

Treatment capitalizes on unique qualities of radioisotope to prolong lives of brain tumor patients

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In a study to determine safe dosages of the isotope astatine-211 for patients with recurring brain tumors, researchers were pleasantly surprised to find that not only was the isotope's potency sufficient to kill residual cancer cells without damaging sensitive healthy brain cells, but the patients experienced longer survival rates.

“Astatine-211 has as much as five times or more cell-killing efficiency than the standard treatments of external beam radiation or beta-particle injection,” said Michael R. Zalutsky, professor of radiology and biomedical engineering at Duke University Medical Center in Durham, N.C. The ability to deliver such a potent cancer killer without causing neurotoxicity (damage to the delicate neurological system that controls brain function) would be a tremendous step forward in combating this lethal disease, he said.

In the past, surgeons have been able to remove the tumor bulk, Zalutsky added, but were unable to see and thereby identify any residual cancerous cells that had escaped into the margins of the healthy tissue surrounding the tumor. It is these cells, however, that continue to grow into new tumors and eventually kill the patient. Scientists have long believed that radioimmunotherapy (RIT) could be the best way to destroy these cells, but demonstrating the feasibility of delivering a sufficiently potent radioactive isotope without harming healthy brain tissue has been heretofore impossible.

In the study, reported in the *Journal of Nuclear Medicine*, astatine-211 was chemically linked to the antibody 81C6, known to seek out and bind specifically to brain cancer cells. It was then administered to 18 patients with recurrent malignant brain tumors by injection into a surgically created cavity from which the visible tumor had been removed. Because alpha particles, such as those emitted by astatine-211, are large and more highly charged, compared to the much smaller and faster beta particles, they are able to travel to a depth of only two to three cells into the affected area, which is enough to deliver the fatal payload. Compared to other alpha emitters, astatine-211 has a relatively short lifespan (approximately 7 hours), which means that the radioactivity falls off rapidly and patients experience few, if any, side effects.

In this first study evaluating astatine-211 as a targeted radiotherapeutic agent in cancer patients, researchers were expecting to determine only dose-limiting toxicity (the amount of isotope necessary to destroy the cancer without killing healthy tissue). In addition, they discovered that many patients experienced an extended survival rate, ranging from an average of 52 weeks to 3 years (compared to 26 weeks for most recurrent brain tumor patients).

Noting that brain tumors recur with an extremely poor prognosis, Zalutsky said, “There is an incredible need for brain cancer treatments, and this finding gives us a potentially valuable weapon in this fight.”

Researchers say future studies may use a “radiotherapeutic cocktail” of both alpha and beta particles attached to the same monoclonal antibody to deliver a treatment with a wider range for larger tumors along with a more focused radiation for smaller tumors or residual cancer cells. Additional studies propose using astatine-211 on other “compartmentalized” cancers, such as ovarian and breast cancers that have spread to the central nervous system. All of these studies, however, will be delayed unless adequate quantities of astatine-211 can be

produced.

“Right now in the United States, there are only three places where the isotope is produced,” said Zalutsky, who contributed to the 2007 National Academy of Sciences report that encouraged Congress to increase funding for nuclear medicine research and treatment, including the production of promising isotopes such as astatine-211. “Patients eligible for such studies will be put on hold until our nation invests significantly in the research needed to eradicate these killer diseases.”

According to the American Cancer Society, brain cancers are some of the most aggressive and deadly forms of cancer because they typically hide from the immune system and grow unchecked.

RIT is the use of an antibody (or protein produced by the immune system) that recognizes foreign substances, or antigens, and attaches to them. When these antigen-binding antibodies are chemically combined with a radioactive substance, they act as a “guided missile” to deliver a lethal dose of radiation directly to the tumor cells. The antibody’s ability to bind to a tumor-associated antigen increases the dose delivered to the tumor cells while decreasing the dose to normal tissues.

Source: Society of Nuclear Medicine

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