Emergency Cancer Care

REVIEWS

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Intracranial emergencies in neurosurgical oncology: pathophysiology and clinical management

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Abstract

Intracranial tumors pose a challenge in neurosurgery, especially when patients present emergently or require emergency surgery. Tackling an acute change in the patient's mental status is the primary reason for seeking an emergency surgery in the setting of an intracranial tumor. In addressing tumor-related complications, the aim of surgery is to relieve elevated intracranial pressure (ICP), confirm a diagnosis, improve or stabilize function, and extend the patient's life by preventing herniation.

Tumors and peritumoral edema form a space-occupying lesion that causes mass effect on nearby structures and elevates ICP. Surgical management involves (1) external ventricular drain (EVD) placement to monitor ICP, lower the volume of cerebrospinal fluid (CSF), and temporarily treat intracranial hypertension, (2) resection of the space-occupying mass responsible for the rise in ICP, and (3) in some patients, decompressive craniectomy (DC). Patients with brain tumors may also present with hydrocephalus due to the tumor's obstructing CSF flow or disrupting CSF absorption. Tumors also cause tumor-associated epilepsy (TAE) and status epilepticus (TASE). TASE is a life-threatening condition characterized by an abnormally prolonged generalized seizure (or a chain of multiple seizures) without recovery of consciousness to baseline. Time is of the essence when managing TAE and TASE, and surgical resection of the tumor-associated epileptogenic focus can be curative. Brain tumors and their treatment can also provoke ischemic stroke, intratumoral hemorrhage, and cerebral venous sinus thrombosis depending on their location. Hemorrhagic infarction of pituitary adenomas leading to rapid expansion of the sellar region and acute pituitary gland dysfunction is known as pituitary apoplexy. Here, optimizing the patient's hemodynamic status and treating adrenal insufficiency are crucial upon presentation. Emergency surgical resection plays an important role in saving nearby neurovascular entities when conservative treatment proves inadequate. Finally, infections of the central nervous system (CNS) occur as a result of immunologic compromise caused by the tumor itself or by its treatment.

In conclusion, in severe and rapidly progressing cases in which the patient presents with altered mental status and neurologic deficits, an emergency neurosurgical procedure is indicated for removal of the cause(s) of the excess ICP, protection of brain function, and monitoring of ICP.

Keywords: Intracranial tumors, Neurosurgical oncology, Acute oncology, Intracranial pressure, Hydrocephalus, Pituitary apoplexy, Intracranial hemorrhage, CNS infections

Introduction

Intracranial tumors remain a daunting challenge in neurosurgery, owing not only to the complexity of their presentation and elective management but also to the countless ways they may wreak havoc emergently. It is

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essential that these neurosurgical oncologic emergencies be identified promptly and treated in a timely manner as they often progress rapidly. In fact, there are multiple reasons as to why an emergency surgery may be sought as treatment for an intracranial tumor, many of which rotate around tackling an acute change in the patient's mental status. In addressing tumor-related complications (Table 1) such as cerebral edema and elevated ICP, seizures and status epilepticus, intra-tumoral hemorrhage, hydrocephalus, complications attributable to treatment such as central nervous system (CNS) infections, coagulopathy, or metabolic derangements, the aim of surgery is to relieve elevated ICP, confirm a diagnosis, improve or stabilize function, and extend the patient's life by preventing herniation (Table 2). Prompt diagnosis and management can prevent detrimental consequences and can even be lifesaving. In this review, we discuss the pathophysiology behind intracranial tumor complications that ultimately constitute a neurosurgical emergency, and summarize current ways of managing them.

Intracranial tumor complications

Increased ICP

Brain tumors are space-occupying lesions causing mass effect on nearby vital structures. In addition, they often provoke cerebral edema. In fact, edema plays a major role in determining symptoms caused by tumors.

