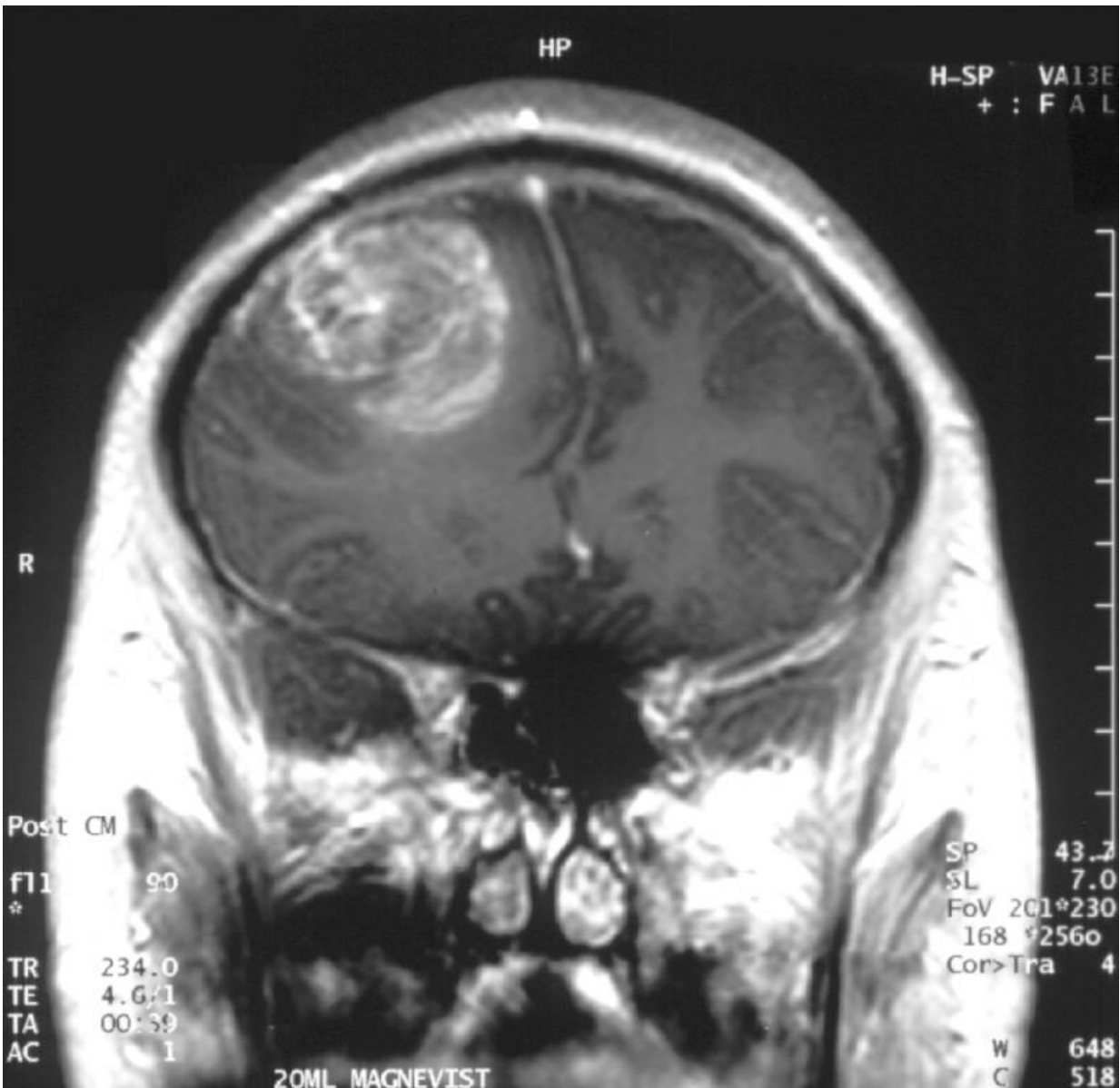


# Case study shows patient on ketogenic diet living fully with IDH1-mutant glioblastoma

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Glioblastoma (astrocytoma) WHO grade IV—MRI coronal view, post contrast. 15 year old boy. Credit: Christaras A/ Wikipedia.

A British man who rejected the standard of care to treat his brain cancer has lived with the typically fatal glioblastoma tumor growing very slowly after adopting a ketogenic diet, providing a case study that researchers say reflects the benefits of using the body's own metabolism to fight this particularly aggressive cancer instead of chemo and radiation therapy.

Published recently in the journal *Frontiers in Nutrition*, the report is the first evaluation of the use of ketogenic metabolic therapy (KMT) without chemo or radiation interventions, on a patient diagnosed with IDH1-mutant glioblastoma (GBM). Ketogenic therapy is a non-toxic nutritional approach, viewed as complementary or alternative, that uses a low-carbohydrate, [high-fat diet](#) to manage a range of cancers, including glioblastoma.

