Chapter 14
Brain Tumors

Raoul J. Aponte, Ankur R. Patel, and Toral R. Patel

14.1 Introduction

Brain tumors encompass a wide range of clinical entities, including primary and metastatic lesions and benign and malignant pathologies. Although they are not nearly as prevalent as other neoplasms, brain tumors often require complex, multidisciplinary care. Furthermore, patients with brain tumors frequently require intensive care unit (ICU) management, both at time of initial presentation and in the post-operative period. Primary brain tumors include lesions that originate in the central nervous system (CNS); in contrast, metastatic (or secondary) brain tumors originate outside of the CNS (Fig. 1).

R.J. Aponte, PA-C (✉)
University of Pennsylvania, Philadelphia, PA, USA
e-mail: Raoul.aponte@uphs.upenn.edu

A.R. Patel, MD • T.R. Patel, MD
University of Texas, Southwestern Medical Center, Dallas, TX, USA
e-mail: ankur.patel@phhs.org; toral.patel@utsouthwestern.edu

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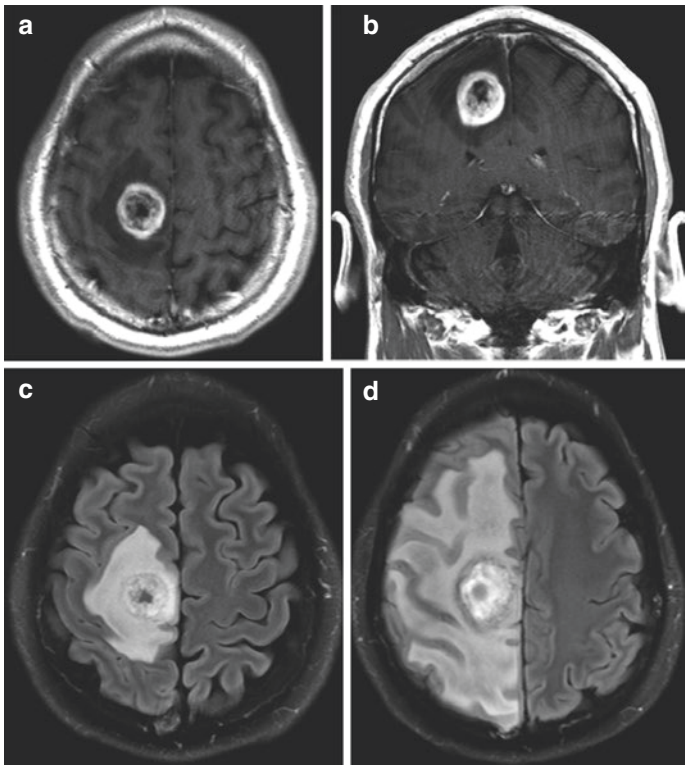

Fig. 14.1 Case 1 Imaging. (**a**, **b**) Pretreatment axial and coronal T1 post-contrast MRIs demonstrate a ring-enhancing intra-axial mass with central necrosis. (**c**) Pretreatment axial FLAIR MRI demonstrates surrounding vasogenic edema that was managed with corticosteroids. (**d**) Posttreatment axial FLAIR MRI demonstrates a significant increase in vasogenic edema, which is now diffuse and encompasses the majority of the right cerebral hemisphere

According to Central Brain Tumor Registry of the United States, the annual incidence of primary CNS tumors is 22.36 cases per 100,000 people. Thus, it is estimated that there will be ~79,270 new cases of primary CNS tumors diagnosed in the

United States (USA) in 2017. This includes both malignant (~26,070 new cases) and benign (~53,200 new cases) pathologies. The most common malignant primary CNS tumor is glioblastoma (GBM), a highly aggressive type of glioma that arises from glial cells. The most common benign primary CNS tumor is a meningioma, which arises from the arachnoid cap cells of the meninges. In the United States, ~17,000 deaths will be attributed to primary malignant CNS tumors in 2017 [1].

