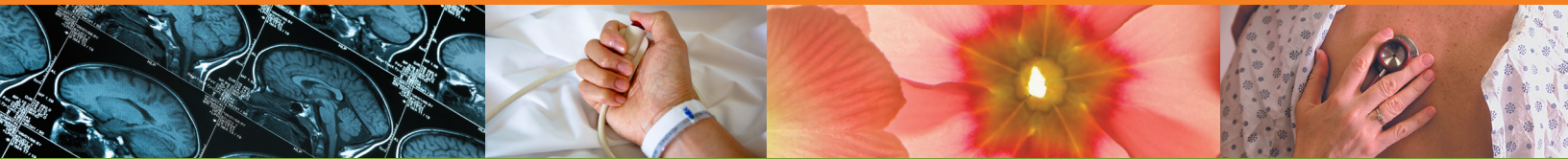


End-of-Life Care for Brain Tumor Patients

Manual for Health Care Providers



AUTHORS:

Susan M. Chang, MD

Erin Dunbar, MD

Virginia Dzul-Church, MD

Laura Koehn, MD

Margaretta S. Page, RN, MS

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Neuro-Oncology Gordon Murray Caregiver Program
UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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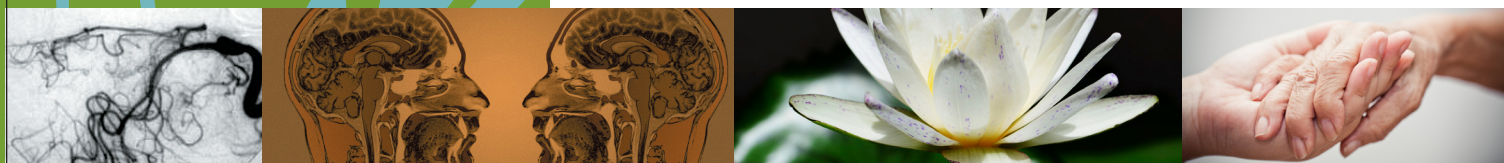
Introduction

The goal of this manual is to provide an overview of what health professionals may expect, as well as offer guidance, in caring for someone with a progressive, life-threatening brain tumor, with a particular focus on end-of-life issues.

Although some of the problems brain tumor patients experience at the end of life are common with many other forms of cancer, there is a subset of challenging problems unique to patients with brain tumors. In fact, the end-of-life phase for brain tumor patients tends to have a different course than general cancer patients.

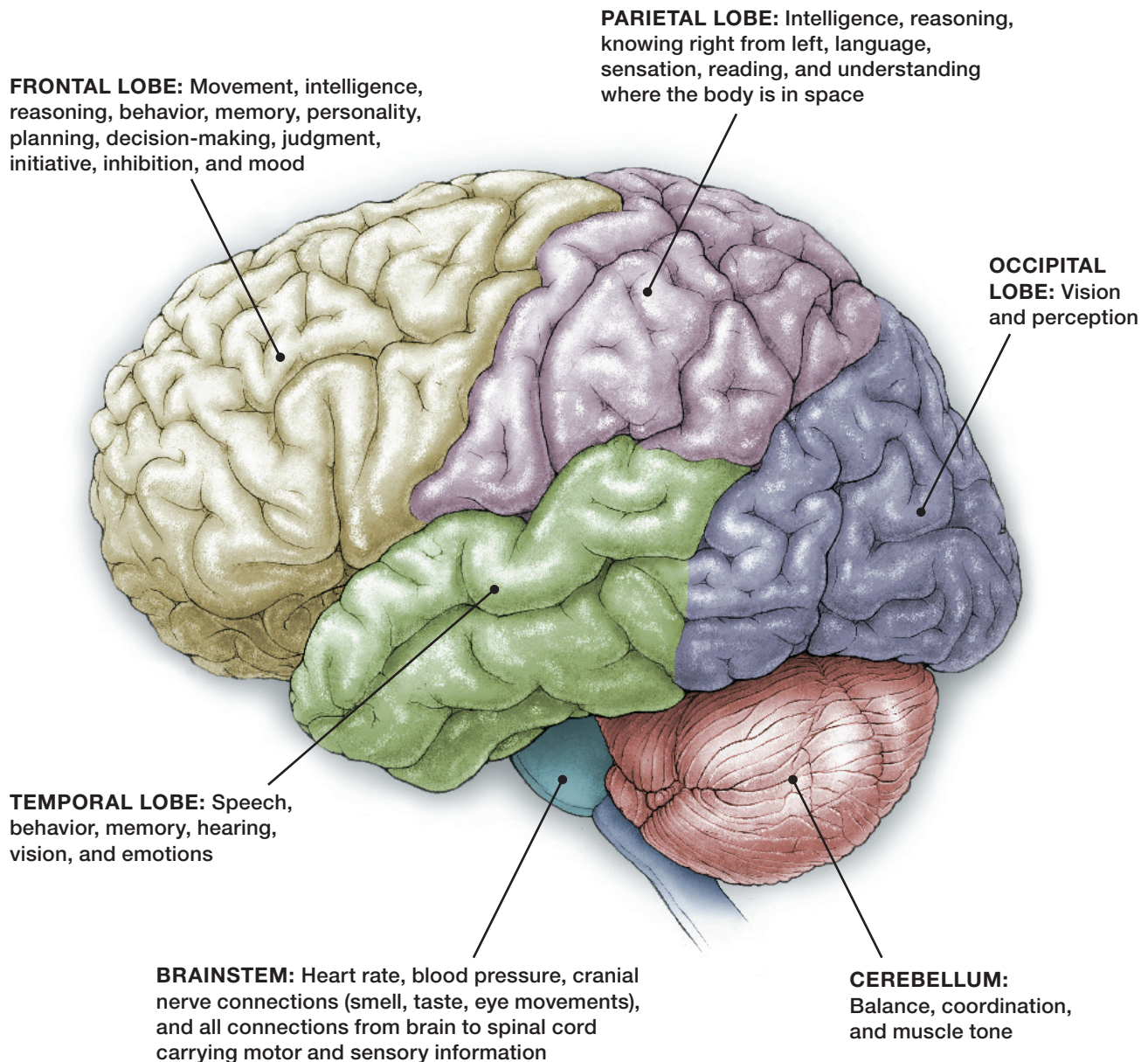
The intent of this manual is to suggest recommendations regarding disease-specific symptoms. Over time, recommendations will likely change as new supportive treatments are incorporated into clinical care. We understand that each patient's situation is unique and that the end of life is different for each patient. Some of these recommendations may not be pertinent to a particular situation.

We hope that you will use this as a guide to supplement your knowledge of end-of-life care.



Neuroanatomy

Brain tumors represent a wide variety of tumor types that either originate in the brain or have metastasized from somewhere else. Because the symptoms commonly seen in the end-of-life phase of brain tumor patients are a consequence of tumor location, it may be helpful to have a general sense of the anatomy of the brain. Knowing where the tumor is located will help you anticipate what type(s) of symptoms you may encounter. Below is a diagram of the brain outlining the major areas and a summary of the major functions.



The Use of Steroids

VIGNETTE:

A 42-year-old woman with glioblastoma multiforme has been noted to have worsening dull headache, which is worst in the morning, with associated nausea and vomiting. She has taken multiple pain medications including acetaminophen, ibuprofen, and oxycodone without relief. She has also taken ondasetron and prochlorperazine with moderate relief of her nausea. What else should you consider to help with her symptoms?

Role of Steroids

What is the role of steroids in treating patients with primary brain tumors? What are indications for use?

A steroid such as dexamethasone is the most common medication prescribed to brain tumor patients to control cerebral edema and in turn manage symptoms. That said, there are many side effects and complications related to taking the drug that are particularly important to be aware of in end-of-life care.

Corticosteroids are hormonal molecules that can cross the blood–brain barrier and act as analgesic agents by (1) decreasing inflammation by inhibiting the synthesis of prostaglandin and (2) reducing tissue edema by decreasing vascular permeability. Due to these mechanisms, corticosteroids are the mainstay of treatment for relief of symptoms of increased intracranial pressure resulting from a brain tumor. These symptoms include nausea, vomiting, and headache, as well as focal neurological deficits such as weakness and language dysfunction.



Managing Steroids

How do you manage steroids? What is the steroid of choice?

Corticosteroids, including hydrocortisone, dexamethasone, prednisone, prednisolone, and methylprednisolone, are the mainstay of treatment of increased brain pressure. Steroid doses should be adjusted to maximize pain relief and minimize side effects.

Dexamethasone (Decadron) is the corticosteroid best supported by clinical experience, evidence, and guidelines issued by expert panel. It causes less fluid retention because of its lesser mineralocorticoid effect, has a longer half-life and thus can be taken once daily, and offers a higher potency.

What is a good trial and how do I titrate the dose?

Each patient warrants a brief trial of corticosteroids for symptom control of headache, nausea, and vomiting. Administration of corticosteroids should preferably not take place later than 2 PM in order to minimize the undesirable effects of insomnia and restlessness as well as to maximize the desirable effects, such as analgesia, support of daytime alertness, and to improve appetite. Common regimens include: 4-6 mg oral daily for mild symptoms; 8 mg oral daily with breakfast for moderate symptoms; and 8 mg orally at breakfast and 8 mg at lunch for severe symptoms. Three days may be an adequate trial for many situations (e.g., headache), with tapering soon after initiation to a minimum effective dose with the least side effects. The corticosteroid should be discontinued if not found to benefit the individual within a week. If effective, the corticosteroid should be maintained at the minimum dose that provides sufficient symptom control with the least side effects. In general, patients should be maintained on the corticosteroid for less than 3 weeks, but the decision of when and whether

to discontinue the corticosteroid should hinge on patient-specific factors (i.e., prognosis, likelihood of side effects from withdrawal, potential to exacerbate other symptoms being masked by the drug).