Table 1 Complications of intracranial tumors

Intracranial tumor complications
A) Increased intracranial pressure
B) Hydrocephalus
C) Tumor-associated epilepsy and status epilepticus
D) Cerebrovascular complications
1) *Ischemic stroke*
2) *Intracerebral hemorrhage*
3) *Pituitary apoplexy*
4) *Cerebral venous sinus thrombosis*
E) CNS infection

Table 2 Reasons for emergency cranial surgery in the setting of neurosurgical oncology

Relieve increased intracranial pressure
- Reduce tumor bulk or remove a space-occupying lesion - Divert trapped CSF - Remove a hematoma - Remove swollen brain
Confirm a diagnosis
Improve or stabilize function
Prevent brain herniation

Cerebral edema is a condition of excess fluid within the brain parenchyma, caused by any of several mechanisms (Table 3). These include *cytotoxic edema* in which failure of the Na^+-K^+ ATPase pump leads to an influx of ions and water and thus to an expansion of intracellular fluid and volume overload in brain parenchyma. This is mainly seen in ischemia, trauma, or liver failure. Another mechanism of edema is *interstitial*, or hydrocephalic, edema in which an imbalance between the production and clearance of CSF leads to an increase in its volume and ultimately to an overflow of CSF into the periventricular extracellular space. This is mainly seen in hydrocephalus, meningitis, or pseudotumor cerebri. A third mechanism of edema is *osmotic* whereby an intravascular solute derangement such as hyponatremia or syndrome of inappropriate secretion of antidiuretic hormone can lead to water diffusion across the blood-brain barrier (BBB). The fourth and final mechanism is *vasogenic* edema wherein the integrity of the BBB is disrupted leading to an increase in capillary permeability that allows interstitial fluid to accumulate. This situation occurs with infections, cerebral edema at high altitude, intracerebral hemorrhage, the late stages of ischemia, or brain tumors. The mechanisms by which tumors cause vasogenic edema are diverse. Tumors secrete vascular endothelial growth factor (VEGF), an angiogenic cytokine that increases BBB permeability as well as neovascularization. The vasculature associated with malignant tumors also has a reduced or abnormal expression of endothelial cell tight junctions due to tumoral secretion of VEGF and matrix metalloproteinases [1–4]. In fact, the aggressiveness of the tumor correlates with the volume of edema more than its size [1–3]. Moreover, tumor-associated edema is affected by tumor type. For instance, peritumoral edema in high-grade gliomas is referred to as infiltrative edema because it represents vasogenic edema in a zone of infiltrating tumor cells [2, 3].

Cerebral edema caused by brain tumors not only adds to the mass effect of the tumor itself but also disrupts tissue homeostasis and reduces local blood flow leading to neurological disturbances [3]. More than two centuries ago, the Scottish surgeons Alexander Monro and George Kellie applied the principles of physics to the intracranial contents and hypothesized that the sum of the individually variable volumes of brain, CSF, and intracranial blood is constant within the fixed volume of a rigid skull. This equation became known as the Monro-Kellie doctrine (Fig. 1) [5, 6], denoted as

$$V_{CSF} + V_{blood} + V_{brain} = V_{intracranial\ space}$$

Hence, an increase in one component, or the addition of an external component to this equation as happens

Table 3 Mechanisms of cerebral edema

Cytotoxic edema	• Failure of the Na^+–K^+ ATPase pump ➔ influx of ions and water ➔ expansion of intracellular fluid and volume overload • BBB integrity: intact • **Example:** ischemia, trauma, and liver failure
Interstitial edema	• Imbalance of production and clearance of CSF ➔ increased intraventricular pressure ➔ overflow of CSF into periventricular extracellular space • BBB integrity: intact • **Example:** hydrocephalus, meningitis, and pseudotumor cerebri
Osmotic edema	• Lower plasma osmolarity compared to intracerebral osmolarity due to intravascular solute derangements ➔ water diffuses across the BBB • BBB integrity: intact • **Example:** metabolic derangements such as hyponatremia and SIADH
Vasogenic edema	• BBB is disrupted ➔ increased capillary permeability ➔ interstitial fluid seeps through • BBB integrity: breakdown • **Example:** tumors, ischemia (late stage), intracerebral hemorrhage, trauma, cerebral edema at high altitudes, and infections