Metastatic CNS neoplasms are much more common than primary CNS neoplasms. It is estimated that 100,000 new cases of metastatic brain tumors are diagnosed in the United States each year. Furthermore, approximately 20–40% of cancer patients will develop brain metastases at some point in their disease course. The most common cancers to metastasize to the brain include lung, breast, and melanoma [2].

Patients with brain tumors present to medical attention with a wide variety of signs and symptoms, depending on the size and location of the tumor. Tumors in relatively ineloquent locations (i.e., right frontal pole) often grow to a large size and present with generalized signs of mass effect such as headache, nausea/vomiting, and fatigue. In contrast, tumors in highly eloquent locations (i.e., left frontal operculum) may present at a much smaller size by causing focal neurologic deficits. Brain tumor patients also commonly present with seizures, vision changes, cognitive decline, sensory or motor deficits, and ataxia.

In general, treatments for brain tumor patients are directed toward two synergistic goals: improvement of neurologic function and improvement of oncologic outcome. These treatments can include surgical resection, chemotherapy, radiation, and medical management. Benign tumors are most often treated with surgical resection alone, although radiation may be required for surgically inaccessible skull base tumors. Malignant tumors most often require a combination of surgical resection, chemotherapy, and radiation. In this chapter, we will focus our attention on reviewing the management of common critical care issues that occur in brain tumor patients.

14.2 Case Presentations

14.2.1 Case 1

Thirty-eight-year-old right-handed male presents to medical attention with a rapidly progressive left hemiparesis. Intracranial imaging revealed a right frontal, intra-axial, enhancing mass lesion within the subcortical motor pathway (Fig. 14.1a–c). The patient was started on high-dose dexamethasone (10 mg initial bolus, followed by 4 mg every 6 h) and noted to have improvements in his motor exam the next day. Due to the location of the lesion, a stereotactic biopsy was performed; pathology revealed a glioblastoma. The patient was subsequently treated with adjuvant chemotherapy (temozolomide) and radiation, and steroids were slowly tapered.

Approximately 3 weeks later, the patient presented to medical attention with headache, lethargy, nausea/vomiting, and increased left-sided weakness. Repeat intracranial imaging revealed a significant increase in peritumoral edema with new mass effect, midline shift, and early obstructive hydrocephalus (Fig. 14.1d). The patient was admitted to the ICU and started on high-dose IV dexamethasone as well as hyperosmolar therapy (3% saline and mannitol). Within 12 h, he reported improvements in his headaches and had objective improvements in his left-sided strength. He was then started on bevacizumab, with resolution of his headaches. He subsequently resumed his combined chemotherapy and radiation therapy 2 weeks after admission.

14.2.2 Case 2

Sixty-one-year-old right-handed female presents to medical attention after experiencing a generalized tonic-clonic seizure at work. Intracranial imaging revealed a large, en plaque right