How and when do I taper steroids?

Because most corticosteroid side effects manifest over the long-term, general consensus holds that these drugs are best used for a limited time, at the lowest effective dose, and with frequent monitoring. Corticosteroids are advised for short-term courses of therapy, from 1 to 3 weeks. Corticosteroids are used for longer than 3 weeks for patients who have a short- to medium-term prognosis (i.e., < 3 months life expectancy) and in whom side effects are unlikely to develop in the time remaining. In most cases steroid doses are maintained through the end-of-life period, until the patient stops taking oral medications. If it was decided to stop the steroid, it must be tapered slowly over a 2-week time period or longer in symptomatic patients. Dexamethasone has a long half-life, therefore it is recommended to decrease the dose by 50% every 4 days. If the patient has been on steroids for an extended period of time, a slower taper may be needed. A common regimen would be decreasing by 2 mg every 2 weeks. For patients with a short- to medium-term prognosis, tapering the medication to the lowest effective dose, but not completely off the medication, provides the best symptom support.

Side Effects

What are the side effects of steroids?

Since side effects of steroids can overlap with side effects of other medicines or symptoms from the brain tumor itself, being aware of common steroid side effects is very important. Some side effects of steroids include blurred vision, headache, mood and personality changes, psychosis, swelling of fingers, hands, feet and

TABLE 1: MAJOR SIDE EFFECTS ASSOCIATED WITH CORTICOSTEROID THERAPY

NEURO-PSYCHIATRIC <i>In general, taper steroid to lowest effective dose.</i> ● Insomnia <i>Schedule last steroid dose before 2 PM.</i> <i>Sleeping aids:</i> ● Melatonin: 1-5 mg at bedtime ● Nortryptiline: 25 mg at bedtime (max 100 mg) ● Mirtazapine: 7.5-15 mg at bedtime ● Lorazepam: 1 mg at bedtime ● Clonazepam: 0.5-2.0 mg at bedtime ● Mania/Psychosis/Agitation <i>Support for low-dose antipsychotics, if unable to taper steroid:</i> ● Haloperidol (Haldol): 2-5 mg daily (or 1-2 mg q6H) ● Olanzapine: 2.5 mg daily, can titrate up to 5-20 mg daily ● Quetiapine (Seroquel): 25-400 mg daily (divided bid or tid). This is the most sedating of the drugs. ● Risperidone (Risperdal): 1-6 mg at bedtime ● Dysphoria/Depression <i>SSRI/SNRI if prognosis > 6 months life expectancy:</i> ● Escitalopram: 5-10 mg daily ● Citalopram: 10-20 mg daily (max 40 mg) ● Sertraline: 25-50 mg daily (max 100 mg) ● Venlafaxine: 37.5 mg daily (max 225 mg) ● Nortryptiline: 25 mg at bedtime (max 100 mg) ● Mirtazapine: 7.5-15 mg at bedtime <i>Psychostimulant if prognosis < 6 months life expectancy:</i> ● Methylphenidate: 2.5-30 mg daily in divided doses (last dose not after 4 PM) ● Ketamine: (oral solution) 0.5 mg/kg in divided doses MUSCULOSKELETAL ● Myopathy; proximal muscle weakness; difficulty standing; falls ● Taper steroid to lowest effective dose. ● Aerobic exercise, resistance training, and physical and occupational therapy may help prevent severity, enhance independence, and reduce falls.	ENDOCRINE ● Hyperglycemia <i>Treat similarly to diabetes mellitus, usually insulin-based. In hospice patients, there may be a higher threshold to treat (i.e., only if blood sugar persistently >350s).</i> ● Adrenal Insufficiency <i>Must taper slowly to prevent crisis and withdrawal (see Steroid Withdrawal Syndrome, page 6).</i> GASTROINTESTINAL ● Gastritis ● Peptic Ulcer Disease ● Visceral Perforation <i>Continue proton pump inhibitor (PPI) if previously indicated. Can consider starting prophylactic PPI if the patient is receiving very high doses of glucocorticoids or if he/she is at high risk for developing peptic ulceration (e.g., previous peptic ulcer disease, concurrent anticoagulation, NSAID therapy).</i> INFECTIOUS DISEASE ● Increased risk of typical and opportunistic infection (fungal, zoster) <i>Consider PCP prophylaxis in patients who are receiving prolonged (more than 6 weeks) courses of glucocorticoids. May not be indicated in hospice patients.</i> <i>Consider oral or topical anti-fungals for prophylaxis or at the development of symptoms.</i> CARDIOVASCULAR ● Hypertension ● Arrhythmia ● Lipid abnormalities <i>Recommend not to check or treat in hospice patients unless they are symptomatic.</i> SKIN ● Thinning and purpura ● Acne, hirsutism ● Be aware of increased skin fragility, higher risk of skin complications, and need for good skin care.
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Note: For all adverse effects: 1) Use the lowest dose of corticosteroid for the shortest period of time needed to achieve the treatment goals. 2) Treatment is needed of those pre-existing co-morbid conditions (e.g., diabetes mellitus, hypertension, arrhythmia, congestive heart failure, brewing infection) that may increase risk when corticosteroids are required.

This table includes commonly used medications to treat side effects of steroids. This list is not meant to be comprehensive. Many of these may or may not be on the hospice formulary and adjustments may be required. Providers are encouraged to be aware of non-tablet routes of administration for common brain tumor treatments, i.e., sub-lingual, transmucosal, subcutaneous, intradermal, rectal, and liquid suspension. Using non-tablet routes of administration often results in improved symptom control especially near the end of life. Furthermore, it improves the ability of the family to participate in symptom management and increases the likelihood that the patient can remain at home.

lower legs, weight gain, proximal muscle weakness (difficulty getting from sitting to standing position, increased risk of falls), trouble sleeping, high blood sugar, increased chance of infection, and gastrointestinal distress (ulcers).

What is Steroid Withdrawal Syndrome?

Consider continuing corticosteroids for patients with advanced or terminal disease in order to prevent the possibility of withdrawal symptoms that may require further medication, including **myalgias, arthralgias, abdominal pain, nausea, conjunctivitis, and Addisonian crisis** (highest risk >6 weeks of use). Discontinuation of steroids may be especially problematic in hospice patients as it could lead to exacerbation of terminal restlessness, hypersomnolence, and potentially contribute to rebound of masked symptoms (e.g., pain, nausea). For these reasons, *when prognosis is short, the patient's safety and experience of the remainder of life may be better maintained by continuing rather than discontinuing corticosteroids.* However, this must always be balanced with corticosteroid side effects such as insomnia, hyperglycemia, psychotropic effects, hypertension, and restlessness.

SUMMARY RECOMMENDATIONS

- For a patient experiencing pain that is insufficiently relieved by NSAIDs or an opioid, conduct a short (i.e., 3-7 days) one-time trial of the corticosteroid in conjunction with the opioid, monitoring results against specific goals in a defined time frame.
- If the patient tolerates the corticosteroid well and reports pain relief, continue therapy at a dose of up to 16 mg orally, daily in divided doses, e.g., breakfast and lunch. Dexamethasone is the current drug of choice.
- Discontinue the corticosteroid if it does not achieve the desired pain relief within a predefined time frame (typically 1 week).
- Maintain the patient on the minimum possible corticosteroid dose to achieve the desired effect, for up to 3 weeks.
- If prognosis is longer than 3 weeks, either (1) taper the patient off of the corticosteroid, carefully monitoring for withdrawal symptoms and return of pain, or (2) maintain the patient on the minimum effective dose based on patient-specific considerations.

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Symptom Management

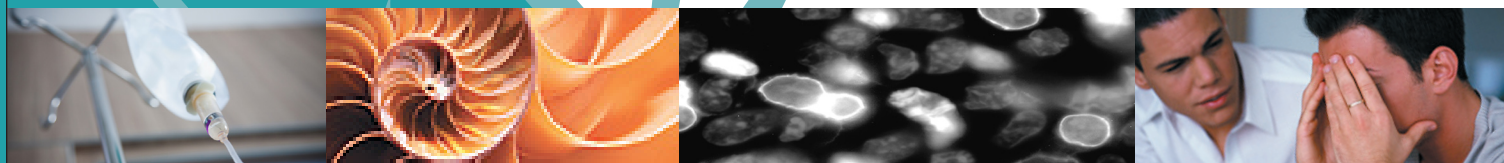
The most common symptoms experienced by patients are often related to tumor location and/or cerebral edema, which can cause increased intracranial pressure.

These symptoms include drowsiness, headaches, cognitive and personality changes, poor communication, seizures, delirium (confusion and difficulty thinking), focal neurological symptoms, and dysphagia.

Some patients may have several of these symptoms, while others may have none. Some of the factors that influence the presence and severity of symptoms are the tumor's location and size, progression of the tumor, and swelling in the brain.

