Glioma Palliation Focuses on Seizure Prevention

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SALT LAKE CITY — The unique challenges of providing palliative care to patients with lethal brain tumors can best be met by anticipating and preparing for functional decline and working with a pharmacist and neurologist to optimize the use of steroid and antiseizure medications, according to joint presentations at the annual meeting of the American Academy of Hospice and Palliative Medicine and the Hospice and Palliative Nurses Association.

Gliomas account for three-quarters of all malignant brain tumors, and half of all gliomas are glioblastomas, which have a 5-year survival rate of 3%, said Dr. Michael E. Salacz, a medical oncologist and board-certified palliative care physician at St. Luke's Cancer Institute in Kansas City, Mo.

Three-quarters of patients with metastatic brain tumors (which outnumber primary brain tumors 10 to 1) die from systemic disease progression and not from brain progression, he explained.

"We're making some preliminary inroads on the treatment of these tumors, but unfortunately what's more common is surgical resection and cancer resurgence," he said, adding that management of seizures is a crucial part of palliative care in such cases.

"About half of these patients are going to have seizures as their initial presenting symptom, and the other half are going to have seizures sometime during the course of treatment," Dr. Salacz said.

While traditional antiepileptic drugs such as Dilantin, Depakote, and Tegretol reduce the risk of subsequent seizures, they do not prevent initial seizures, he said, pointing to American Academy of Neurology Guidelines, which state that patients who have not had a seizure after surgery should not be on an antiseizure medication.

"The reality is that over half of physicians use antiepileptic drugs prophylactically. Even though the data show no benefit, many patients will come to palliative care and hospice with seizure prophylaxis. Neurosurgeons have been trained to give Dilantin. As a result, any patient who has had a craniotomy is on Dilantin, and a good portion of these patients are going to have side effects and toxicity as a result of these drugs," Dr. Salacz said, adding that palliative care doctors treating brain tumor patients who no longer take anything by mouth and have no intravenous line must decide how and whether to give antiepileptic drugs.

Anticipating functional decline is the goal care for a brain tumor patient at the end of life.

DR. SINCLAIR

"This is a common dilemma in this patient population because the alternative routes of dosing have relatively little data to support them. What I can tell you is that I used transdermal phenobarbital in an advanced patient who would not tolerate oral medications and had a history of seizure disorder," Dr. Salacz said, adding that after application of the topical paste, the patient was seizure free for his remaining 2 weeks of life.

"While there are no data on use of transdermal phenobarbital, we do know how much of each milligram applied to the skin will get into the bloodstream," he said.

Short-term corticosteroids, though they have no antitumor effect, can be beneficial at reducing symptoms caused by peritumoral edema.

However, steroids may produce gastrointestinal toxicity, steroid myopathy and, occasionally, lymphopenia or Pneumocystis carinii pneumonia, said Dr. Salacz.

Describing the use of dexamethasone as more art than science, Dr. Salacz said, "There are no magic doses when you're using dexamethasone to reduce brain edema. Oral absorption is rapid and excellent, so you don't need to do [intravenous] steroids when you have an oral rate that you can use."

Dexamethasone is given every 6 hours, which requires that the patient be awakened at 2 a.m. to take his medication. Dr. Salacz uses a loading dose, though he conceded that doing so is not supported by research data.

"The half-life of dexamethasone is 36-50 hours and pharmacologically it takes about five half-lives for the drug to be out of your system, so the dose I give the patient is going to be gone 7-10 days later," he said, adding that dexamethasone can be given daily or twice a day.

Steroid-induced insomnia can be minimized by dosing at 8 a.m. and 4 p.m., Dr. Salacz said, adding that neurologic changes follow 1-4 days after a dexamethasone dose change, which can be confusing to a patient on a steroid taper who suddenly develops symptoms.

Cognitive dysfunction occurs in half to three-quarters of brain tumor patients secondary to the disease or to treatment, and has been shown to predict radiographic progression and worse survival.

Although many trials use the Mini-Mental Status Exam (MMSE), Dr. Salacz said that by the time cognitive dysfunction shows up on this screening test, it already has become significant. An alternative is neuropsychiatric testing, which is not widely available or covered by Medicaid. "So I'm stuck trying to help these patients as best as I can out of our clinic," he said.

Palliative care for brain tumor patients at the end of life also is preventive medicine that involves anticipating and getting the jump on functional decline, said Dr. Christian T. Sinclair, a palliative care and hospice physician.

"Our job is to maximize benefits for the patient and family by discussing alternative services that are available and getting physical or occupational therapy involved early to strengthen the patient as much as possible," said Dr. Sinclair, with Kansas City Hospice and Palliative Care. Although little can be done to slow functional decline, supplementing a corticosteroid with short-term methyl-phenidate can help increase energy and help cognition, he said.

"Start methylphenidate at 5 mg in the morning and 5 mg at noon. You'll know within a day if it works. If it does, go to 10 mg b.i.d. and top out at 30 mg a day. If the patient gets jittery and anxious, you may want to discontinue the drug," he said.

Dr. Sinclair's "simple medication regimen at the end of life" was presented as an example: Dexamethasone 4 mg by mouth b.i.d., valproic acid 500 mg by mouth b.i.d., subcutaneous Lovenox daily, morphine ER 15 mg by mouth b.i.d., and morphine 5 mg by mouth every 2 hours p.r.n. for pain. And, he emphasized, some of these doses exceed FDA's normal dosage recommendations, therefore always use the lowest effective dose. ■

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