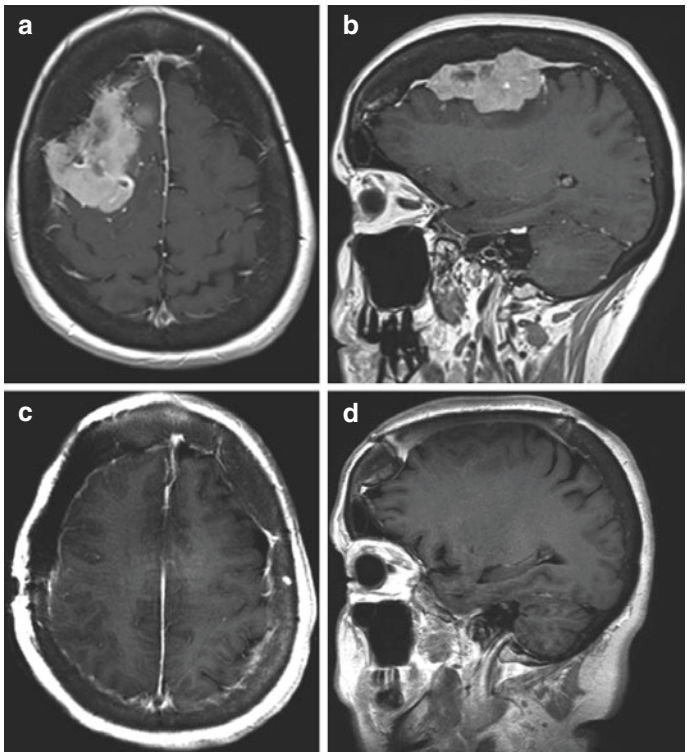

Fig. 14.2 Case 2 Imaging. (**a**, **b**) Preoperative axial and sagittal T1 post-contrast MRIs demonstrate an extra-axial enhancing right frontal mass with a "dural tail" and local mass effect, consistent with an en plaque meningioma. (**c**, **d**) Postoperative axial and sagittal T1 post-contrast MRIs demonstrate gross total resection with resolution of the mass effect

frontal meningioma with hyperostosis of the overlying calvarium (Fig. 14.2a, b). She was started on levetiracetam and taken to the operating room several weeks later for elective surgical resection (Fig. 14.2c, d).

Immediately postoperatively, she remained clinically stable and was neurologically intact. Subsequently, on the first night after surgery, the patient developed focal motor seizures of her left arm. Intracranial imaging was obtained and revealed expected changes, without evidence of hematoma or infarct. The seizures persisted despite several 2 mg boluses of lorazepam and increasing doses of levetiracetam. Over the next several hours, she developed focal status epilepticus and soon became lethargic. She was intubated, started on continuous video EEG, and ultimately required burst suppression with propofol and a fosphenytoin load to control seizures. Approximately 48 h later, the sedation was lifted and the patient was noted to slowly awaken. Over the next 24 h, she became fully alert and was noted to be neurologically intact. She was maintained on levetiracetam and phenytoin and has remained seizure-free.

14.2.3 Case 3

Thirty-two-year-old right-handed female presented to medical attention with a 1-week history of progressive headache, nausea/vomiting, and blurry vision. Intracranial imaging was obtained and revealed a colloid cyst with resultant obstructive hydrocephalus (Fig. 14.3a, b).

The patient was admitted to the ICU and noted to be awake and alert. Given her preserved mental status, an emergent external ventricular drain (EVD) was not required; however, an EVD kit was placed at bedside while operative preparations were made. The patient was started on high-dose IV dexamethasone and taken to the operating room the following morning for resection of the colloid cyst. Postoperatively, the patient had complete resolution of her symptoms; intracranial imaging revealed gross total resection of the lesion and resolution of the hydrocephalus (Fig. 14.3c, d).