Brain tumor patients tend to develop significant and progressive neurological symptom burden in the final weeks of life.

The following are strategies and guidelines for managing some of the symptoms that are common in brain tumor patients at the end of life and differ from the terminal symptoms seen in the general oncology population.



Drowsiness, Decreased Level of Consciousness

VIGNETTE:

A 46-year-old male patient with recurrent glioblastoma has recently transitioned to hospice care. His wife called to report that lately all the patient wants to do is sleep. He wakes for his morning meal, which he takes with assistance. He then showers or sponge bathes, which he follows with a nap until lunch. At lunch, his caregivers wake him again for meal, which he eats with assistance. He then naps until dinner, at which time he eats and remains awake and able to interact with family for about 2 hours. He then returns to bed and sleeps soundly for 12-13 hours until the next day. What should you tell his wife?

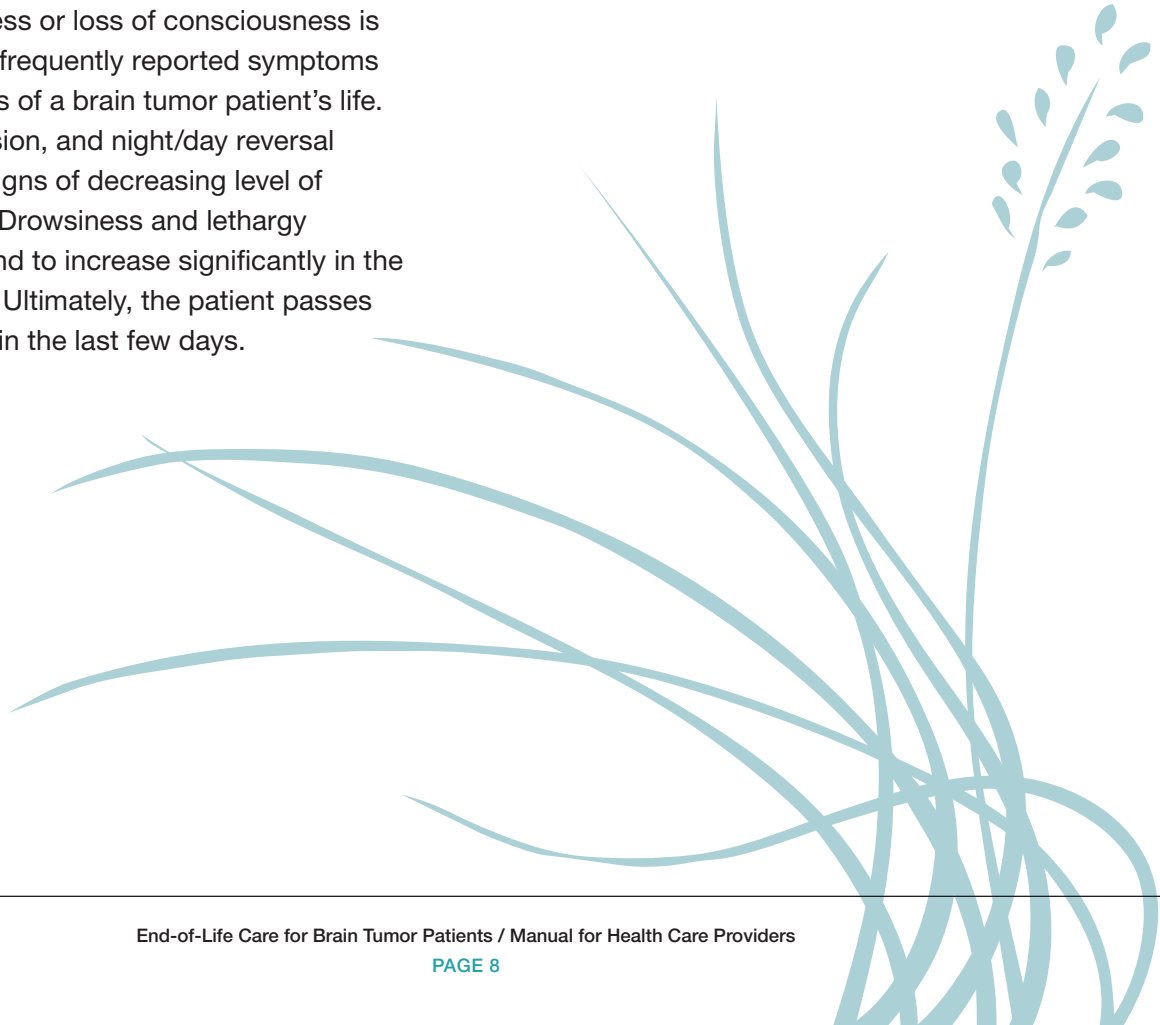
Epidemiology

Patients with progressive brain tumor suffer from increasing intracranial pressure as the tumor grows. Drowsiness or loss of consciousness is one of the most frequently reported symptoms in the final weeks of a brain tumor patient's life. Lethargy, confusion, and night/day reversal are often early signs of decreasing level of consciousness. Drowsiness and lethargy progress and tend to increase significantly in the last week of life. Ultimately, the patient passes into deep coma in the last few days.

Concerns Related to the Symptom

One word of practical advice is to always look at the big picture. Ask yourself: *Is there anything else going on with the patient?* Although it is likely that the drowsiness and decreased level of consciousness are direct results of tumor growth and increasing intracranial pressure, one must remember that **drowsiness can be part of delirium**, and delirium can be caused by mass effect, hydrocephalus, herniation, metabolic disorders (such as electrolyte disorders and diabetes), sepsis, pain, other medications, or dehydration. Symptoms of decreased level of consciousness can also be due to non-convulsive seizures. Care must be taken to ensure that there is consideration of reversible causes for the change in level of consciousness. This is particularly important in the early phases of hospice when treating such symptoms is consistent with the goals of care, less so as death approaches.

In addition, *somnolence*, or decreased level of consciousness, can hamper the use of oral



medications and increase the risk of aspiration. If the patient has occasional periods of waking and is able to swallow, it is recommended to continue steroids and anticonvulsants whenever the patient wakes up, not necessarily on a strict time schedule. In most cases, as the patient progresses into a deeper coma, oral medications are then suspended. Patients who have been using anticonvulsants may benefit from switching to alternate routes of this medication (i.e., rectal, intranasal, transdermal, or buccal) through the end stage of illness to prevent seizures at end of life. Using non-tablet routes of administration often results in improved symptom control especially near the end of life. Furthermore, it improves the ability of the family to participate in symptom management and increases the likelihood that the patient can remain at home. Aspiration can be minimized by having the head of the bed elevated to about 30 degrees, refraining from administering liquid and tablet medications during times of severe drowsiness and experimenting with which consistency of liquids/solids are best swallowed.

Early in the hospice phase it is important to remember the need for good skin care. Provide frequent position changes and incontinence materials if not already in use. As the patient begins “actively dying” this recommendation is revised and position changes are often reduced to a minimum.

Treatment

Steroids can be used or increased if already in use, if not at maximum dose, to treat and possibly improve the symptom for a short time. This is a temporary measure and in most cases this is not recommended. If there is no treatable cause for the lethargy, somnolence, or decreased level of consciousness, other than progressive tumor, there is usually no treatment offered for the symptom. It is assumed that this is the natural progression of the disease and an end-stage sign.

SUMMARY RECOMMENDATIONS

- Drowsiness or loss of consciousness is one of the most frequently reported symptoms in the final weeks of life
- Care must be taken to ensure that there is no other reversible cause for the change in consciousness
- If due to tumor progression, the condition is not reversible and utmost care must be provided to prevent aspiration (head of the bed 30 degrees) and maintain skin integrity.

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Headaches

VIGNETTE

You are treating a 52-year-old woman with a 6-year history of anaplastic astrocytoma. She is wheelchair-bound as a result of her tumor and has recently suffered another recurrence. She has been on 4 mg dexamethasone per day for increased weakness of her right upper extremity. She has opted for hospice care. In addition to her right-sided weakness, she notes that for the last few weeks her headaches have been increasing. She has been using over-the-counter non-steroidal anti-inflammatories with less and less success. Today, she reports that her headache is a 6 out of 10 on a scale of 1 to 10, with 10 being the worst. What advice would you give her regarding her headache?

Epidemiology

About half of all brain tumor patients experience headache at some point during their illness. Patients' headaches can be variable in frequency, intensity, and quality. Typically, headaches that are caused by the build up of pressure in the skull from the brain tumor are worse in the morning (or at night) and can be worsened by bending over or coughing. Headaches from the tumor itself and from increased brain swelling can be any type of headache, the most common being a dull ache. Headaches are thought to be due to a combination of increased intracranial pressure and traction on sensitive structures such as blood vessels and the overlying lining of the brain (dura mater). Since headaches are a symptom of increased intracranial pressure, this is a common symptom experienced by patients at the end of life as both the size of the tumor and the associated edema increase.

Concerns Related to the Symptom

With decreased level of consciousness, patients are often unable to communicate whether or not they have a headache. Family members often

worry that their loved one is in pain. It is recommended to observe the patients for signs of discomfort, like wincing or grimacing, and medicate as appropriate.

