

Malignant Gliomas in Adults

TO THE EDITOR: In their Medical Progress article, Wen and Kesari (July 31 issue)¹ review the molecular pathogenesis of gliomas yet do not mention the role that DNA tumor viruses may play in tumor formation. In the same issue, Prins et al.² provide evidence that strongly supports prior research findings that link cytomegalovirus to glioma. Other DNA viruses, such as JC virus, have been implicated in glioma pathogenesis.³ In this regard, it is also important to note that detection of atypical nuclei and high-proliferation indexes in a brain biopsy led to, in at least one instance, the misdiagnosis of a grade III astrocytoma; subsequent polymerase-chain-reaction studies led to a diagnosis of progressive multifocal leukoencephalopathy related to JC virus.⁴ Further research is therefore needed to understand the link between DNA viruses and glioma.

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3. Boldorini R, Pagani E, Car PG, et al. Molecular characterisation of JC virus strains detected in human brain tumours. *Pathology* 2003;35:248-53.
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THE AUTHORS REPLY: Because of space limitations, our review was largely restricted to information that was strongly supported by data. We agree that the studies regarding the potential role of

tumor viruses in the pathogenesis of malignant gliomas are intriguing. However, much more research is required to confirm such a link. Although some studies indicate the presence of cytomegalovirus in malignant gliomas,¹ other studies have failed to confirm these findings.^{2,3} In addition, the detection of viruses such as cytomegalovirus in malignant gliomas may not necessarily indicate that these viruses contributed to the transformation of the tumor. An alternative explanation could be reactivation of virus as a result of immunosuppression related to the tumor, corticosteroids, or chemotherapy.² With the advent of genomewide analytic tools and the recent advances characterizing the glioblastoma genome,⁴ we may now be able to address the issue of the presence of infectious agents in human cancer by using newer approaches, such as genomic subtraction technologies.⁵

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1. Mitchell DA, Xie W, Schmittling R, et al. Sensitive detection of human cytomegalovirus in tumors and peripheral blood of patients diagnosed with glioblastoma. *Neuro Oncol* 2008;10:10-8.
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Case 20-2008: Abdominal Pain and Weakness after Gastric Bypass Surgery

TO THE EDITOR: In the discussion of the Case Record by Bonkovsky et al. (June 26 issue)¹ about a patient with porphyria who became symptomatic after gastric bypass surgery, there was no mention of the patient's nutritional care, which may have played a major contributory role. The persistent ketonuria before hospitalization indicates a daily carbohydrate intake of less than 100 g, where-

as the very low serum creatinine level on admission indicates limited meat intake and a marked reduction in skeletal muscle, reflecting severe protein-calorie malnutrition.² These findings are consistent with limited energy and protein intake postoperatively, which was at least 18 days before a subsequent hospital admission that was more than 5 weeks in duration. If the patient remained

in a semistarved state in terms of protein and energy for that entire period, this would contribute substantially to the extreme motor weakness that increased with time and perhaps contributed to the continued activity of the porphyria. An additional factor is the possible contribution of deficiencies of thiamine and other micronutrients; these deficiencies have been observed previously after gastric bypass and are associated with polyneuropathy and encephalopathy.³⁻⁵

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4. Juhasz-Pocsine K, Rudnicki SA, Archer RL, Harik SI. Neurologic complications of gastric bypass surgery for morbid obesity. *Neurology* 2007;68:1843-50.
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TO THE EDITOR: Bonkovsky et al. report an interesting case of a 57-year-old woman with abdominal pain and weakness 1 month after gastric bypass surgery for morbid obesity. The cause of the

symptoms could have been a primary disease or a consequence of the bariatric surgery. Abdominal pain is a frequent symptom after surgery for obesity and is caused by a variety of postoperative complications (shown in Table 2 of the article). Neurologic complications (Table 1) are not uncommon after bariatric surgery and have been reported in 5 to 10% of patients.¹ Any part of the nervous system may be involved, with a broad variety of symptoms. The majority of neurologic complications after bariatric surgery are caused by nutritional deficiencies, particularly deficiencies of iron, folate, vitamin B₁, and vitamin B₁₂, and they are mostly recognized as late complications.² Vitamin B₁ deficiency is a rare but important cause of early acute polyneuropathy after bariatric surgery.³ Furthermore, neurologic disorders may be the result of accelerated fat metabolism. Some authors suggest that a toxin from the fast metabolism of fat, a loss of carnitine, or lactate acidosis is responsible.^{1,2}

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Table 1. Progressive Weakness after Bariatric Surgery.