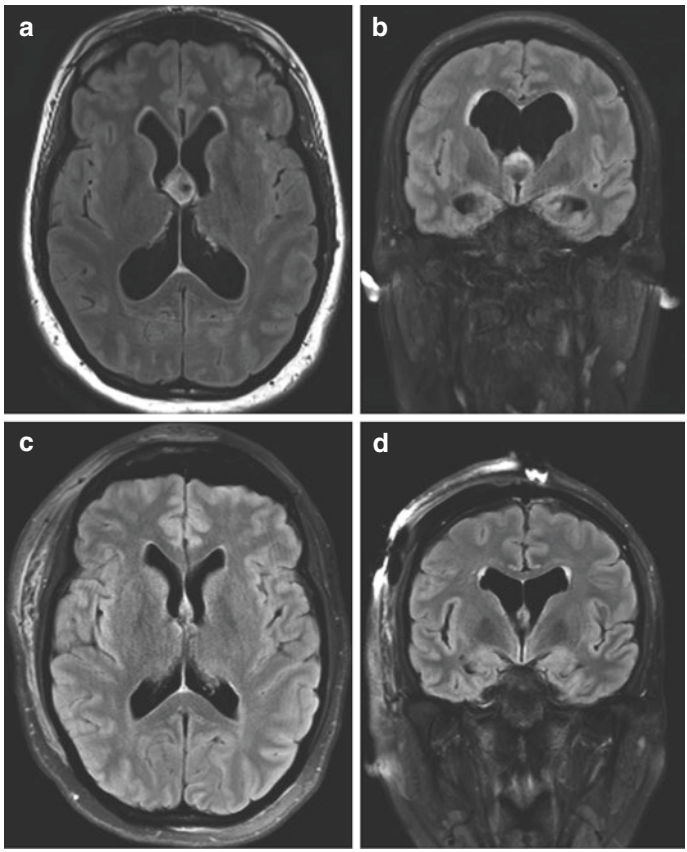

Fig. 14.3 Case 3 Imaging. (**a**, **b**) Preoperative axial and coronal FLAIR MRIs demonstrate an intraventricular mass centered at the foramina of Monro, consistent with a colloid cyst. Note the dilated ventricular system, a sign of obstructive hydrocephalus. (**c**, **d**) Postoperative axial and coronal FLAIR MRIs demonstrate gross total resection with resolution of the hydrocephalus

14.3 Initial Evaluation

As with all neurocritical care patients, the initial evaluation of a brain tumor patient should begin with a thorough neurological exam. In particular, providers should focus on the patient's mental status and assess for the presence or absence of focal neurologic deficits. The initial evaluation should also include a review of the available intracranial imaging, typically a CT and/or MRI. In general, if a brain tumor patient presents in an emergent fashion, a non-contrast CT of the head should be obtained to evaluate for an acute neurologic emergency (i.e., hemorrhage, infarct, herniation). However, in non-emergent cases, the preferred imaging modality is an MRI of the brain with and without contrast, which provides superior delineation of the tumor and brain parenchyma. Most brain tumors have unique imaging characteristics, which help to identify them from one another (Fig. 14.4). Following review of the exam and imaging findings, the patient should be quickly stabilized and treated in accordance with the interventions described below.

14.4 Interventions and Management

14.4.1 Routine Postoperative Management

The majority of brain tumor patients are admitted to the ICU for routine postoperative care. In most hospitals, patients undergoing a cranial tumor surgery will spend one night in the ICU immediately after surgery. This allows for close monitoring and rapid identification of changes in neurological exam. If a change in neurologic status is identified, brain imaging (typically, a non-contrast CT Head) must be obtained expeditiously to

