TREATMENT UPDATE:

Glioblastoma

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Treatment Update: Glioblastoma

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Each year, about 24,000 adults in the United States are diagnosed with a malignant primary brain tumor, a cancer that begins in the brain's cells, membranes, nerves or glands.

Tumors arising from the supportive tissue of the brain are called gliomas. Approximately 75 percent of malignant brain tumors are gliomas. Glioblastomas (also called glioblastoma multiforme, or GBM) are the most common form of this cancer, accounting for about 55 percent of cases.

The symptoms of primary brain tumors vary. Not everyone with a brain tumor will have these symptoms, and having some of these symptoms doesn't necessarily mean that a brain tumor is the cause. Talk with your doctor if you experience any of these general or specific signs and symptoms.

General signs and symptoms

- Headaches
- Seizures
- Changes in personality
- Memory lapses
- Nausea and vomiting
- Changes in vision

Specific signs and symptoms, depending on the location of the tumor

- A feeling of pressure in the head or headache
- Loss of balance
- Impaired fine-motor skills, such as the ability to button a shirt
- Impaired judgment
- Muscle weakness or paralysis
- Changes in speech, hearing, memory or emotional state
- Problems understanding or retrieving words
- Extreme sensitivity to touch
- Arm or leg weakness on one side of the body
- Confusing the left and right sides of the body

An MRI (magnetic resonance imaging) is often performed if a brain tumor is suspected. An MRI uses magnetic fields to detect tumors within the body. Other imaging tests, such as PET (positron emission tomography) and CT (computerized tomography) may also be conducted.

If a tumor is found, it is removed surgically (if possible) and tested for cancer cells in order to decide on a treatment approach. If the tumor is located in a part of the brain where surgery would pose a serious risk, a biopsy may be performed. In a biopsy, surgeons use computers to guide a needle into the skull, allowing for a small piece of the tumor to be removed. That sample is then examined under a microscope to see if it contains cancer cells.

Treatment Options

This booklet will focus on the treatment of glioblastoma, the most common type of malignant brain tumor. The standard of care for glioblastoma is surgery, followed by radiation and chemotherapy. By removing or shrinking the glioblastoma tumor, doctors relieve the pressure on the brain these tumors can cause. Treatment also reduces other symptoms such as seizures, headaches and difficulty with balance.

Surgery

Using a procedure called a craniotomy, the surgeon opens the skull and removes as much of the tumor as possible. Special computers hooked up to MRI monitors allow surgeons to view a "map" of different parts of the brain, helping to find and remove tumors more easily and safely.

Swelling in the brain (edema) can be caused by surgery or by the tumor itself. After surgery, doctors usually prescribe dexamethasone or another steroid medication to reduce edema and its symptoms, which can include seizures, memory problems and confusion. Because they are powerful medications, the use of steroids must be carefully monitored by a doctor.

Radiation

After the tumor is surgically removed, some cancer cells may still remain. These cells can act as seeds, sparking the growth of another tumor. To help destroy these cells, the area of the brain which surrounded the tumor is usually treated with radiation. Radiation works by damaging the DNA of cancer cells. People with glioblastomas typically get 30 radiation treatments, spaced over the course of six weeks.

"External beam radiation" is commonly used in treating glioblastomas. Standard external beam radiation uses a machine that directs a beam (or multiple beams) of radiation to the tumor. The use of CT, MRI and PET scans allows radiation oncologists to accurately target tumors, shaping the radiation beams to the size and dimensions of the tumor to help spare healthy tissue.

Intensity-modulated radiation therapy (IMRT) is a form of external beam radiation that allows a higher dose of radiation to be directed to the tumor, while minimizing the amount of radiation received by healthy brain tissue. The use of IMRT may result in fewer side effects compared to standard external beam radiation.

A newer form of radiation called SBRT (stereotactic body radiation) is sometimes used in the treatment of glioblastoma. SBRT delivers higher doses of radiation over a shorter period of time, which minimizes the impact on healthy tissue.

Chemotherapy

Either during or following the 6-week course of radiation, people with glioblastoma are typically prescribed temozolomide (Temodar), a chemotherapy taken in pill form. Temozolomide was approved by the U.S. Food and Drug Administration (FDA) in 2005 for the treatment of adult patients with newly-diagnosed glioblastoma. The goal of temozolomide is to stop or slow cell growth.

The chemotherapy carmustine (Bicnu, Gliadel) is sometimes used to treat certain types of brain tumors, including glioblastoma. Carmustine is administered as a wafer, placed in the area where the tumor was removed during surgery.

Targeted Therapy

Targeted therapies focus on specific molecules and cell mechanisms thought to be important for cancer cell survival and growth, taking advantage of what researchers have learned in recent years about how brain tumors grow. Targeted therapies are meant to spare healthy tissue and cause less severe side effects than chemotherapy.