Treatment

It is recommended to always attempt to treat mild to moderate headaches with over-the-counter analgesics, i.e., acetaminophen (Tylenol) or non-steroidal anti-inflammatories, first. As the tumor progresses, headaches may increase and not respond to the over-the-counter analgesics or become more severe. In this case, steroids are the mainstay of treatment and the dose should be adjusted to maximize pain relief and minimize side effects. It may take 5-7 days at one dose to assess the full effect of the steroid medication. Additional information about using steroids can be found in the medication management section. Sometimes, headaches are very severe, in which case, in addition to steroids, opioids are recommended. Providers can choose between oral medications if the patient is able to swallow or transdermal pain control systems if needed.

SUMMARY RECOMMENDATIONS

- Half of all patients experience headaches at some time during their illness.
- Attempts should be made to treat the pain with over-the-counter analgesics.
- Dexamethasone can be used for headaches that are moderate to severe and do not respond to oral pain medications (see *"The Use of Steroids" section on pages 3-6*).
- Opioids are recommended when pain control with dexamethasone is not sufficient.

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Focal Neurological Symptoms

VIGNETTE

A 71-year-old man had a progressive left parietal lobe glioblastoma. At diagnosis, he presented with significant right-upper extremity weakness and some mild-to-moderate, right-sided lower extremity weakness. At the time of diagnosis, he also reported occasional difficulties with finding words. Although the tumor was described as located in the left parietal lobe, his symptoms seemingly correlated to what one would think were frontal lobe symptoms. It is likely that the tumor was at the edge of the frontal lobe and had compressed or invaded the motor strip and, over time, Broca's area, the part of the brain responsible for speech production. He actively participated in speech, occupational therapy, and physical therapy 3 times per week. His functional status never improved, but he was able to maintain a steady functional status for over 2 years. Finally, as the disease progressed, he had increased aphasia to the point of being unable to communicate at all and developed increased urinary incontinence. His right-sided weakness remained significant throughout his illness, although did not significantly worsen until the last 2 weeks of his life. Prior to losing more function on the right, he developed confusion, complete aphasia, and nausea and vomiting, all signs of progressive tumor and increasing intracranial pressure. Were there any additional interventions that could have been provided for this patient?

Epidemiology

All brain tumor patients suffer from progressive neurological deficits. The specific symptom depends primarily on the tumor location. Focal symptoms are a result of either compression or infiltration of the surrounding brain tissue by the tumor and/or associated edema. In addition to tumor invasion, the patient can suffer symptoms related to surgical complications, radiation necrosis, or even medications like steroids, which can cause proximal muscle weakness. Over and above the general symptoms of increased intracranial pressure (headache, nausea, vomiting, and decreased level of consciousness), patients may demonstrate symptoms related to the specific tumor location. These include but are not limited to: uni-lateral motor weakness (particularly in the arm), sensory alterations, speech disturbances, visual disturbances, gait disturbances, cognitive changes that include memory and behavioral changes, and cranial nerve palsies. It is common for the symptom burden to increase rapidly in the last 2 to 3 months of life.

Most people are left-side dominant for speech, which means that left hemispheric tumors can affect speech, particularly if near Broca's area, which is responsible for the motor production of speech. Patients often know what they want to say but are frustrated because they are unable to speak. The dominant parietal lobe contains Wernicke's area. For patients with damage in this area, they may have more problems with processing speech, known as receptive aphasia. In addition, the parietal lobes are involved with the processing of all sensory information, so symptoms can include numbness and tingling, hemi-neglect, and cognitive issues around right-left confusion and reading and math problems due to the inability to read or process

letters and numbers in the correct order. Frontal lobe tumors may impact memory, decision-making, inhibition, and mood. Occipital lobe tumors may impact vision, temporal lobe tumors may significantly impair memory, and brainstem tumors may cause cranial nerve dysfunction.

Concerns Related to the Symptom

The biggest concerns when thinking about neurological deficits revolve around quality of life, safety, mobility, and ability to communicate. It is always important to be aware of where the tumor is located in order to look for, anticipate, and identify symptoms as well as provide patients and families with anticipatory guidance on what to expect. Patients may need assistance with transfers and activities of daily living. Families may need education on use of adaptive devices. Families may need instruction on care if patients have developed hemi-sensory neglect. Lastly, due to confusion and impaired communication, **advanced care planning should be addressed as early as possible in the illness.**

Treatment

The mainstay of treatment for neurological deficit is targeted at the cause, which is either cerebral edema or tumor invasion. Steroid doses may be titrated up to provide maximal symptom relief with minimal negative impact. However, many patients are already on high-dose steroids so this treatment is not always an option. As always, the benefits of the higher dose of steroid must outweigh the significance of the symptom. Compensatory and adaptive devices, like walkers, transfer boards, shower chairs, special utensils, and communication tools, may be tried to assist with mobility, transfers, feeding, and communication, if needed. Cranial nerve deficits that interfere with vision, sensation or muscle control of the face, swallowing, and speech are

particularly problematic. Eye patches, eye lubrication (saline/ointment), alterations of solid/liquid food/medicines, aspiration precautions, and close attention to oral hygiene, etc. can be used. The excessive collection of saliva during both attempted conversation and resting (audible “rattling”, including the “death rattle”) can be ameliorated by altering liquid/solid intake, positioning of the patient (head of bed at 30-degrees or positioning to one’s side), the use of muscarinic receptor blockers (anti-cholinergic agents), and near the end of life, minimizing liquid intake.

SUMMARY RECOMMENDATIONS

- All brain tumor patients suffer from progressive neurological deficits as a result of tumor invasion or compression of the brain by edema.
- The deficits demonstrated by the patient may be predicted by tumor location.
- Dexamethasone can be used to mitigate deficits to a point.
- Patients and families can be counseled on what to expect, based on tumor location, and how to safely care for a patient with certain deficits, such as with the use of adaptive devices, positioning the patient, and occasionally medicines.
- Advanced care planning conversations should happen as early as possible.

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Cognitive, Behavioral, and Emotional Changes

VIGNETTE:

A 42-year-old woman has glioblastoma multiforme and is experiencing short-term memory loss and difficulty maintaining focus to complete ADLs/IADLs, such as dressing, cooking, and shopping. She is more impulsive and leaves to go on walks, has gotten lost on more than one occasion, and has frequent episodes of agitation. She now needs constant supervision for her own safety. What are important things for her family to know?

Epidemiology

In addition to focal neurological deficits from the brain tumor (weakness, vision changes, speech changes) or acute delirium, patients can have chronic and progressive changes to their cognition and behavior as a result of the tumor itself and tumor-related treatments. These changes are similar to what is observed in patients with

progressive dementia and produce comparable challenges (episodes of agitation and emotional volatility, loss of function and independence, and memory loss) for families and practitioners taking care of patients with primary brain tumors.

Concerns Related to the Symptom

Because the behavioral disturbances are often consequences of the tumor location, it may be helpful as a provider to have a general sense of the anatomy of the brain. Knowing where the patient's tumor is may allow you to anticipate and explain various behaviors or cognitive changes. This can also be helpful when discussing the patient with the family. Some of the behaviors, while frustrating, are not the patient's fault but are really a consequence of the brain tumor just like pain in a patient with pancreatic cancer or shortness of breath in a patient with lung cancer. Cognition, behavior, and emotion are controlled by several areas of the brain (see *illustration on page 2*). The types of cognitive and behavioral challenges one might observe are described in Table 2 below.

TABLE 2: COGNITIVE AND BEHAVIORAL CHALLENGES

SYMPTOM LOBES INVOLVED	DESCRIPTION	TREATMENTS
Emotion & Personality <i>Frontal, temporal</i>	● Psychiatric symptoms: depression, anxiety, obsessive-compulsive behaviors ● Emotional volatility: irritability, mood swings, withdrawal ● Socially inappropriate behavior ● Denial that behavior is a problem	● Cognitive rehabilitation therapy ● Psychotherapy ● Medication therapies ● Early advanced care planning
Learning & Memory <i>Frontal, temporal, parietal</i>	● Difficulty processing, storing and retrieving information ● Short-term memory loss	● Cognitive rehabilitation therapy ● Speech and language therapy
Attention & Concentration <i>Frontal</i>	● Confusion ● Easy distraction ● Difficulty multi-tasking and planning	● Cognitive rehabilitation therapy ● Medication therapies
Executive Functioning <i>Frontal</i>	● Decreased reasoning ability ● Impaired judgment ● Inability to apply consequences from past actions ● Requires frequent monitoring for safety and appropriateness of actions	● Cognitive rehabilitation therapy ● Problem-solving therapy
Language & Communication <i>Frontal, temporal</i>	● Difficulty with verbal fluency, speaking, reading, and/or writing	● Speech and language therapy ● Cognitive rehabilitation

Treatment

In many cases, the symptoms are related to damage in a specific area of the brain and are not reversible. It is important to counsel the family that behaviors are not intentional, but a direct result of the disease. It may be helpful to share with the family the following strategies.

Instruct family on providing a calm and structured environment

- Sometimes, patients can get predictably agitated at certain times of day. Consider trying to do the same things at the same time each day.
- Continue structured, predictable routine. Sudden changes to routine, rushing, or stress can contribute to fear and disorientation.
- Encourage the family members to take mental notes. Do behaviors mean something? Is the person feeling stressed, hungry, tired, scared, cold, or hot? Do they need to use the bathroom? Are they in pain?