in pathological states, should in theory displace another component to maintain a constant ICP within the confines of the skull. However, this reaches its limits when a maximal compression of other compartments is reached leading to decompensation and increased ICP (Fig. 2) [7]. The traditional pressure-volume relationship suggested by Monro and Kellie emphasized the role of CSF and intravascular blood as dynamic components, and the brain tissue as a static component that cannot change its volume in response to elevated ICP. In this theory, vascular blood and CSF are displaced to maintain normal pressure within the rigid cranium, but the brain parenchyma remains unchanged. However, modern observations show that neurons are, in fact, able to change their volume, and that brain is deformable especially when the ICP is elevated. Because brain parenchyma occupies around 80% of the cranium, its shrinkage frees up significant volume capable of buffering the high ICP triggered by a space-occupying lesion. Hence, high ICP drives tissue compliance [8]. The pioneering work by Marmarou

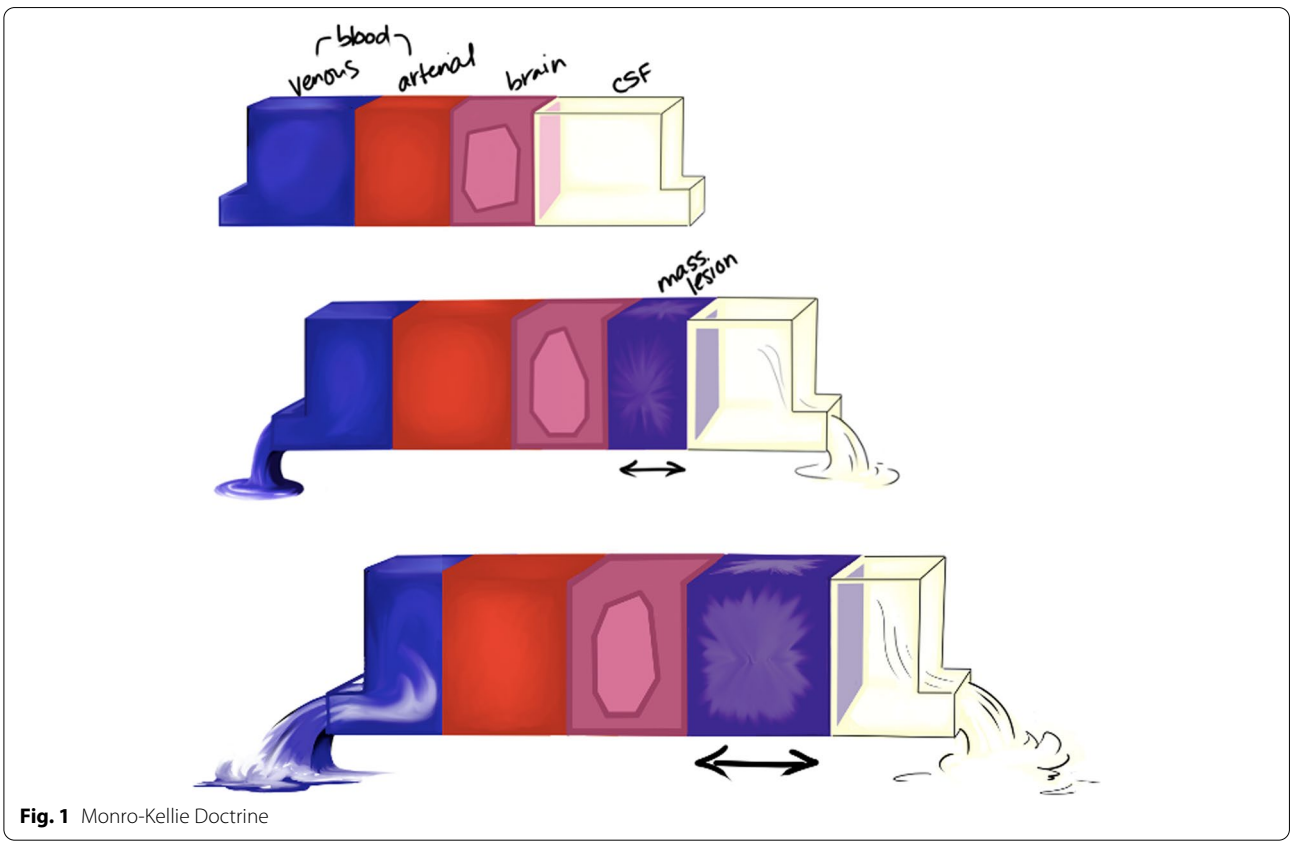

Fig. 1 Monro-Kellie Doctrine

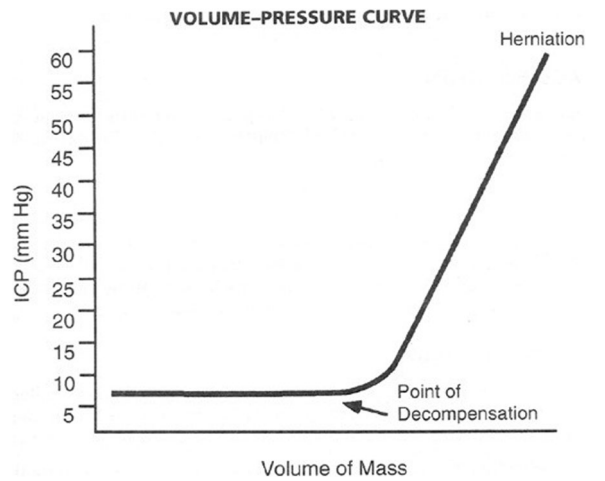

Fig. 2 Non-linear relationship between ICP and volume of the space-occupying lesion. An initial increase in volume results in a small increase in pressure because of intracranial compensation obtained by displacement of blood and CSF. Once intracranial compensation is exhausted, additional increases in intracranial volume result in a dramatic rise in ICP

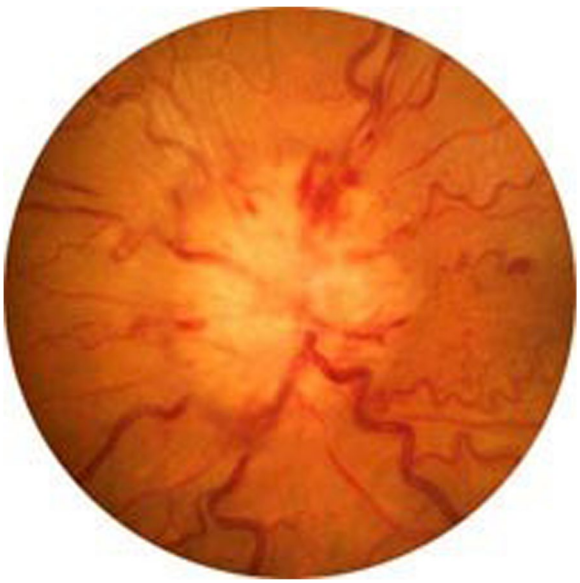

Fig. 3 Papilledema

and colleagues also elaborated on the dynamic aspects of ICP by introducing the concept of intracranial compliance in which volume changes, and the rate of change, within the closed cranium lead to pressure changes [9]. A system with high intracranial compliance can accommodate higher volumes, but as compliance decreases, ICP rises exponentially. Subsequently, new models have added further to the building blocks of our understanding of ICP [10–12].