Signs and Symptoms	Cause
Paresthesia, loss of cutaneous sensation, decreased reflexes, ataxia	Vitamin B ₁₂ deficiency
Peripheral neuropathy	Folate deficiency
Peripheral neuropathy (predominantly affects the lower limb; sensory and motor)	Vitamin B ₁ deficiency
Confusion, cerebellar dysfunction, oculomotor abnormalities (e.g., Wernicke's encephalopathy)	Vitamin B ₁ deficiency
Fatigue, hallucinations, encephalopathy, pellagra (i.e., symmetric rash with hyperpigmentation, hyperkeratosis, and desquamation)	Niacin deficiency
Polyneuropathy	Hypokalemia, hypophosphatemia, hypomagnesemia
Polyneuropathy and ataxia	Extensive demyelination with extensive accumulation of lipofuscin
Confusion, abnormal behavior, diminished or absent muscle reflexes	Rapid metabolism of fat
Myalgia	Autoimmune process
Guillain-Barré syndrome	Parainfectious process (intraabdominal infection)
Acute disseminated encephalomyelitis	Parainfectious process

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TO THE EDITOR: The reduction in food intake, frequent vomiting, and the loss of absorptive surface puts patients at risk of vitamin deficiency after bariatric surgery. In the case described, the patient's anorexia and severe peripheral neuropathy, which developed a few weeks after surgery, are consistent with thiamine deficiency. One of the most serious consequences of this deficiency is Wernicke's encephalopathy. The well-known triad of confusion, ophthalmoplegia, and ataxia plus typical laboratory or radiologic findings is not always present.^{1,2} The diagnosis of Wernicke's encephalopathy is usually missed clinically.³ Intravenous administration of dextrose or carbohydrate loading may worsen the course of this deficiency syndrome.¹ Parenteral thiamine prevents or treats thiamine deficiency in poorly nourished patients.^{1,2}

Perhaps thiamine deficiency played some part in the confusing and serious clinical course of this patient. It would be interesting to know whether she received parenteral vitamins at any point in her complicated course after bariatric surgery.

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TO THE EDITOR: Genetic testing may have established the diagnosis of variegate porphyria in this patient, but the apparent fact that there was no history of skin lesions before she received parenteral iron-containing heme suggests newly unmasked porphyria cutanea tarda superimposed on variegate porphyria. (The occurrence of variegate and cutanea tarda porphyria in the same family has been described in persons with mixed Dutch and Bantu ancestry.¹) Further genetic testing for mutations in the *HFE* hemochromatosis gene would help corroborate that porphyria cutanea tarda also was present in this patient.

In addition, there are two errors in Table 4 of the article. The deficient enzyme for protopor-

phyria (ferrochelatase) is missing from the table. "Hepatocarbonylporphyrin" should be heptacarboxylporphyrin (shown correctly in Table 5).

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1. Dean G. *The porphyrias*. Philadelphia: J.B. Lippincott, 1963.

THE DISCUSSANT AND A COLLEAGUE REPLY: Bistrrian, Baierlein et al., and Frankenburg point out the most common causes of neurologic disorders after gastric bypass surgery. Thiamine deficiency is an important consideration, especially in patients with recurrent vomiting; however, vomiting was not a feature of this patient's presentation. During the first 6 weeks after surgery, she was consuming the recommended liquid nutritional drinks, eating soft food without difficulty, and taking multivitamins regularly.

When weakness suddenly developed, thiamine was administered intravenously and vitamin B₁₂ was administered intramuscularly. The serum thiamine level obtained before thiamine administration was 72 nmol per liter (normal range, 87 to 286); the levels of vitamins A, B₂, B₆, B₁₂, and folate were normal. Within 24 hours after intubation, a nasogastric tube was placed; 10 days later, laparoscopic exploration was performed that showed normal anatomy after gastric bypass, and a gastrostomy tube was placed in the bypassed gastric remnant. Thus, we believed her nutrition was adequate.

In response to the comment of Kalivas: subsequent testing for mutations in the gene for familial hemochromatosis (*HFE*) showed no mutations. However, the serum ferritin levels were persistently high after discontinuation of heme infusions, and regular phlebotomy was recently begun for a presumptive diagnosis of acquired porphyria cutanea tarda. Kalivas also correctly points out in Table 4 the omission of ferrochelatase (the gene and enzyme that are defective in erythropoietic protoporphyria) and the misspelling of heptacarboxylporphyrin.

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