Need for supervision of activities

- Provide a safe environment.
- Provide structure and routine.
- Keep things simple: Break down complex tasks into many small, simple steps that the person can handle.
- Redirect: Sometimes the simplest way to deal with agitation is to give the person something else to do as a substitute.
- Distract: Sometimes it is enough to offer a snack or put on a favorite videotape or familiar, soothing music when behaviors are becoming too disruptive (See “101 Activities” on the Alzheimer’s Association Web site at: www.alz.org/living_with_alzheimers_101_activities.asp)

- Be flexible: They may refuse to do something you want them to do. Before trying to interfere, ask yourself whether it is really important to do so.
- Soothe: Help family members experiment with simple, repetitive actions (massage, hair brushing).

Help families learn to communicate with the patient

Many times, patients have difficulty speaking or coming up with words to use for expressing what they want and may communicate only by gestures and expressions.

- You might feel angry. Try counting to ten, remembering that the person has a disease and is not deliberately trying to make things difficult.
- Identify yourself by name and call the person by name.
- If a subject of conversation makes a person frustrated or angry, better to drop the issue than correct a specific misunderstanding.
- If the person seems frustrated and you don’t know what he or she wants, try to ask simple questions that can be answered with yes or no or one-word answers.
- Speak slowly and distinctly.

Medication strategies

Agitation or changes in behavior can be helped mostly by behavioral strategies, though medications can also be helpful. Medication use is typically targeted to the likely cause of the agitation. Table 3 on the next page lists some commonly used medications to be considered. It is understood that hospice formularies may vary and substitutions or modifications may be required.

TABLE 3: MEDICATIONS USED TO TREAT COGNITIVE AND BEHAVIORAL SYMPTOMS

INSOMNIA OR “SUNDOWNING”

Sleeping aids:

- Melatonin: 1-5 mg at bedtime
- Nortryptiline: 25 mg at bedtime (max 100mg)
- Mirtazapine: 7.5-15 mg at bedtime
- Lorazepam: 1 mg at bedtime
- Clonazepam: 0.5-2.0 mg at bedtime

Consider zolpidem for short-term use.

Antipsychotics (see *below*) can also help reduce sundowning and work quickly so can be used in emergencies.

PSYCHOSIS/MANIA/AGITATION

Support for low-dose antipsychotics

- Olanzapine: 2.5 mg daily, can titrate up to 10-15 mg daily
- Seroquel: 25 mg daily and 12.5mg q6H prn
- Haldol: 2-5 mg daily (or 1-2mg q6H)

DEPRESSION

SSRI/SNRI if prognosis > 6 months life expectancy

- Escitalopram: 5-10 mg daily
- Citalopram: 10-20 mg daily (max 40mg)
- Sertraline: 25-50 mg daily (max 100mg)
- Nortryptiline: 25 mg qhs (max 100mg)
- Mirtazapine: 7.5-15 mg qhs

Psychostimulant if prognosis < 6 months life expectancy

- Methylphenidate: 2.5-30 mg daily in divided doses (last dose not after 4 PM)
- Ketamine: (oral solution) 0.5 mg/kg in divided doses

ANXIETY

SSRI/SNRI if prognosis > 6 months life expectancy:

- Escitalopram: 5-10 mg daily
- Citalopram: 10-20 mg daily (max 40mg)
- Sertraline: 25-50 mg daily (max 100mg)
- Consider short-term use of the benzodiazepines lorazepam 0.5-2 mg q6H prn or clonazepam 0.5-2 mg every 8-12 hours.

PAIN

Ensure the patient has been adequately treated for pain (e.g., known arthritis, tumor burden, etc.) using a stepwise pain algorithm.

SUMMARY RECOMMENDATIONS

- Emotional, behavioral, and cognitive changes are common in patients with primary brain tumor and present challenges similar to those encountered with patients with progressive dementia. It is important for families and providers to remember that these changes are caused by a medical illness; it is not the fault of the patient.
- It is important to provide a calm, structured, safe, and caring environment.
- Carefully chosen medications can relieve distress and help the person function.

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Seizures

VIGNETTE:

A 54-year-old woman with glioblastoma multiforme has had two generalized tonic clonic seizures over the past 24 hours. She was previously taking levetiracetam, but she has become more somnolent over the past weeks and is unable to swallow the pills. What are the next steps in managing her seizures? How would you counsel the family?

Epidemiology

Seizures are a common and often disturbing complication of both primary and metastatic brain tumors. Seizures have been found to occur in up to 56% of patients with primary brain tumors at the end of their lives. They are less common in patients with metastatic lesions. Of those with metastatic brain lesions, seizures are most common in patients with melanoma and least common in those with breast cancer. Seizures in patients with metastatic lung cancer are intermediate in prevalence. While seizures often occur simply because of the location of the brain lesion, this is not the only cause of seizures in patients with brain tumors. Any person's seizure threshold may be lowered by changes in electrolytes such as with hyponatremia, hypernatremia, hypomagnesemia, or hypoglycemia or by conditions such as poor sleep, infection, or increased stress.

What is a seizure?

Seizures are an abnormal neuronal discharge, often with physical manifestations. Epilepsy refers to a condition in which a person experiences two or more seizures. Seizures are divided into two main types based on how the neuronal discharges originate: focal seizures and generalized seizures. This distinction is relevant for many reasons. First, it is helpful when communicating with other medical providers. Second, focal and generalized seizures respond differently to certain medications. Third, while focal seizures are distressing to patients and families and should be treated very seriously, they are thought to be less harmful to the brain, whereas prolonged, generalized seizure activity is thought to be harmful to neurons.

FOCAL SEIZURES (previously called *partial seizures*) originate in a localized area of the brain's cortex. The seizure will appear different physically depending on where the seizure originates. For example, if a patient has a brain tumor located in the left side of his brain, which affects his motor cortex, he may develop a focal seizure that looks like rhythmic jerking of his right arm and leg (left motor strip, right side of the body affected). If the seizure only affects a very small amount of the motor cortex, it may be less dramatic, such as twitching of a pinky finger on the right side or twitching of the right lip. In these simple focal seizures, the patient does not lose consciousness.

If more cortex is involved or a different area of the cortex, the patient may experience altered mental status. This is a subtype of focal seizures called a *focal seizure with dyscognitive features* (previously termed *complex partial seizure*). The seizure may look like a simple focal seizure except the patient is unable to respond and is unable to recall the event. Because brain tumors



are located in specific parts of the brain, they are more likely to cause irritation of the cortex where the tumor is located. Thus, most patients suffer from focal seizures (with or without dyscognitive features). However, sometimes these focal seizures quickly spread across the cortex and become generalized seizures. These are considered secondarily generalized seizures.

GENERALIZED SEIZURES are often called grand mal seizures and considered synonymous with tonic-clonic seizures. (These are often called *grand mal seizures* and considered synonymous with *tonic-clonic seizures*). There are many physical manifestations of generalized seizures. Generalized simply means that the electrical discharge originated in a widespread area of the cortex as opposed to a focal site.

Generalized seizures include many subtypes. *Absence seizures* appear as if a patient is staring

blankly into space. *Myoclonic seizures* are characterized by brief periods of shock like jerks that are not necessarily rhythmic. The most commonly recognized generalized seizure is the generalized *tonic clonic seizure*. They are generally characterized by a tonic phase: eyes open and roll upward, pupils dilate, and patients flex, then pronate and stiffen their arms. It is sometimes accompanied by a moan or “ictal cry.” This is followed by a clonic phase: generalized clonic movements (rhythmic jerking). Patients may experience tongue biting and incontinence, which may be markers of nocturnal seizures if a patient wakes up with these features.

Generalized seizures (even if limited motor involvement) are often followed by a post-ictal phase in which the patient notes significant fatigue/lethargy, drowsiness, confusion, and muscle soreness.

***TIPS:** Evaluating a patient with a seizure disorder*

- If you are unsure if a person is having a focal seizure, test if the movement is suppressible or changes with movement. If you are able to stop the movement by changing positions or holding the person’s involved limb, this is not a seizure. It is more likely to be a tremor.
- Ask if they experienced an aura. Some people note a sense of foreboding, déjà vu, experience odd smells (burning tires) or tastes (metallic) at varying times before an event. This can be helpful to either guide them to take an abortive medication such as lorazepam if there is time, or at least move the patient to a safe place.
- The most feared complication of seizures is status epilepticus, which may be convulsive or nonconvulsive (a patient no longer has physical manifestations but does not reawaken). The formal description of status epilepticus is a seizure that persists or seizures that recur without interictal recovery of consciousness within 30 minutes. However, most practitioners become concerned for continuous seizure activity lasting greater than 5 minutes or two or more discrete seizures between which there is incomplete recovery of consciousness. These patients require urgent administration of medications in order to stop the seizure.

Concerns Related to the Symptom

Counseling and supporting patients' families around acute seizure management is paramount for the safety of patients and their caregivers. Families should be educated that seizures in a brain tumor patient are not uncommon and family members should be taught how to manage a seizure in the home, should one occur. An important consideration is to have a "seizure kit" in the home that includes instructions on when/how caregivers can administer medications and how to contact hospice for further instructions. In case of seizures simple suggestions to discuss include:

- Turn the patient to his or her side. This attempts to reduce the patient's aspiration risk.
- DO NOT place an object in the patient's mouth. This is a choking hazard for the patient and may also cause harm to the caregiver.
- If a seizure lasts greater than one minute, benzodiazepines should be available for use as an abortive medication. Rectal diazepam 0.2 mg/kg or 10-20 mg can be repeated hourly until the seizure stops. Sublingual lorazepam is also available. We would recommend starting with 1-2 mg orally depending on the patient's size and seizure type (higher if generalized).
- If their standing seizure medication was missed, administer the medication when able.