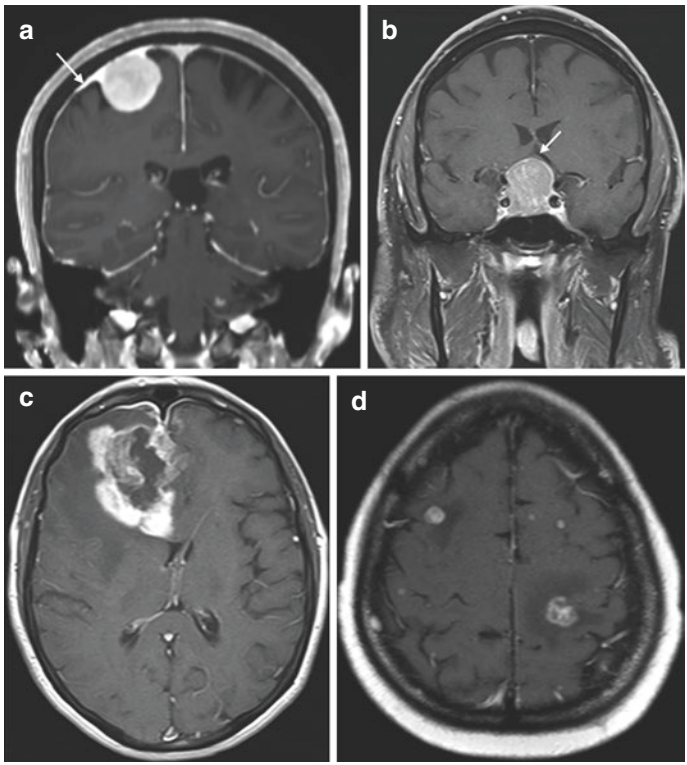

Fig. 14.4 MRI images depicting the most common primary and secondary CNS tumors. (**a**) Coronal T1 post-contrast MRI demonstrating a convexity meningioma. Note the extra-axial location, homogenous enhancement, and presence of a "dural tail" (*arrow*). (**b**) Coronal T1 post-contrast MRI demonstrating a pituitary macroadenoma with suprasellar extension and compression of the optic chiasm (*arrow*). (**c**) Axial T1 post-contrast MRI demonstrating a glioblastoma. Note the intra-axial location, thick peripheral enhancement, and central necrosis. (**d**) Axial T1 post-contrast MRI demonstrating multiple brain metastases. Note the numerous intra-axial enhancing lesions near the grey-white junction with associated vasogenic edema

evaluate for frequent postoperative complications, including hemorrhage, infarct, and pneumocephalus. Additionally, the ICU setting allows for prompt treatment of pain, nausea, and vomiting, symptoms which are common in the first 24 h following cranial surgery. The routine care of most postoperative brain tumor patients includes the administration of intravenous fluids, corticosteroids (most commonly, dexamethasone), narcotics, and antiemetics. Additionally, TED hoses and sequential compression devices are utilized to decrease the risk of deep venous thrombosis. Neurological exams are performed every hour. Systolic blood pressure is typically maintained <140 mmHg (using labetalol, hydralazine, and/or nicardipine). Foley catheters are utilized to record strict urine input and output. A non-contrasted CT of the head is typically obtained 24 h after the procedure to evaluate the surgical cavity. If the CT scan demonstrates expected findings and the neurological exam is stable, the patient can be transferred to the general floor.

14.4.2 Management of Cerebral Edema

Brain tumor patients often present with symptomatic peritumoral edema. Edema is defined as the abnormal accumulation of fluid within tissues. Cerebral edema can be subdivided into two main types: vasogenic and cytotoxic. Cytotoxic cerebral edema occurs when fluid accumulates within cells as a result of injury, most commonly, an ischemic event. Vasogenic edema occurs when a disruption in the blood-brain barrier (BBB) allows plasma proteins and fluid to shift into the brain parenchyma and is commonly associated with brain tumors (particularly high-grade gliomas and metastatic lesions) [3].

Vasogenic edema can be a major cause of morbidity and mortality in brain tumor patients. Significant vasogenic edema may result in elevations in intracranial pressure (ICP), mass effect on critical neurovascular structures, and herniation

syndromes [4]. The initial treatment for vasogenic edema is corticosteroids. Since the 1950s, dexamethasone has been the steroid of choice due to its longer half-life and low mineralocorticoid effects [5]. When starting dexamethasone, most patients are given an initial bolus of 10 mg intravenously, followed by a maintenance dose of 4 mg every 6 h. However, this dosing schedule may vary considerably depending on provider preference. Improvements in neurologic symptoms are typically seen within the first 24 h. Once maximum clinical benefit has been achieved, steroids should be slowly tapered to the lowest effective dose [6]. In addition to their use for symptomatic vasogenic edema, corticosteroids are also used in the immediate postoperative care of brain tumor patients. This practice has been demonstrated to decrease perioperative morbidity and mortality. Typically, patients are placed on a dose of 4–6 mg every 6 h following surgery, and this is tapered over the subsequent 1–2 weeks.

Although corticosteroids have improved clinical outcomes for brain tumor patients, these medications can have significant adverse effects that must be recognized, especially with prolonged use. Although relatively uncommon, these include gastrointestinal (GI) issues (bowel perforation, gastric ulcers), proximal myopathy, pneumocystis pneumonia, and osteoporosis. Other more common but less severe side effects include hyperglycemia, behavioral changes, weight gain, insomnia, and immunosuppression. Thus, for patients on corticosteroids, frequent blood glucose checks and either proton pump inhibitors or H2 blockers should be included in the treatment plan.