In this particular case, the patient's tumor contained a mutation, known as the IDH1. This mutation is acquired by chance and is known to improve overall survival. So the findings are particularly relevant to other patients whose tumors contain this mutation, according to Boston College Professor of Biology Thomas Seyfried, a co-author of the report and a leading researcher who has long advocated the benefits of KMT to treat disease.

"As GBM, like most malignant cancers, is dependent on fermentation for energy synthesis and survival, the simultaneous restriction of fermentable fuels, such as glucose and glutamine, while elevating non-fermentable ketone bodies, offers a non-toxic therapeutic strategy for managing GBM," said Seyfried. "Further studies will be needed to test this hypothesis in other patients diagnosed with GBM."

Glioblastoma kills about 15,000 people each year and remains largely unmanageable. While the standard of care has shifted to new immunotherapies, the median survival time of 11 to 15 months for GBM has not improved significantly for more than 100 years, according to the co-authors.

A number of high-profile cases have illustrated the deadly progression of GBM. The late U.S. Sen. John McCain was diagnosed at age 80 with glioblastoma in July 2017, and died in August 2018. U.S. Sen. Edward M. Kennedy lived for a year after his diagnosis with GBM, dying at age 77. Beau Biden, son of U.S. President Joe Biden, was diagnosed at age 44 with GBM in August 2013, and died in May 2015.

The current standard of care for GBM involves surgical resection, radiation, and chemotherapy, which have been shown in studies to result in significant toxicity. However, large-scale clinical trials for alternative therapies are difficult to initiate, leading researchers to carefully examine individual cases.

The patient in this case was diagnosed with glioblastoma in 2014 and eschewed the traditional standard of care and instead embarked on a self-directed ketogenic diet—low in carbohydrates and high in fat—in an effort to manage his cancer.

The researchers found "the patient's tumor continued to grow very slowly over a three-year period without expected vasogenic edema until 2017," according to Seyfried and his co-authors, Boston College researcher Purna Mukherjee, Aditya Shivane, MD, of University Hospital Plymouth NHS Trust, in the United Kingdom, U.S.-based nutritionist Miriam Kalamian, Joseph Maroon, MD, of the University of Pittsburgh, and Giulio Zuccoli, MD, of the Drexel University School of Medicine

At that point, the patient underwent "surgical debulking" of his tumor. The pathology specimen confirmed the diagnosis of GBM and that the patient's tumor also contained the IDH1 mutation.

"Following surgery, the patient continued with a self-administered [ketogenic diet](#) to maintain low Glucose Ketone Index (GKI) values, indicative of therapeutic ketosis," the researchers report. "In light of continued slow progression of the residual tumor, the patient intensified his KMT starting in October, 2018 with inclusion of mindfulness techniques to reduce stress. While Magnetic Resonance Imaging (MRI) shows slow interval tumor progression, the patient remains alive with a good quality of life at the time of this report." He is now at 82 months from original diagnosis.

"We were surprised to discover that KMT could work synergistically with the IDH1 mutation to simultaneously target the two major metabolic pathways needed to drive the growth of GBM," said Seyfried. "Glucose drives the glycolysis pathway, while glutamine drives the glutaminolysis pathway."

He added: "No tumor, including GBM, can survive without glucose and glutamine. Our study has identified a novel mechanism by which an acquired somatic mutation acts synergistically with a low-carbohydrate, high-fat diet to provide long-term management of a deadly brain tumor."

Despite the compelling interest in such individual case studies, the co-authors note, "We cannot predict if the therapeutic response to KMT seen in our GBM patient will also be seen in other similarly treated GBM patients. For those GBM patients not fortunate enough to have acquired the spontaneous IDH1 mutation in their tumor, glutamine targeting drugs used with KMT will be necessary to reduce tumor growth."

The researchers noted that additional studies they've conducted have shown that the simultaneous targeting of glucose and glutamine availability, using KMT and the a pan-glutaminase inhibitor—known as 6-diazo-5-oxo-L-norleucine (DON)—can significantly prolong survival in preclinical syngeneic glioblastomas in mice. Earlier research has shown that ketogenic diets can facilitate delivery of small-molecule therapeutic drugs through the blood brain barrier without toxicity.

**More information:** Thomas N. Seyfried et al, Ketogenic Metabolic Therapy, Without Chemo or Radiation, for the Long-Term Management of IDH1-Mutant Glioblastoma: An 80-Month Follow-Up Case Report, *Frontiers in Nutrition* (2021). [DOI: 10.3389/fnut.2021.682243](https://doi.org/10.3389/fnut.2021.682243)

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