Treatment

There are many antiseizure medications, each with their own unique set of side effects. Table 4 on the next page lists some of the most commonly used antiepileptics and their most commonly encountered side effects. It is not meant to be comprehensive. These may or may not be on the hospice formulary and adjustments may be required.

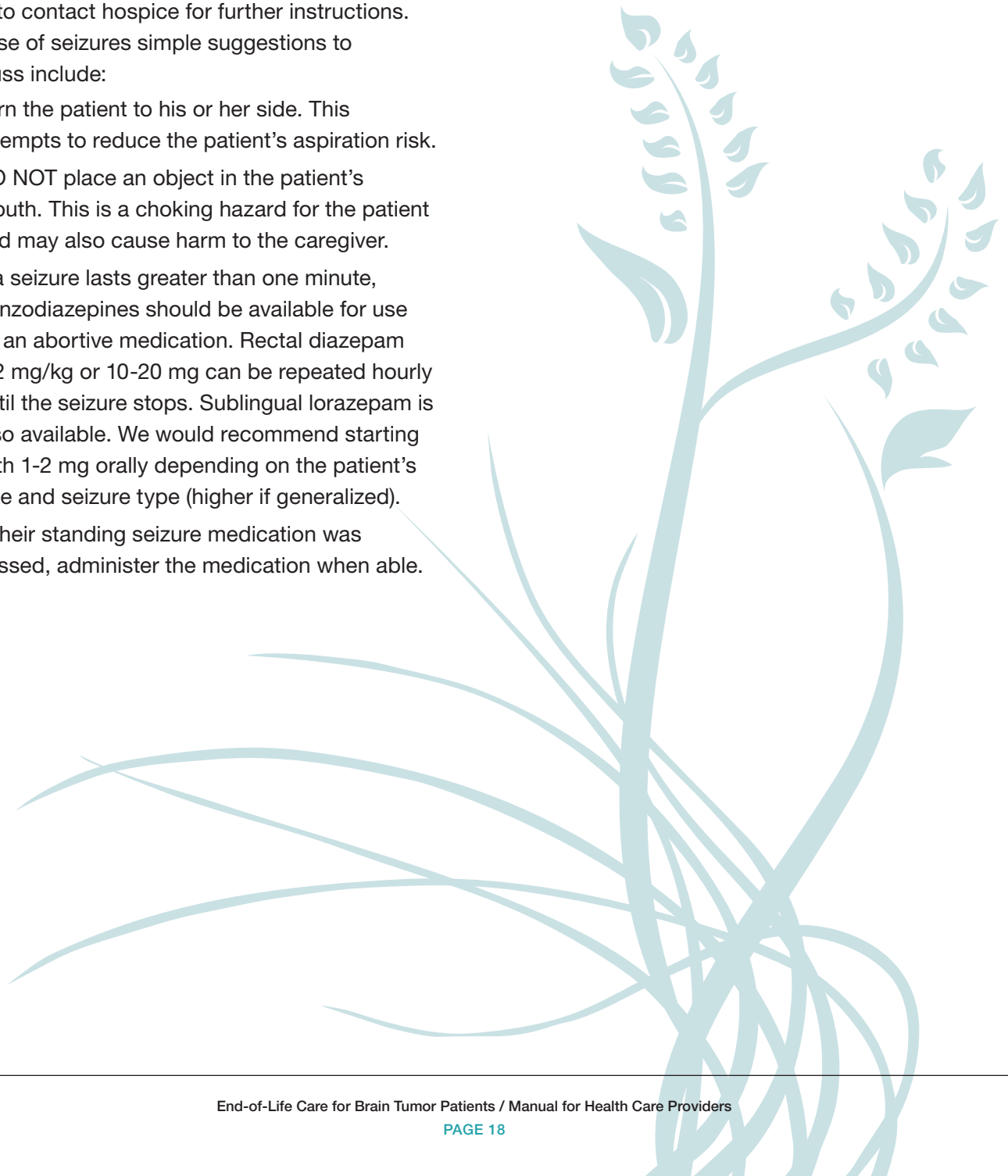


TABLE 4: COMMON ANTIEPILEPTIC DRUGS (AEDS)

MEDICATION	COMMON MAINTENANCE DOSING	COMMON SIDE EFFECTS
Carbamazepine (Tegretol)	300-600 mg TID (BID if XR)	- Chronic: hyponatremia, weight gain/edema, behavioral changes - Idiosyncratic: Steven's Johnson Syndrome (SJS)
Clonazepam (Klonopin)	0.5-2 mg TID	Somnolence, respiratory suppression
Diazepam (Valium)	Variable	Somnolence, respiratory suppression
Gabapentin (Neurontin)	400-1200 mg TID	Weight gain, peripheral edema, behavioral changes, myoclonus
Levetiracetam (Keppra)	500-1000 mg BID	Agitation, psychosis, depression
Lamotrigine (Lamictal)	200 mg BID	Headache, insomnia, incoordination, tics, SJS
Lacosamide (Vimpat)	100-200 mg BID	Headache, tremor, incoordination, depression
Oxcarbazepine (Trileptal)	400-1200 mg BID	Hyponatremia, insomnia, headache, SJS
Phenobarbital	30-60 mg BID	Nausea, vomiting, respiratory depression, somnolence
Phenytoin (Dilantin)	300 mg at bedtime (ER)	Gingival hyperplasia, coarse features, neuropathy, cerebellar ataxia, hypothyroidism, SJS
Pregabalin (Lyrica)	75-300 mg BID	Weight gain, peripheral edema, behavioral changes, myoclonus
Topiramate (Topamax)	100-200 mg BID	- High risk for adverse cognitive effects at higher dosing: word-finding difficulties and memory loss - Weight loss, paresthesias (tingling in hands/feet)
Valproic acid (Depakote)	250-1000 mg TID or QID	Weight gain, alopecia, amenorrhea, pancreatitis

TIPS: *When thinking about a seizure medication*

- Antiepileptics are often divided into categories of “old” drugs or “newer” drugs. The more conventional, older medications include phenobarbital, phenytoin, primidone, carbamazepine, and valproate. Many of these influence the liver’s metabolism (either inhibit or induce or both depending on their drug level), thus should be used thoughtfully with other medications.
- Most antiepileptics are dosed orally but may be compounded into a rectal suspension (see below). Antiepileptics that come in intravenous formulations include lacosamide, levetiracetam, phenytoin, and valproic acid.
- As you can see in Table 4 on the previous page, there is a wide range of accepted dosing. Always attempt to use the lowest dose with the greatest seizure control and least amount of side effects.
- Not all patients with brain tumors need antiepileptic medications. They are recommended if a patient has a history of seizures or is immediately post-operative (should be tapered off after 2 weeks post-op). There is no evidence to support the use of prophylactic antiepileptics in a patient who has been seizure-free outside of the peri-operative setting.
- Patients with brain tumors undergoing radiation therapy have a higher likelihood of drug rash with AEDs. The combination of phenytoin, cranial irradiation, and gradual reduction of concomitant steroid therapy may be particularly associated with erythema multiforme and/or Stevens-Johnson syndrome.
- For refractory seizures at the end of life, consider a sedating anti-epileptic such as midazolam (0.1-0.3 mg/kg po/sq/nasal or a barbiturate with the goal of deep sedation)

Recommendations for when patients are no longer able to swallow:

As mentioned above, seizures are relatively common in patients with brain tumors at the end of their life and are distressing to the patient and family. Thus, if desired by the patient with a history of seizures, they should continue their drug therapy as long as they are able to take oral medications. However, difficulty swallowing is also common in patients with brain tumors at the end of their life, so the route of AED delivery may need to be adapted.

When patients can no longer take medication orally, it is first important to use one’s own clinical judgment to decide whether to continue an AED, and then discuss with the family member(s) who have medical directive. It may be appropriate to stop the AED if the patient’s life expectancy is short and they have a remote history of seizures, which are not an active problem. If they have a more recent history of seizure activity, it is recommended to continue antiepileptic medications.

- Phenobarbital, carbamazepine, valproic acid, and lamotrigine can be given rectally without the need for dose adjustments. Valproic acid also comes in sprinkles.
- Rectal administration of levetiracetam suspension should be dosed 2:1 (if taking 500 mg BID of oral levetiracetam, one should take 1000 mg BID of rectal medication).
- For patients who have frequent seizures, consider scheduling doses of diazepam or lorazepam to be given around the clock rectally or buccally.

SUMMARY RECOMMENDATIONS

- Seizures are a common and often disturbing symptom in patients with primary and metastatic brain tumors at the end of life. A “seizure kit” is recommended.
- Seizures are classified by where they originate as either focal or generalized.
- There are multiple antiseizure medications, each with their own toxicity profile and interactions with other drugs.
- It may become difficult to maintain antiepileptic therapy once patients are no longer able to swallow medications. First, consider if the medication is still necessary. If so, investigate if it may be delivered in a rectal suspension. If not, consider dosing a benzodiazepine such as lorazepam or diazepam around the clock to prevent seizure activity.
- It remains important to counsel caregivers regarding management of a patient during a seizure in addition to providing emotional support.