In addition to corticosteroids, other medications can be considered for the treatment of peritumoral cerebral edema. Hyperosmolar agents can reduce the amount of edema by increasing serum osmolality and drawing fluid out of the brain via an osmotic gradient. The most commonly used hyperosmolar agents are hypertonic saline and mannitol. When administering these medications, the patient's serum osmolality, osmolar

gap, and sodium should be carefully monitored; these measurements should not exceed 320 mOsm/kgH_20, 12, and 160 mEq, respectively. Additionally, because these medications are administered intravenously, they can only be utilized transiently in an emergent setting. See Chap. 11 for further information on use of osmotic agents for edema management. Another pharmacologic option for the treatment of refractory peritumoral edema is the VEGF-A inhibitor, bevacizumab. In randomized trials, this medication was found to have only modest oncologic benefit in malignant gliomas; however, it was found to have remarkable efficacy in the treatment of vasogenic edema [7]. Thus, for patients with severe edema that cannot be controlled by steroids alone, bevacizumab may be a valuable adjunctive option.

14.4.3 Management of Seizures

Many brain tumor patients frequently experience seizures; as a result, good seizure control is essential for patient management. Approximately 20–40% of brain tumor patients will present with seizures, while another 20–45% of patients will develop seizures at some point during their clinical course [8]. There are several factors that influence the likelihood of developing a seizure. In general, primary brain tumors tend to have a higher incidence of seizures as compared to metastatic lesion. Of the primary tumors, low-grade gliomas are more epileptogenic than high-grade gliomas. The location of tumors also correlates with risk of seizures; cortical and temporal lobe lesions have higher rates of seizures than infratentorial or deep, subcortical tumors [9].

If a brain tumor patient experiences a seizure, the risk of developing a subsequent seizure is high. Thus, it is important to start antiepileptic drugs (AEDs) immediately. Seizures themselves can lead to profound neurologic morbidity and significantly impact a patient's quality of life. Choosing an anticonvulsant regimen can

present a challenge; both its therapeutic efficacy and potential side effects must be considered [10]. The newer AEDs (including levetiracetam, lacosamide, lamotrigine, topiramate, zonisamide, gabapentin, pregabalin) are generally preferred over older medications (phenytoin, valproic acid, phenobarbital) because of their fewer side effects and drug-drug interactions [3, 10]. Most often, brain tumor patients experience localization-related epilepsy, due to the physical presence of the tumor. Thus, if the tumor can be surgically resected, this has the potential to cure the patient's seizure disorder.

The available data suggests that prophylactic AEDs are not effective in preventing first seizures, and given that many AEDs have significant side effects, prophylactic use is not supported [8]. Despite the lack of supporting data, many providers still prescribe prophylactic AEDs in the perioperative period, arguing that a seizure during this critical time could have significant clinical impact. If AEDs are given prophylactically in the perioperative period, it is generally accepted that they should be discontinued within 7 days following surgery [11].

14.4.4 Management of Hydrocephalus

Hydrocephalus is defined as the abnormal accumulation of cerebrospinal fluid (CSF) within the ventricular system of the brain. Broadly, hydrocephalus can be either obstructive (non-communicating) or communicating in nature. Obstructive hydrocephalus occurs when there is a blockage within the ventricular outflow system. Depending on the location of the obstruction, various parts of the ventricular system will be dilated, while other portions may be normal in caliber. Communicating hydrocephalus occurs when the entire ventricular system is dilated; there is no focal point of obstruction. Thus, the anatomic abnormality lies within the absorptive portion of the CSF pathway, at the level of the arachnoid granulations.

Overall, obstructive hydrocephalus is more common in brain tumor patients than communicating hydrocephalus, although both conditions may occur. Obstructive hydrocephalus is caused by physical compression of the ventricular outflow pathway by the tumor itself. Communicating hydrocephalus occurs when a tumor secretes abnormal proteinaceous material into the CSF, which impairs the ability of the arachnoid granulations to absorb the CSF.