Papilledema (Fig. 3), headaches that are worse in the morning, nausea and vomiting, abnormal eye movements, pupillary changes, seizures, and altered mental status are classic signs of intracranial hypertension [2] but not all patients with raised ICP present similarly [13]. In addition, not all patients presenting with signs of intracranial hypertension demonstrate such an increase on non-invasive ICP monitoring [14]. Infratentorial lesions may require urgent attention because small amounts of edema can result in severe neurological compromise and altered mentation given their proximity to the brainstem and aqueduct of Sylvius. Moreover, increased ICP may ultimately lead to brain herniation beneath major dural folds such as the falx cerebri or tentorium cerebelli [2, 13]. Although clinical signs of increased ICP can suggest an impending or *de facto* herniation (Table 4), this causal relationship is not always established as some patients have such signs without radiologic evidence of herniation and vice versa [13].

The most common herniation syndromes encountered in patients with brain tumors are classified as uncal, subfalcine, central, or tonsillar herniation (Fig. 4). In uncal herniation, the most common type, the uncus in the mesial temporal lobe herniates over the tentorial edge as a result of mass effect within the middle cranial fossa. In doing so, it compresses the oculomotor nerve (cranial nerve III) and causes a fixed and dilated ipsilateral pupil. In addition, the uncus can herniate against the midbrain leading to a decreased level of consciousness and contralateral hemiplegia. In patients with large temporal lobe tumors and prolonged uncal herniation, the posterior cerebral artery can be compressed between the uncus and the midbrain, and cause ischemia and cerebral infarction. Subfalcine herniation occurs when supratentorial space-occupying lesions such as metastases or low- or high-grade gliomas cause local mass effect leading to cingulate gyrus displacement under the falx. When this happens, the pericallosal branches of the anterior cerebral artery may be compressed as they run near the free edge of the falx. In central transtentorial herniation, the

Table 4 Signs of impending herniation

Signs of impending herniation
Mental status change
Decreased consciousness
Hypertension
Vomiting
Pupillary changes
Localizing signs
Papilledema
Posturing

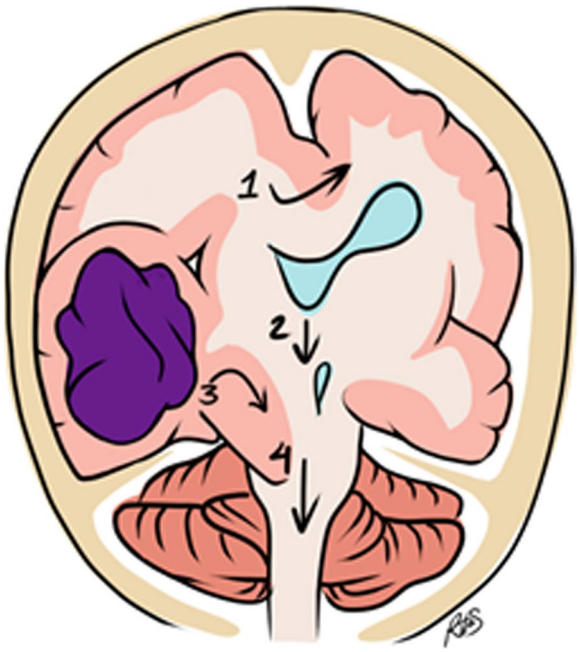

Fig. 4 Types of brain herniation: (1) subfalcine herniation; (2) uncal herniation; (3) central transtentorial herniation; (4) tonsillar herniation

entire midbrain herniates downward due to generalized mass effect leading to pinpoint pupils and loss of upward gaze. Finally, in patients with an infratentorial mass and expansion of the contents of the posterior fossa, tonsillar herniation occurs whereby the cerebellum herniates through the foramen magnum to compress the caudal medulla and upper cervical spinal cord [2, 15]. This form of herniation can be a terminal event. Although tonsillar herniation can be provoked or worsened by a large-volume lumbar puncture (LP) that causes an increased pressure gradient across the foramen magnum, LP can be done safely in most patients with a posterior fossa mass if a small (25-gauge) needle is used for the dural puncture and if the volume of CSF taken is limited to $\leq$ 5 mL.