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Delirium

VIGNETTE:

A 72-year-old man with a history of mild cognitive impairment and anaplastic glioma is discharged from the hospital to hospice after progression is noted on a recent MRI in the setting of altered mental status. During his hospital stay he was treated for a urinary tract infection without improvement in his mental status. His chronic opioids were also weaned off. You receive a phone call that he is sleeping during the day and awake and agitated all night. What do you recommend?

Epidemiology

Delirium is an acute cognitive impairment associated with medical illness. It is characterized clinically by decreased attention span and waxing/waning confusion. While it is considered a global disorder of cognition, personality and behavior are often involved. The prevalence of delirium is dependent on the population being studied. Delirium has been shown to be present in as high as 88% of patients near the end of life. In a separate study, hospice nurses were asked if their patients were confused during the prior week. They reported 50% of the patients were confused during that time. In spite of these large numbers, clinicians often fail to recognize delirium. In some reports, more than 70% of cases were unrecognized. This is especially true when hypoactive and often mimics decreased level of consciousness, depression, elevated ICP, and edema.

Delirium is associated with multiple negative outcomes. The most striking complication of delirium is an increase in mortality. Patients admitted to the hospital with delirium have mortality rates 10-26% higher than similar patients without delirium at hospital admission. Delirium has a large impact on caregivers as well as patients. It is associated with increased distress among caregivers, decreased quality

Delirium risk factors

Risk factors associated with delirium may be classified as predisposing factors that increase baseline vulnerability and those that precipitate the disturbance.

Predisposing factors:

- Cognitive impairment (dementia, Parkinson's disease, stroke)
- Advanced age
- Need for surgery
- Psychiatric symptoms
- Medical comorbidity
- Poor renal or liver function
- Sensory impairment (hearing or vision loss)
- Advanced cancer
- Being near death

Precipitating factors:

- Medications (polypharmacy, anticholinergics, opioids, benzodiazepines)
- Infections
- Metabolic disturbances
- Dehydration
- Immobility (restraints, IVs, catheters)
- Malnutrition
- Untreated pain
- Being in an ICU
- Room changes

of life, and increased risk for developing anxiety disorders. **It is the most common reason palliative sedation is requested.**

Diagnosing Delirium

The *Diagnostic and Statistical Manual of Mental Disorders* 4th edition defines delirium as follows:

- Disturbance of consciousness with reduced ability to focus, sustain, or shift attention.
- A change in cognition or the development of a perceptual disturbance that is not better accounted for by a preexisting, established, or evolving dementia.
- Disturbance that develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.
- There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition.

The above criteria may be used as a practical framework for assessing delirium. Delirium is further subdivided into hyperactive and hypoactive states, with hyperactive delirium being more commonly appreciated. When in doubt about the diagnosis, formal mental status testing should be performed such as the Mini-Mental State Examination or brief bedside tests of attention such as serial sevens (ask the patient to subtract 7 backwards starting at 100), spelling a word backwards, or digit span (at least 5 is normal). Additional clinical instruments may be used such as the *Confusion Assessment Method* (CAM), which is a simple 4-question tool to evaluate for delirium.

Concerns Related to the Symptom

The work-up of a patient's delirium while receiving hospice care is highly dependent on the patient and family's goals of care. However, because delirium is an uncomfortable symptom, it is important to consider if there are any easily reversible causes of delirium. As in any patient,

consider if pain is being undertreated, review the patient's medication list for common offenders, evaluate for constipation, and consider if it is related to an easily treatable infection such as a urinary tract infection.

Cognitive dysfunction in general may occur for a myriad of reasons in patients with brain tumors. Not all dysfunction may be attributable to delirium. Similarly, it is important to consider if there are other contributing factors leading to the delirium that are unique to patients with brain tumors, particularly given their medication list. It is essential to distinguish the direct effects of the tumor from other potentially treatable etiologies such as anticonvulsant toxicity, side effects of corticosteroids, seizures (perhaps subclinical), postictal state, systemic infection, metabolic derangement, or depression.

Prevention of Delirium

As established above, delirium is a common and disturbing symptom in patients at the end of life. Thus it is important to avoid factors known to cause or aggravate delirium as possible. Some simple suggestions include frequent reorientation by loved ones, environmental modifications, non-pharmacological sleep aides, early mobilization, visual and hearing aides, and medication review. There is no evidence to support prophylactic use of cholinesterase inhibitors and insufficient evidence for the use of antipsychotic agents and anticonvulsants (gabapentin) in preventing delirium.

Treatment

The treatment of delirium may be divided into non-pharmacologic and pharmacologic therapies. Delirium is reversible in 50-80% of patients with terminal illnesses. A certain percentage of cases resolve spontaneously.

- **Non-pharmacologic therapies:** education and support of families decreases distress and should be repeated often during the course of a patient's delirium. Non-pharmacologic interventions include reorientation to date

and time, clear simple instructions, frequent eye contact, proper introduction by all staff, application of working glasses and hearing aides, limiting or removing Foley catheters or oxygen as possible, oral rehydration, limiting room and staff changes, allowing uninterrupted sleep, and starting a sleep protocol before bedtime (warm milk, relaxation tapes, back massage) and evaluation of safety and restlessness at night, consider baby monitor/sitter.

- **Pharmacologic therapies:** the most frequent reason to initiate a medication is agitation followed by disturbing hallucinations. If the patient is a danger to self or others, or the symptoms of delirium are distressing, a cautious trial of an antipsychotic agent may be used. Unfortunately, there is limited data available to guide use or dosing. Most authors recommend haloperidol be used first (except in Parkinson's disease in which an atypical antipsychotic such as quetiapine should be tried first). Typical starting doses for haloperidol (Haldol) are 2 mg for mild agitation, 5 mg for moderate, and 7.6-10 mg for severe agitation (*see Table 3 on page 15 regarding other medications*). Reduce these doses by one-third in elderly patients. Doses may be repeated every 30 minutes until the patient is calm yet arousable to voice. If serious agitation persists, the previous dosage may be doubled 30 minutes later. When symptoms are controlled, calculate the 24-hour amount of medication needed for good control and provide as a single daily dose or divided BID. If agitation remains difficult to control with haloperidol alone, consider adding lorazepam 1-2 mg every 2-4 hours. Ideally, the dose should be slowly decreased over 5-7 days once two normal assessments have occurred. Smaller studies have evaluated newer atypical antipsychotics and these appear to be similarly efficacious. It is important to recognize that antipsychotic agents have numerous side

effects and risks and should be used cautiously and tapered as possible once symptoms are stabilized.

SUMMARY RECOMMENDATIONS

- Delirium is a common problem in patients with medical illnesses in general and even more common among patients at the end of life.
- Delirium is characterized by an acute change in a patient's mental status including changes in arousal, impaired attention, and cognition, related to a general medical condition.
- There are many risk factors associated with delirium. The most common predisposing risk factors include advanced age and preexisting cognitive impairment, which is common in patients with brain tumors. Medications and undertreated pain are often cited as precipitating factors.
- In patients with brain tumors, consider if their delirium may be related to specific treatable causes such as anticonvulsant toxicity, seizures, side effects of corticosteroids, systemic infection, or depression.
- Efforts to treat delirium involve non-pharmacologic and pharmacologic modalities.
- Haloperidol is the most studied pharmacologic agent used to treat delirium. If symptoms remain uncontrolled, a benzodiazepine such as lorazepam may provide added benefit.

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Dysphagia

VIGNETTE

A 53-year-old woman was diagnosed with a glioblastoma in the left parietal lobe. She had significant paresis on her right side throughout her illness, which progressed over time, making her wheelchair-dependent. She underwent nonsurgical therapies for 3 tumor recurrences, and 2 additional craniotomies, until the tumor recurred in her corpus callosum. It was at this time, 2.5 years after initial diagnosis, that she was referred to hospice. At the time of referral she was lucid, communicative, and still feeding herself. Over the next 10 weeks, she became increasingly lethargic, sleeping more and more. She began to wake only for meals and had more and more difficulty staying focused on the task at hand, which included swallowing and eating. Often in the morning, her husband was successful in getting her to swallow her medications, but as the day progressed she often pocketed her medications in her cheeks and her husband would later find her medications in her bed. Ultimately, she stopped waking up and her husband stopped feeding her. What would you recommend regarding her anticonvulsants and other medications at this time?

Epidemiology

Dysphagia or difficulty swallowing is a symptom that is most common with brainstem tumors as a result of compression or invasion of cranial nerves and other areas critical for the swallowing reflex (nucleus solitaries and ventromedial reticular formation). It is also a very common symptom in the late stage of illness; in the last two weeks of life, the incidence has been reported as high as 79%. It is postulated that it is related to decreased level of consciousness and/or an apraxia. It is thought that supratentorial lesions may decrease levels of oral sensory awareness or feedback cues that assist with swallowing.

Concerns Related to the Symptom

There are two major concerns. The first is protecting the patient from aspiration of food and fluids into the lungs, which can lead to pneumonia. In addition, trouble swallowing or inability to swallow affects patients' ability to take medications orally and so alternate routes must be used. Many patients are taking steroids and anticonvulsants and it is desired to continue these medications as long as possible, short of administering them intravenously.