Patients with hydrocephalus most often present with signs and symptoms of elevated ICP. This typically includes headaches, nausea/vomiting, vision changes, and lethargy. On physical exam, notable findings may include papilledema and altered mental status. The severity of symptoms is related to the degree of hydrocephalus and the rapidity of onset. Slowly evolving hydrocephalus allows the brain time to accommodate, while rapidly evolving hydrocephalus does not. Similarly, mild hydrocephalus can often be compensated for, while severe hydrocephalus is typically symptomatic.

While the definitive treatment of hydrocephalus is generally surgical in nature, several medical interventions are important during the initial stages of management. Patients with symptomatic hydrocephalus should be admitted to the ICU for close neurologic monitoring. Additionally, they should be placed on high-dose corticosteroids to reduce any peritumoral edema that may be contributing to an obstructive phenomenon. Finally, bedside placement of an external ventricular drain (EVD) may be required, to temporarily divert CSF from the ventricular system and control ICPs. After the patient has been stabilized, obstructive hydrocephalus is typically treated by resection of the tumor, while communicating hydrocephalus often requires placement of a ventriculoperitoneal shunt, even if the tumor has been removed.

14.4.5 Prevention of Venous Thromboembolism

Brain tumor patients are known to have an increased risk of postoperative deep venous thrombosis (DVT) and pulmonary embolism (PE), with a reported incidence of 3–8% in the immediate postoperative period [12, 13]. It is postulated that the increased rates of DVT and PE in brain tumor patients are due to the local synthesis of tissue factor and/or higher rates of immobility in this population. Despite this, there is no consensus recommendation regarding the use of mechanical and/or chemical prophylaxis for these patients [14].

Numerous retrospective reviews have demonstrated that a practice of combined mechanical and chemical prophylaxis in the immediate postoperative period can reduce the risk of DVT and PE by more than half [14]. While almost all surgeons initiate mechanical prophylaxis in the operating room via TED hoses and sequential compression devices, there is considerable variability in the administration of subcutaneous chemical prophylaxis (both heparin and low-molecular-weight heparin, LMWH) [13]. Some surgeons begin chemoprophylaxis in the operating room, others wait until postoperative day 1, and others do not ever utilize chemoprophylaxis. In general, the reluctance to start chemoprophylaxis is due to the perception that this class of medications increases the risk of surgical site hemorrhage. While some case series do report an increased risk of minor bleeding with chemical prophylaxis, there have been no consistent reports demonstrating an increased risk of clinically significant surgical site hemorrhages with chemoprophylaxis [14]. Thus, at most institutions, for brain tumor patients, the practice has evolved to begin mechanical prophylaxis in the operating room and chemical prophylaxis on the morning of postoperative day 1.

14.4.6 Hospice/Palliative Care

Most patients with malignant brain tumors will eventually succumb to their disease. This is particularly true for glioma patients. As their disease progresses, these patients may experience a myriad of neurologic symptoms, including seizures, focal weakness, lethargy, cognitive changes, and headache. These symptoms may, in turn, prompt ICU admission. Thus, it is critical for the ICU provider to understand the natural progression of malignant brain tumors and to be prepared to provide supportive care to these patients via corticosteroids and AEDs, as needed. In addition to medical management, the critical care provider should engage the patient's primary oncologist to assist with family discussions regarding goals of care, and, when appropriate, consult the hospice/palliative care team. Although these efforts are not livesaving, by design, attention to end-of-life care is critical to the overall management of brain tumor patients and may start in the ICU. Keen attention to maintaining the comfort of both the patient and their family cannot be overemphasized.

Summary Points

- Brain tumor patients represent a wide range of clinical pathologies and can present to medical attention with a variety of signs and symptoms.
- Many brain tumor patients will require ICU care for the initial management of cerebral edema, seizures, and/or hydrocephalus.
- Almost all brain tumor patients will require transient ICU care in the immediate postoperative period.
- Close neurologic monitoring is essential; most neurologic changes, when identified early, can be treated with good long-term outcomes.

- Critical care providers who are treating brain tumor patients should be comfortable with the use of dexamethasone, hyperosmolar agents, and anticonvulsant medications.
- The ability to read and interpret intracranial imaging is essential to the management of brain tumor patients.

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