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Opinion

Nutrient Deprivation: A Cancer Treatment of Last Resort

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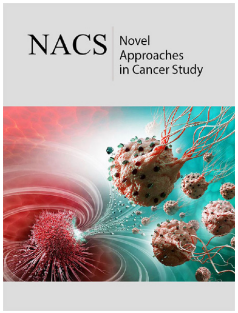

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Opinion

A West Hartford high school senior was diagnosed with brain cancer, "a high-grade glioma." Her parents brought her to Dana Farber Institute in Boston Massachusetts seeking the world's best treatment. They took an apartment in Boston to support her through the ordeal. The patient received surgery and radiation, and, at five months after diagnosis, showed improvement, but, at seven months, relapsed. She received more surgery and radiation but died nine months after diagnosis [1]. It's a tragic horror story that plays out in this way for some 3,000 young and many more, older adults each year. The patient's parents did all they could to get their daughter the best treatment. But, in the end, it was inadequate. And it would have been inadequate at any cancer center. There simply is no dependable treatment for end-stage glioma. "Clearly, there exists an unmet need for innovative approaches" [2].

After the above patient's relapse, it was unreasonable to imagine that more surgery or radiation would effect a cure: "As soon as they took it out, there was evidence that it had already spread" (patient's father). To have a shot at curing advanced cancer, therapeutic thinking has to be out-of-the-box. Experts, however, are not famous for such thinking. In medicine, thinking out-of-the-box is the province of amateurs like Leeuwenhoek, Jenner, Pasteur, Koch, Ehrlich, and Fleming. I suggest we begin with what makes gliomas so hard to kill, the hypoxia and poor perfusion. This impairs radiation, which depends on oxygen for efficacy, as well as chemotherapy, which depends on circulation for access to the tumor. It's no wonder that the magnitude of hypoxia predicts prognosis [3]. Let's imagine how we might turn tumor hypoxia and poor perfusion to the patient's advantage. Key nutrient deficiency has such potential: Remove an essential nutrient from the diet, tolerate the side effects as long as possible, and then, restore the nutrient in trace amount. The difference in blood supply between cancer and normal tissue should deliver the nutrient to normal cells, while depriving the cancer. Start with folate deprivation. It's simple, inexpensive, relatively safe, inherently promising, does not require regulatory approval, and allows for unlimited variations on the basic theme. But no variation has yet been tested, so this innovation would of necessity be restricted to cases of last resort, such as the above. But it should work against advanced solid hypoxic tumors of all varieties.

Methotrexate inhibits cell proliferation by blocking the conversion of dihydrofolate to tetrahydrofolate, which is essential to DNA replication. It ranks among the oldest and most effective anti-cancer agents. Benefits are often short-lived, however, because cancer cells almost inevitably become resistant. Folate deprivation will prevent tetrahydrofolate synthesis and should accomplish the same benefits as Methotrexate without the possibility of cancer becoming resistant. The side effect of folate deprivation is anemia, which can be tolerated when mild, or treated with trace doses of folate when serious. Blood should take the added folate to normal cells preferentially, while permitting it only to trickle into the cancer. If, for some reason, the cancer fails to respond to folate deprivation, or if the anemia from it does not respond to trace folate supplementation, then restore the folate to full normal

levels, and remove another key nutrient from the diet, such as thiamine or an essential amino acid, e.g., phenylalanine. Thiamine is required for ribose synthesis. All eight essential amino acids are required for protein synthesis. Deficiency of either thiamine or an essential amino acid should stop cell division. Omacetaxine is an FDA-approved inhibitor of global protein synthesis that has shown activity against cancer. But I suspect impaired blood flow to solid tumors inhibits its efficacy by blocking access to its targets. It's the same problem that stifles Methotrexate and other chemotherapeutic agents. Deprivation of essential amino acids should inhibit global protein synthesis, while avoiding any such blood-tumor barriers. When side effects of thiamine or essential amino acid deficiency become serious, restore the vitamin or amino acid in trace amounts. Blood should take the nutrient to normal cells preferentially. Combinations and schedules of essential nutrient deprivation are limitless.

Hypoxic tumors are dependent on glycolysis for ATP, and, therefore, require some 18X more glucose to produce the same amount of ATP as normal, well-oxygenated, tissue. Diets devoid of glucose, i.e., ketogenic diets, should stress hypoxic tumors more than normal tissue. The drop in dietary glucose will drop plasma insulin and release Free Fatty Acids (FFA) from adipose tissue. But there are no anaerobic pathways by which FFA can produce ATP. Hypoxic tumors should starve, therefore, in response to ketogenic diets, while normal tissue feasts on FFA. Trials of ketogenic diets, however, were not curative [4]. I suspect gluconeogenesis is the problem. Fortunately, alcohol or Metformin can be used to inhibit gluconeogenesis. It is essential that the alcohol be distilled and not contain any sugar or carbohydrates. I suggest vodka. If the combination of ketogenic diet with vodka or Metformin works, the tumor would die quickly. But there are risks, and patients must beware of them, such as potentially lethal hypoglycemia and tumor lysis syndrome. Inhibition of gluconeogenesis should only be undertaken with close supervision of a physician, who is prepared to maintain hypoglycemia at a safe level and protect against tumor lysis syndrome by hydration and other means.

A ketogenic diet can be both folate- and thiamine-free. For a time, it can even be protein-free. In combination with vodka or Metformin, this folate and thiamine and protein-free ketogenic diet, i.e., a total fast, would constitute the all-out, maximum attack on cancer. Eat nothing, or only fat, and every hypoxic, solid tumor should die as a consequence. There's legitimate hope in that. But close physician supervision is essential to protect against life-threatening consequences of fasting. Consume water and electrolytes with sips of vodka until the plasma glucose begins to fall below normal. Maintain plasma glucose concentration at a safe, but hypoglycemic level. Sip olive oil for energy. Use masks, gloves, gowns, and isolation to protect the patient from infection. Consider total body hyperthermia both to protect against the hypothermia that accompanies fasting, and as an added stress on the cancer [5]. When protein deficiency becomes a problem, serve egg whites from humane-certified farms. But hold egg consumption to a minimum because amino acids in excess become carbohydrates, that will feed the tumor.

Fever is the body's response to infection. In the old era, it was thought to be part of the problem and was attacked with antipyretics. Now fever is known to be an ally in fighting infection. Cachexia is the body's response to cancer. Even now, it tends to be thought of as part of the problem and is often attacked with nutritional supplements. But such supplements do not improve survival. I suspect cachexia is, like fever to infection, an ally. Encourage patients to work with this natural response by deleting key nutrients from their diets as described above. Bolster patients' spirits with nature appreciation, music, art, team-spirit, humor, and empathy. Find hope in truth. Nutrient deprivation is the best chance at stopping advanced cancer. It's untested and risky but carries the potential for remission or cure. As a treatment of last resort, nutrient deprivation is worthy of consideration.

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