In 2009, the FDA approved the targeted therapy bevacizumab (Avastin) as a treatment for glioblastomas that continue to grow following standard therapy. Bevacizumab is designed to stop angiogenesis (the growth of new blood vessels that feed tumors) by binding to and inactivating a protein called vascular endothelial growth factor (VEGF). Studies have shown that, when added to chemotherapy, bevacizumab can help extend the time until glioblastomas start growing again after surgery.

Tumor Treatment Fields

In 2011, the FDA approved Optune, a portable, wearable device designed to treat glioblastoma that recurs or progresses after being treated with chemotherapy and radiation therapy. Electrodes placed on the surface of the patient's scalp deliver low-intensity electrical fields called "tumor treatment fields" (TTFs) to the site of the tumor, which disrupt the rapid division exhibited by cancer cells.

In 2015, Optune's FDA approval was extended to treat people with newly-diagnosed glioblastoma. Following surgery and radiation, Optune is administered along with the chemotherapy temozolomide.

The Importance of Clinical Trials

Clinical trials are the standard by which we measure the safety and effectiveness of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Many clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- Participation is voluntary and does not affect your access to treatment in other settings. You can stop taking part in a clinical trial at any time for any reason.

Treatments Being Studied

There is promising research being done on treatment approaches for glioblastoma, including:

- **Genomic drivers.** Researchers have intensified their efforts to learn more about the genomic drivers of brain tumors (the identification of genes that carry mutations). It is thought that a deeper understanding of this process can lead to the development of additional, more effective treatments. For example, one large study recently identified a gene called IDH1, which is often involved in the growth of glioblastoma tumors.

- **New ways to deliver chemotherapy.** When anti-cancer drugs are given in pill form or through a vein, they have to travel throughout the body before getting to the brain. As the drugs travel, they can cause side effects, such as nausea. Researchers continue to develop chemotherapy that can be delivered directly into the brain tumor itself. One technique that is being explored is "convection-enhanced delivery of chemotherapy," in which doctors put one to four tiny tubes into a brain tumor and connect the tubes to a pump that delivers large doses of chemotherapy directly into the brain.

- **Radiation sensitizers.** These are drugs that make the cells of a brain tumor more likely to be treated successfully by radiation. As a result, doctors can use lower doses of radiation, reducing treatment side effects.

- **New targeted therapies**:
  - In 2016, a study was published suggesting that a protein called RSK2, which regulates cell growth, is heightened in many patients with glioblastoma. This protein can "push" malignant cells into the surrounding healthy brain tissue. This discovery may help researchers develop new therapies targeting this protein.
  - In August 2020, the FDA granted a fast track designation to paxalisib for the treatment of people with glioblastoma who have finished initial radiation in combination with the chemotherapy temozolomide. Fast track status is a process designed to facilitate the development and expedite the review of drugs that treat serious conditions.

Additionally, immunotherapy is an exciting area of research for the treatment of glioblastoma. The immune system is the body's natural defense against disease, but is usually not strong enough to stop tumor growth. A number of treatments intended to strengthen the immune system are being studied, including:

- **Vaccines,** designed to attack cancer cells bearing antigens (molecules that can suppress the body's immune system).
- **Immune checkpoint inhibitors.** Tumor cells often have "immune checkpoint" molecules that act as a shield, allowing the cancer to evade an attack by the immune system. This can be countered by immune checkpoint inhibitors, such as nivolumab (Opdivo, others). These drugs are designed to remove the shield and allow the immune system to attack the cancer cells.
- **Biological therapies** stimulate the immune system and stop cancer cells from growing. Ongoing research suggests that oncolytic viruses (a type of biological therapy) can be used as a potent treatment of glioblastoma.

- **Adoptive T-cell transfer** (also called CAR T-cell therapy) is an approach in which T-cells are removed from the patient and genetically modified so that they target a particular protein that may be found on cancer cells. These reprogrammed T-cells are infused back into the patient with the goal of improving the immune system's anti-cancer response. This type of imunotherapy is being actively studied for the treatment of glioblastoma.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects that you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to maintain your treatment plan. It's important to remember that not all patients experience all side effects, and patients may experience side effects not listed here.

Side Effects of Chemotherapy

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are used, and can include:

- Fatigue
- Nausea or vomiting
- Hair loss
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding (from having a low platelet count)
- Changes in memory or thinking
- Peripheral neuropathy (numbness or tingling in hands and feet)

Side Effects of Radiation Therapy

Changes to the skin are the most common side effects of radiation therapy. The changes can include dryness, swelling, peeling, redness and blistering. If a reaction occurs, contact your health care team so the appropriate treatment can be prescribed. It's especially important to contact your health care team if there is any open skin or painful area, as this could indicate an infection. Infections can be treated with an oral antibiotic or topical antibiotic cream.