An infratentorial mass can also cause upward transtentorial herniation which ultimately compresses the basilar artery and its upper branches (most notably the posterior cerebral artery, which is vulnerable to pressure) against the tentorium, and the midbrain and upper pons against the clivus. Such shifts can cause obstructive hydrocephalus. Upward herniation can occur spontaneously, but it is more commonly iatrogenic due to a pressure gradient across the tentorium created by supratentorial CSF diversion or lumbar puncture for CSF analysis [16].

Diagnosis of intracranial hypertension

A thorough neurological exam is imperative in determining when a patient has high ICP. The clinical signs are largely found in the patient's level of awareness, their cranial nerve reflexes, and whether obtundation is accompanied by such pathological reflexes as extensor posturing. The Glasgow Coma Scale (GCS) is calculated by assigning points to each of three categories of response: eye opening (1–4 point), verbal (1–5 points), and motor (1–6 points) [2]. Thus, a fully awake and oriented patient who opens his or her eyes spontaneously and obeys requests for movement of limbs receives a perfect score of 15. A patient who is completely unresponsive (and thus, in a profound coma) would receive the lowest score, which is 3. The GCS does not show causation, simply the depth of coma, which correlates with prognosis and also drives decisions to treat. A deeper understanding of cause is obtained by computed tomography (CT) or, if more detail is needed for surgical planning, by magnetic resonance imaging (MRI). CT is quicker, more widely available, and shows whether a patient has an intracranial lesion such as a tumor, abscess, or hematoma, the location of the lesion, and the degree of mass effect it induces. It also shows hydrocephalus, when it is present. CT of the head is the first and most important radiographic study done by a clinician assessing a patient in whom neurological impairment suggests an intracranial disease process warranting urgent treatment. When LP is needed to rule in or out the presence of meningitis or to quantify the ICP, it is done only after CT shows it is safe to do.

Management of intracranial hypertension (Table 5)

Non-surgical management Optimizing patient outcomes through prompt and proper initial resuscitation techniques is crucial. Generally, therapies that lower ICP are administered in a stepwise manner (Table 6). Initially, if the patient has a declining neurologic status, a GCS of less than 8, or requires sedation, intubation is warranted (Table 7) [2].

Patient positioning is an important pillar in the management of ICP. Elevating the head of bed to 30° decreases ICP by facilitating venous blood drainage. Jugular obstruction should be eliminated by placing the head in neutral position and adjusting or removing any constrictions around the patient's neck. Moreover, partial pressure of CO_2 (pCO_2) is a potent cerebral vasodilator and by reducing pCO_2 through hyperventilation, brain volume decreases and thus the ICP does as well. However, it is important not to induce aggressive hyperventilation (i.e., to $pCO_2 < 28$) as this may critically decrease cerebral blood flow (CBF) and can lead to cerebral dysfunction and in extreme cases to stroke.

Table 5 Emergency management in patients with elevated intracranial pressure and signs of impending or de facto cerebral herniation

