Neurologic and Medical Management of Brain Tumors

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KEYWORDS

• Bevacizumab • Brain tumor • Chemotherapy • Cognition • Corticosteroids
• Fatigue • Mood • Seizure

KEY POINTS

- Prophylactic anticonvulsants are not recommended for patients with seizure-naive brain tumor.
- Monotherapy with a nonenzyme-inducing anticonvulsant is the preferred initial treatment for patients with tumor-related epilepsy.
- Asymptomatic patients with brain tumors do not require corticosteroids.
- Low-molecular-weight heparins are safer and more effective than oral anticoagulants for the management of venous thromboembolism in patients with brain cancer.
- Bevacizumab has steroid-sparing properties that often permits steroid taper.

INTRODUCTION

The complexity of the care of patients with neuro-oncologic disorders demands a multidisciplinary approach, where the neurologist may play a major role. An understanding of the spectrum of neurologic and systemic complications associated with brain cancer and cancer therapy is essential for guiding appropriate treatment.[1] We review aspects of relevance to the neurologist regarding the supportive care of patients with brain tumors, with attention to the management of seizures, brain edema, venous thromboembolism (VTE), fatigue and mood alterations, cognitive dysfunction, as well as the deleterious effects of antitumor and supportive therapy.

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SEIZURES

Epilepsy and its treatment is a frequent cause of morbidity in patients with intracranial neoplasm. Approximately 30% to 50% of patients with brain tumor present with seizures and 30% will become intractable.[2] The incidence will vary according to the type (**Table 1**) and location of the tumor. Focal seizures occur in about 60% of the cases with secondary generalization in 40%.[3] In the pediatric and young adult population, gangliogliomas and dysembryoplastic neuroepithelial tumors are more frequently associated with intractable epilepsy.[4,5] Seizures are a common manifestation of low-grade gliomas (LGG) because of their indolent growth rate and location,[6] with cortically located oligodendrogliomas carrying a higher risk than deep midline-located tumors.[7] Furthermore, in LGG, the accumulation of 2-hydroxyglutarate in isocitrate dehydrogenase 1–mutated tumors has been postulated as a driver of epileptogenesis.[8] Only about one-third of patients with brain metastases present with seizures, but when the primary is melanoma the incidence of seizures is approximately 67% possibly related to the cortical predilection, widespread distribution, and the tendency for hemorrhage.[6]

Oncologic treatment plays an important role in the management of tumor-related epilepsy. Antitumor therapies have a favorable impact on seizure control in patients with brain tumor. In LGG, complete resection predicts favorable seizure outcome.[6] Gross total resection is the most important factor for predicting seizure freedom; however, preoperative seizure control during antiepileptic drug (AED) administration as well as the duration of seizures of $\leq$ 1 year also confers favorable seizure control.[9] Conventional radiotherapy[10] and Gamma Knife radiosurgery[11] have a positive influence on seizure control. In addition, significant seizure reduction during chemotherapy in patients with LGG has been observed.[12,13] Furthermore, seizure response during antitumor therapy has been proposed as a metric in brain tumor trials.[14]

Use of Antiepileptic Drugs

AED administration after seizure secondary to brain tumor is the standard of care. In seizure-naive patients, however, prophylactic AEDs are not recommended. A meta-analysis did not justify prophylactic AED administration,[15] and this has been corroborated in more contemporary systematic reviews.[4,15–18] In neurosurgical practice, the goal of AED prophylaxis is to prevent acute postoperative seizures, but it remains unclear whether prolonged prophylactic AED therapy reduces seizure frequency after craniotomy. Several studies have failed to demonstrate efficacy of postoperative

Table 1
Estimated seizure frequency by tumor type

Tumor Type	Frequency
Glioneuronal tumor[33]	80%–100%
Oligodendroglioma[33,124]	70%–90%
Diffuse low-grade glioma[33]	60%–85%
Anaplastic astrocytoma[124]	60%–70%
Glioblastoma[33,124]	40%–60%
Meningioma[6,124]	20%–50%
Metastasis[6,29]	20%–35%
Primary CNS lymphoma[125]	10%

Abbreviation: CNS, central nervous system.