Side Effects of Targeted Therapy

Targeted therapy doesn't have the same effect on the body as do chemotherapy drugs, but they can still cause side effects. Side effects of targeted therapies can include diarrhea, liver problems (such as hepatitis and elevated liver enzymes), nerve damage, high blood pressure and problems with blood clotting and wound healing.

General Side Effects

Some side effects may occur across treatment approaches. This section provides tips and guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals that are chilled, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- Choose fiber-dense foods such as whole grains, fruits and vegetables, all of which help form stools.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Managing loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks during the day.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.
- Save your energy for things you find most important.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis and depression. So be sure to ask your doctor if they think any of these conditions may be contributing to your fatigue.

Managing Pain

To help your doctor prescribe the best medication, it's useful to give an accurate report of your pain. Keep a journal that includes information on:

- Where the pain occurs
- When the pain occurs
- How long it lasts
- How strong it is on a scale of 1 to 10, with 1 being the least amount of pain and 10 the most intense
- What makes the pain feel better and what makes it feel more intense

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication to determine if they are safe and will not interfere with your treatments.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.

Communicating With Your Health Care Team

As you manage your glioblastoma, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and get to know the members of your health care team, including doctors, nurses, nurse practitioners, physician assistants, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook (either on paper or in a digital format) will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, ask your most important questions first and be as specific as possible.

Bring someone with you to your appointments. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person you bring may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. You can also ask the person who accompanies you to take notes for you, either in your journal or on a tablet or smartphone.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team. Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your glioblastoma treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have or any pain you are experiencing so that they can consult with your primary care physician or specialists as needed.

Remember, there is no such thing as over-communication.

Cancer*Care*'s Free Support Services and Programs

It can be very difficult to receive a diagnosis of glioblastoma, and adjusting to the necessary changes in your life can be challenging.

Cancer*Care*® can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system and offer information on support groups and other resources.

To learn more about how Cancer*Care* helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network composed of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store, or ask a friend who's a good listener to come over for a chat.

Frequently Asked Questions

Q: I've just been diagnosed with glioblastoma. I know I should seek treatment at a cancer center with experience treating this type of brain tumor. What questions should I ask when I meet with a specialist?

A: The following questions are good to ask during your first meeting. Other questions, specific to your situation, will likely arise during your course of treatment.

- What are my treatment options?
- What are the risks and benefits of the recommended treatment?
- What research has been done on this treatment?
- What are the likely side effects?
- Do I have time to get a second opinion before starting treatment?
- Can treatment wait?
- At this center, who is the key nurse or doctor I can talk to if there's a problem?

Q: Is it common for people with glioblastoma to have seizures?

A: It is not unusual for people with brain tumors, including glioblastomas, to have seizures. Many times, a seizure is what leads a person with an undiagnosed brain tumor to seek medical care. Seizures can also occur after diagnosis and treatment. To prevent seizures, doctors may prescribe an anti-seizure medication such as phenytoin (Dilantin and others).

Q: Does cognitive therapy have benefits for people with glioblastoma?

A: It is not uncommon for people being treated for glioblastoma to experience some degree of cognitive change, including problems with attention, memory and information processing. Cognitive therapy (also called cognitive remediation) can help people cope with and overcome these challenges. Cognitive therapy includes:

- Teaching strategies to help you carry out daily activities, such as using a notebook or daily planner.
- Using "task analysis"—breaking tasks into steps to make them easier to achieve.
- Incorporating attention-enhancing games and exercises, designed to improve retention and recall, into your daily life.

Q: Can eating organic foods and taking nutritional supplements help treat brain tumors?

A: There is no scientific evidence that organic foods and nutritional supplements help treat brain tumors, but one of the best things a person with a brain tumor can do is eat as healthily as possible and stay physically active. People who have not been particularly active can start by walking regularly. Be sure to talk with your doctor about how vigorous your activity should be. Also, be sure to tell your doctor about any vitamins, minerals, herbs or other supplements you take. Some over-the-counter supplements can interact with medications, particularly anti-seizure drugs; other supplements may raise the risk of excess bleeding.

Resources

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www.cancercare.org

American Cancer Society
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www.cancer.org

Cancer.Net
Patient information from the American Society of Clinical Oncology
888-651-3038
www.cancer.net

National Cancer Institute
800-422-6237
www.cancer.gov

Cancer Support Community
888-793-9355
www.cancersupportcommunity.org

CLINICAL TRIALS WEBSITES

EmergingMed
www.emergingmed.com

National Cancer Institute
www.cancer.gov

National Coalition for Cancer Survivorship
877-622-7937
www.canceradvocacy.org

American Brain Tumor Association
800-886-2282
www.abta.org

Brain Tumor Foundation
212-265-2401
www.braintumorfoundation.org

Medicine Assistance Tool
www.medicineassistancetool.org

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