1) Positioning: • Elevate head of bed to 30°, adjust or remove jugular obstruction, and maintain head in neutral position • Facilitates venous blood drainage
2) Securing airway and hyperventilation: • Intubate for airway protection and hyperventilation • Establish a secure airway to allow the physician to identify and treat apnea quickly • Hyperventilation reduces pCO_2, a potent cerebral vasodilator, and decreases cerebral blood volume. Over-aggressive hyperventilation should be avoided as it may critically decrease CBF and lead to ischemia/stroke • Hyperventilation has a fast onset and is effective for lowering high ICP, but its effect only lasts for a short duration and may be harmful if applied aggressively
3) Neuromuscular paralysis: • Facilitates intubation and prevents shivering
4) Fluid management: • Monitor fluid balance, body weight, serum electrolytes, and serum osmolality • Correct electrolyte disturbances and maintain euvolemia by giving isotonic (0.9%) saline • Avoid free water including D5W, half normal (0.45%) saline, and enteral free water • Serum osmolality should be kept > 280 mOsm/L (it is often kept in the 295 to 305 mOsm/L range)
5) BP control: • Maintain BP, minimize large shifts in BP, and avoid hypotension (may lead to ischemia) • BP should be sufficient to maintain CPP > 60 mmHg • Vasopressors and inotropes (e.g., dopamine or norepinephrine) can be used to increase MAP and achieve optimal CPP
6) Sedation: • Titrate propofol to a Ramsay score of 4. Do not exceed 5 mg/kg/h for more than 24 h. If maximum dose of propofol is reached while ICP > 20 mmHg, fentanyl drip can be started • Reduces metabolic demand, ventilator asynchrony, venous congestion, and the sympathetic responses of hypertension and tachycardia
7) Maintain normothermia and treat temperature > 37.5 °C by giving antipyretic agents (e.g., acetaminophen)
8) Hyperosmolar therapy (mannitol or hypertonic saline): • Give mannitol at dose of 1 g/kg IV for rapid reduction of ICP. Monitor fluids and electrolytes every 4 h (twice after each bolus) • Hypertonic saline can be alternatively used to maintain hyperosmolarity and rapidly reduce ICP. It may be effective when mannitol is not. It needs central line placement for administration. Adverse effects: congestive heart failure, hyperchloremic acidemia, hypernatremia, and seizures
9) Glucocorticoids: • Give dexamethasone (10–20 mg IV) followed by maintenance dose of 4–6 mg every 4–6 h • Reduces cerebral vasogenic edema • Adverse effects: hyperglycemia, insomnia, immunosuppression, mood fluctuations, myopathy, Cushing syndrome
10) Head CT as soon as possible. Moderate hyperventilation is advisable during transport and initial evaluation
11) Barbiturate coma therapy for refractory intracranial hypertension: • Pentobarbital is generally used with a loading dose of 5 to 20 mg/kg as bolus, followed by 1–4 mg/kg/h • Continuous EEG monitoring with EEG burst suppression as a guide to optimal dosage • Additional boluses can be given during infusion for acute spikes in ICP • Moderate doses cause sluggish pupils; large doses cause 3–5 mm nonreactive pupils • Watch for hypotension • Treatment should be assessed based on ICP and CPP response and development of unacceptable side effects
12) ICP monitoring: • Performed when GCS ≤ 8 with signs of elevated ICP on CT scan • Ventriculostomy performed to drain CSF in case of hydrocephalus, and to monitor ICP
13) Surgical management: • Resection of space-occupying lesion • Decompressive craniectomy • Trephination

CBF cerebral blood flow, *BP* blood pressure, *CPP* cerebral perfusion pressure, *MAP* mean arterial pressure, *ICP* intracranial pressure, *CSF* cerebrospinal fluid, *IV* intravenous, *GCS* Glasgow coma scale, *EEG* electroencephalography

In patients with brain tumors, it is crucial to maintain hemodynamic stability. Fluid balance should be rigorously monitored through measurement of the patient's fluid input and output, body weight, and serum electrolytes. Sodium alterations are the most common electrolyte abnormalities in patients with brain tumors and should be monitored closely. Euvolemia should be maintained by giving isotonic fluids. Hypotonic fluids should be avoided as free water passes into the brain and exacerbates any pre-existing edema. Furthermore, systolic blood pressure (SBP) should be maintained and hypotension avoided in patients with elevated ICP as it can lead to ischemia. CBF is related to systemic blood pressure and is defined with regard to cerebral perfusion

Table 6 Factors affecting intracranial pressure

Increase ICP	*Decrease ICP*
Hypercarbia	Hyperoxia
Hypoxia (pO_2 < 50 mmHg)	Hypothermia
Seizures or shivering	Barbiturates
Arousal (pain, anxiety)	Hypocapnia
Venous congestion	Hypovolemia

pressure (CPP) by the cerebrovascular resistance (CVR) as per the equation below (Table 8):

$$\mathrm{CBF} = \mathrm{CPP}/\mathrm{CVR}$$

CPP is a derived value and is the difference between mean arterial pressure (MAP) and ICP. MAP is calculated from measured systolic (SBP) and diastolic blood pressure (DBP).