Treatment

Some would suggest a swallowing evaluation so that behavior changes could be made. In thinking about this option, one must consider the stage of the illness and the condition of the patient. If it is a patient with a newly diagnosed tumor of the brainstem who is cognitively intact, such an evaluation makes good sense. Swallowing techniques and thickeners may allow the patient to keep up oral intake. If, however, the patient is cognitively impaired, so that their memory is impaired or that following a series of instructions is difficult, it is unlikely that the evaluation would be useful. Most evaluations are followed by

recommendations for behavior modifications that the patient would not be capable of making. In addition, if the patient is at late- or end-stage, the symptom is common, expected, and progressive. It is time to consider refraining from oral intake and switching only the absolutely necessary medications to an alternate route, i.e., rectal, topical, or intranasal. Good oral hygiene must be maintained to minimize halitosis, thrush, and dental/gingival disease. Depending on the patient's history of seizures and the family's concern about seizures, anticonvulsants may or may not be continued as a rectal medication (see section on seizures). If the patient is losing consciousness or has lost consciousness, the decision is usually made to stop steroids. Pain medications can and should be provided either in highly concentrated liquid form or transdermally, based on prescriber preference.

SUMMARY RECOMMENDATIONS

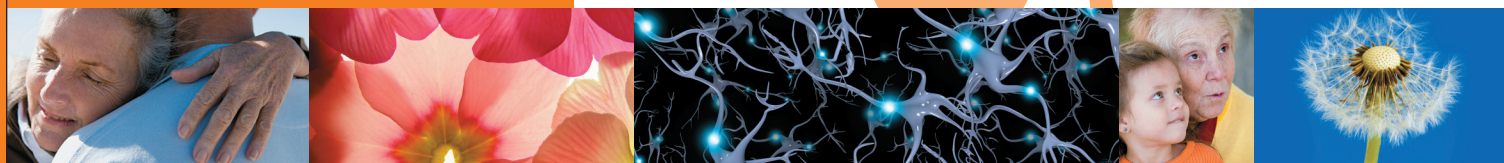
- Dysphagia is a common symptom at the end of life.
- Dysphagia can be related to involvement of the cranial nerves, but it is also thought to be somehow related to decreasing levels of consciousness and decreased oral sensory awareness.
- Dysphagia can be very distressing to family members.
- Family members require counseling regarding natural progression of disease, risk of aspiration, and consulted on strategies and decisions to continue medications.

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Social Issues

Some of the issues that are difficult at end of life for brain tumor patients revolve around the fact that many of the symptoms involve neurological deterioration. Often the patient loses significant neurological function and is no longer the same person as he or she was prior to the illness. This can be especially difficult for children who know the patient as well as the caregiver.



Children in the Home

VIGNETTE

A 48-year-old male with a progressive left parietal glioblastoma recently stopped active treatment and will pursue comfort care. Presently, he suffers from numbness on the right side. He has right-sided weakness and decreased coordination on the right. He has decreased short-term memory, word-finding difficulty, and decreased stamina. At present, he is able to ambulate with a cane. His wife reports that he does not tolerate loud noises or commotion in the home. He is sensitive to overstimulation. He is irritable and asks the same questions over and over. He wears noise-cancelling headphones at all times in the house. Prior to his illness, he was a soft-spoken, gentle, active parent who loved to explore the outdoors, ski, read, and play games with his children. He and his wife have three children, 9-year-old twin boys and a 6-year-old daughter. What suggestions could you to provide the well parent to help her with her parenting role?

Epidemiology

In addition to physical handicaps like the right-sided symptoms described above, many, if not most, brain tumor patients suffer from some cognitive and behavioral changes at the end of life. Most often these are due to the tumor, but can be exacerbated by the medications the patient is taking, particularly steroids and/or some anticonvulsants. At the end of life, many patients are very different, both physically and cognitively, from the person they were prior to the illness.

Concerns

Impending death combined with neurological deterioration can be particularly challenging for children in the home. In addition to expected concerns regarding children with a dying parent,

brain tumor patients often experience physical handicaps, cognitive changes, and personality changes. All of these can add an additional layer of distress. Children are often confused, frightened, embarrassed, and sometimes lonely because of the changes in the patient, as well as the fact that the healthy parent is often very involved in caring for the patient and may be less attentive to their parenting duties. Children may be experiencing grief and sadness about what is happening and the loss of their parent as the person he or she was before. They may even feel responsible for the negative mood or behaviors a patient may exhibit.

Treatment

The healthy parent in the home often wonders what to say to the children. In cases like this, it may help to offer advice or coach the parent. They need to know that children need to be informed of the status of the disease and the plan. Help the parent understand that it helps children to know how this next phase of illness will affect their lives. Encourage them to use age-appropriate language to explain the disease and the effects it may have on the person. Remind them to give the child a chance to ask questions and express how they feel. Finally, remind the healthy parent that they may need to do this repeatedly as symptom burden progresses. There are excellent resources available through American Cancer Society (cancer.org) titled “Helping Children When a Family Member has Cancer.” As mentioned before, the fact that brain tumor patients undergo cognitive and behavioral changes adds another level of complexity. With that in mind, additional suggestions for parents include the following:

- Inform the child that the symptoms that the patient is experiencing are due to the tumor or the medications.
- Make sure that they understand that the behavior is part of the illness and not directed at them.

- It is important for children to understand that that they are not to blame for the behavior.
- It is also very important that they feel safe asking questions.

SUMMARY RECOMMENDATIONS

- Remind the child that the ill parent loves him/her. Find photos of times together before the illness that bring memories of good times.
- Identify triggers that exacerbate the negative behaviors (i.e., too much noise, overstimulation). Coach the parent and the children to modify their behaviors if possible and/or work with the patient. Sometimes, you have to be creative. The patient in the vignette above found that noise-cancelling headphones made his home, which was full of young life, tolerable.
- Look for activities that the child and the ill parent can still share together, like watching a cooking show together, coloring, or looking at a picture book together.
- Lastly, encourage the child to continue normal activities with friends and family outside of the home.

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Caregiver Concerns

VIGNETTE

A 40-year-old woman is married to a 45-year-old man with a glioblastoma multiforme. He was diagnosed in April. By September, his wife is reporting that he has significant cognitive impairment, with poor short-term memory, poor judgment, irritability, difficulty with complex problem-solving, and visual-spatial issues. He is unable to sort the boys' and girls' laundry, suffers from profound anxiety, and loses track of time and continues with things like brushing teeth for 10 minutes until instructed to stop. The patient is no longer able to work. The couple has two children, ages 4 and 7 years. The wife reports feeling overwhelmed by the need to manage the patient's health, her work, and her children, and is very sad about the loss of the person that was once her husband. He was very intellectual, "knew something about everything," managed the family finances, and was her best friend. What advice and information can you provide the caregiver?

Epidemiology

Cognitive, personality, and communication changes are particularly challenging for caregivers. Unfortunately they are quite common symptoms in brain tumor patients, particularly at the end of life. They may be subtle or, as described above, severe. Caregivers of patients with neurological symptoms are at greater risk than other caregivers for distress and depression. In addition to dealing with the life-threatening nature of caring for someone with a brain tumor, caregivers are often dealing with the loss of the person that they once knew. Caregivers state that the loss of a loved one's memory, identity, and awareness is "equal to a death, yet it is not." This has been described as an "ambiguous loss."

Caregivers of brain tumor patients suffer from role strain, loss of relationship quality, and significant financial burdens.

Concerns

Symptom burden increases significantly at end of life. As stated above, caregivers of brain tumor patients are at significant risk for distress, burden, depression, fatigue, and insomnia. Younger females are at the greatest risk. If left unchecked, these have the potential to affect the caregiver's health and ability to provide quality care to the patient. In addition, advance care planning may or may not have been addressed at the beginning and the burden is left to the caregiver to make important end-of-life decisions for the patient.

Treatment

There is increasing awareness of the significance of the impact of illness on the health and well-being of the caregiver. For this reason, there is a movement to promote conscious efforts to support the caregivers as part of the care plan for a brain tumor patient. This starts by identifying those at greatest risk for distress. In addition to younger females, caregivers of patients with neuropsychological sequelae are at risk, as are caregivers of patients moving through transitions in their illness, such as to a new care setting, or hospice care. Caregivers need support in their new roles, with information, education, and connection to resources and others who are having a similar experience. They need guidance to renegotiate relationships with the patient as well as assistance with advanced care planning and decision-making whenever possible.

TIPS: Providing caregiver support and improving coping skills

- Social support is important for caregivers, whose own physical and mental health can be affected by stress and sadness of caring for a patient with brain tumor.
- Encourage them to join a support group.
- Personal therapists can help caregivers deal with stress, anxiety, and depression or sort out conflicts about priorities in time or living arrangements.
- Religious organizations can also help through support groups.

SUMMARY RECOMMENDATIONS

- Support caregivers in their new roles with information, education, and connection to resources as well as to others who are in similar situations.
- Encourage use of support groups, one-on-one therapy, or peer-to-peer support.
- Encourage caregivers to make time for self-care and respite.

Conclusion

In summary, the needs for brain tumor patients continue and change across the trajectory of the illness. When caring for a brain tumor patient at the end of life, one must remember that most of the symptoms that the patient will experience are a direct result of increased intracranial pressure or invasion of brain tissue by tumor. Due to the nature of the disease, the majority of the symptoms experienced are neurological and patients often experience rapid cognitive and functional decline. For most patients, the symptom burden increases dramatically in the last several weeks to months of life.



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