American Brain Tumor Association

ADVANCES IN BRAIN TUMOR DIAGNOSIS AND TREATMENT

There are many different types of brain tumors. These tumors range from small, benign tumors requiring no treatment to very malignant, aggressive tumors needing a wide array of advanced, and sometimes experimental, therapies. Our understanding of brain tumors has advanced greatly in the past few years, primarily due to basic and clinical research leading to new and innovative ideas. This article reviews some of the most recent advances in diagnosing and treating brain tumors.

Years ago, most people assumed that a diagnosis of a "brain tumor" was the worst possible news that one could hear. Proper functioning of one's brain is certainly key to good quality of life, and anything that might disturb the normal functioning of this organ is naturally thought to lead to a shortened life with poor mental and physical capacities. The reality is that a large number of individuals with brain tumors have a good outcome following treatment and, with help from their family, friends and healthcare team, are able to return to a good quality of life.

Brain tumors are unique because they occur in the skull -- a confined space with rigid walls. A brain tumor takes up space normally allocated to the brain. As the tumor continues to grow, it pushes aside or compresses the brain. This can cause a build up of pressure in the skull that leads to symptoms such as headaches, seizures and strokes. Brain tumor treatment is designed to eliminate the tumor or reduce tumor size, thus allowing the surrounding brain to resume its normal functions.

Brain tumors are referred to as "benign" or "malignant." An example of a benign brain tumor is a meningioma – a generally slow-growing, localized mass which is actually located outside the structure of the brain but can compress the brain. These tumors can often be removed completely with microneurosurgical techniques, and may require no further surgical treatment. In some cases, these tumors are tucked away in areas that cannot be reached safely, or they are wrapped around critical structures such as the carotid artery or the optic nerve. In these situations, specialized radiosurgical techniques might be considered to either shrink these tumors or stop their growth.

"Malignant" brain tumors can either be primary brain tumors which arise directly from the cells in the brain, or metastatic tumors arising from a cancer elsewhere in the body which spread to the brain (such as lung cancer or breast cancer). Many types of primary brain tumors are capable of invading the surrounding brain tissue. Metastatic brain tumors are generally distinct from the brain tissue itself. Significant advances in diagnosing and treating all of these brain tumors have been made, and as one can imagine, there is substantial overlap between these two areas.

Diagnosis*:* The field of neuroimaging brought us new and improved methods for visualizing the anatomy and physical characteristics of brain tumors. CT and MRI imaging of the brain revolutionized the diagnosis and treatment of brain tumors in the 1970's and 1980's. In this decade, advances in MR spectroscopy (MRS) now assist in revealing the chemistry and physiology of brain tumors while helping discern active, growing tumor from necrotic tissue. Functional magnetic resonance imaging (fMRI) can now be used to map the function of the area surrounding a tumor, which in turn helps the neurosurgeon design surgical approaches that avoid areas of critical brain function. In this technique, fMRI is obtained while the patient performs tasks such as reading words or tapping their finger. The scan detects very subtle increases in blood flow and oxygen utilization in the specific areas of the brain that control these tasks, mapping these changes on the image of the brain. Diffusion tensor imaging (DTI) is another new form of MR imaging which shows the relationship of a brain tumor to nerve pathways in the brain. This technique can also be used by a neurosurgeon to avoid unnecessary deficits from surgery.

Another major advance in diagnosis is better characterization of the genetic makeup of brain tumor cells. As researchers look more critically at the chromosomes and genes of brain tumor tissue, they have identified characteristics that may greatly influence the treatment of these tumors. For example, individuals with oligodendroglioma might respond well to chemotherapy if cells in their tumor show a loss of genetic material in two different chromosomes. Other gene expression studies are leading to the development of drugs specifically targeted to either stop tumor growth by interfering with specific biologic pathways or are aimed at killing specific tumor cells.

Treatment: Advances have been made in new and improved methods in surgery, radiation and chemotherapy and in various combinations of these treatments. It has been known for some time that primary malignant brain tumors are difficult tumors to treat, and neither surgery alone, radiation alone, nor chemotherapy alone can treat these tumors successfully. On the other hand, it is also well established that various combinations of these modalities can have a significantly favorable impact on these tumors.

For many years, standard chemotherapy for brain tumors involved the injection of alkylating agents, such as BCNU, which worked by scrambling the DNA in cells ready to divide. This prevented cellular division and eventually led to cell death. Unfortunately these drugs were not very specific, affecting normal dividing cells as well as tumor cells, and causing significant side effects. Some of these drugs were also unable to pass through the blood-brain barrier which serves as a filter between the blood and the brain. A newer generation oral drug, temozolomide (Temodar), passes through the blood-brain barrier and has already been shown to be a major advance in the treatment of brain tumors.

It has always been felt that the ideal anti-brain tumor drug or agent would be a substance that selectively seeks out and destroys tumor cells, leaving normal cells alone. Antibodies are natural immune system molecules that perform such a function when they seek out and destroy invading bacteria, but until recently, scientists were unable to engineer these molecules to effectively and selectively recognize and destroy only brain tumor cells. In recent years, great strides were made toward accomplishing this "selectivity" feat and research now focuses on the best way to deliver these molecules. Current studies inoculate or "vaccinate" patients with their own tumors, building up the patient's immune system and stimulating it to make antibodies against the tumor cells.

New therapies have also been developed which combine surgery and a drug delivery system that bypasses the blood brain barrier obstacle. An example is convection enhanced delivery (CED) of new anti-tumor drugs in individuals with malignant tumors. In this technique, a drug can be delivered through 3 to 4 small catheters implanted into the brain surrounding a resected tumor. The drug is slowly pumped directly into the brain tissue, bypassing the challenges of getting the drug past the blood brain barrier. Other study designs combine an anti-tumor antibody with a radioactive agent that attaches itself to the tumor cells, and then kills them with radioactivity. In some trials, these agents are delivered using CED. In other trials, the agents are injected into the space left behind after the tumor has been removed.

Advances in radiation delivery have also made it possible to more effectively and safely treat brain tumors. New ways of focusing radiation beams allow the delivery of more radiation to the tumor and less radiation to the surrounding normal brain. Computerized robotic radiation delivery systems make these advances possible. These highly focused radiation systems are called stereotactic radiosurgery (SRS) since the ultimate effect is similar to a surgical resection. The most recent advances in radiosurgery combine the abilities of several pieces of radiation equipment into one unit.

New therapies are tested in organized research studies called clinical trials. For information about clinical trials for your type of tumor, call the National Cancer Institute's Cancer Information Service at 800-422-6237, or visit www.clinicaltrials.gov.

Scientists are also exploring the role of stem cells in the origins of brain tumors. It is thought a certain population of cells in a brain tumor act very much like normal stem cells seen elsewhere in the body -- except these stem cells are out of control and are programmed to produce brain tumor cells. These cells, characterized by a marker called CD133, are being intensively investigated in the hope future drugs can be designed to stop these stem cells from producing tumor cells.

Finally, the most important advance is the recognition that the successful treatment of brain tumors requires a dedicated team of researchers, neurosurgeons, neurologists, radiation oncologists, neuroradiologists, neuropathologists, medical oncologists, nurses, social workers, neuropsychologists, and rehabilitative medicine specialists all working together with the patient and his or her family. It is through this team effort that the best results, and highest quality of life, are achieved.

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