emerging evidence also suggests that neoplastic macrophages/microglia, arising through possible fusion hybridization, can comprise an invasive cell subpopulation within GBM. Glucose and glutamine are major fuels for myeloid cells, as well as for the more rapidly proliferating **cancer** stem cells. Therapies that increase inflammation and energy metabolites in the GBM microenvironment can enhance tumor progression. In contrast to current GBM therapies, metabolic therapy is designed to target the metabolic malady common to all tumor cells (aerobic fermentation), while enhancing the health and vitality of normal brain cells and the entire body. The calorie restricted **ketogenic** diet (KD-R) is an anti-angiogenic, anti-inflammatory and pro-apoptotic metabolic therapy that also reduces fermentable fuels in the tumor microenvironment. Metabolic therapy, as an alternative to the standard of care, has the potential to improve outcome for patients with GBM and other malignant brain cancers.

KEYWORDS: Brain tumor; Caloric restriction; Energy metabolism; Glioma; **Ketogenic** diet

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