Table 7 Glasgow Coma Scale (GCS)

Score	Eyes (E)	Verbal (V)	Motor (M)
6			Follows command
5		Oriented and appropriate	Localizes to pain
4	Eyes open spontaneously	Confused	Withdraws to pain
3	Eyes open to verbal command	Incoherent words	Decorticate positioning
2	Eyes open to pain	Incomprehensible sounds	Decerebrate positioning
1	No eye opening	Not verbal	No movement to pain

The GCS is scored between 3 and 15, 3 being the worst and 15 the best. It is composed of three parameters: eye response (E), verbal response (V), and motor response (M). Each component should be recorded individually. A score of 13 or higher represents mild brain injury. Scores of 9–12 and of 8 or lower represent severe and moderate injury, respectively

Table 8 Cerebral blood flow thresholds

CBF (mL/100 g/min)	Effects
> 60	Hyperperfusion (more than tissue demand)
45–60	Normal
< 20	Ischemia
12	Brainstem changes
10	Cell death

$$\begin{aligned}\mathrm{CPP} &= \mathrm{MAP} - \mathrm{ICP}\\ \mathrm{MAP} &= 1/3\,(\mathrm{SBP} - \mathrm{DBP}) + \mathrm{DBP}\end{aligned}$$

Within a CPP range of 50 to 150 mmHg, the CVR will vary to maintain a constant CBF, a physiological mechanism known as cerebral autoregulation (Fig. 5). A CPP ≤ 50 mmHg should be avoided to prevent cerebral ischemia. CPP is increased either by lowering ICP while maintaining MAP, or by increasing MAP. Ideal CPP values depend on the level of ICP. When ICP drops below

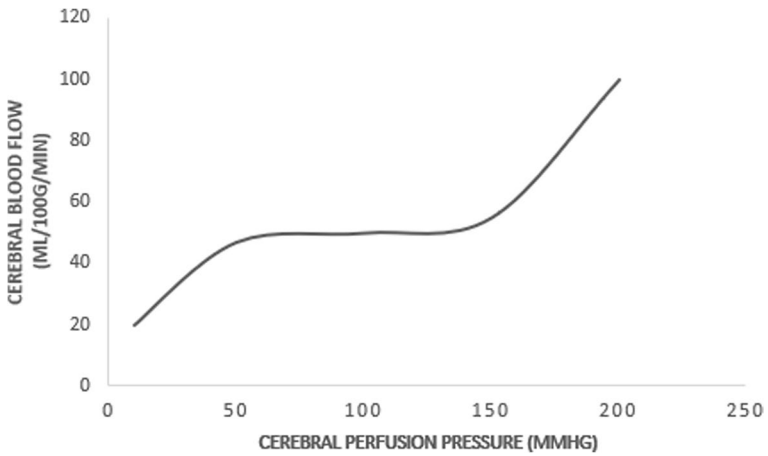

Fig. 5 Cerebral autoregulation. Initial changes in CPP are associated with maintenance of CBF due to appropriate changes in arteriolar resistance. More marked changes in CPP are eventually associated with loss of autoregulation, leading to a reduction (with hypotension) or an elevation (with marked hypertension) in CBF

22 mmHg, a CPP of ≥ 60 mmHg is targeted. If ICP is at or above 22 mmHg, a higher CPP threshold of 70 mmHg is targeted instead.

Moreover, avoiding fever in patients with intracranial hypertension is crucial as a rise of 1 °C in body temperature increases the cerebral metabolic rate by 10% and raises the ICP by several mmHg. Antipyretic agents should be used to prevent fever and maintain normothermia [2]. Hypothermia has historically been used to lower ICP as it reduces cerebral metabolic activity and has cytoprotective effects, but it can adversely cause arrhythmias, coagulopathies, hypokalemia, and a higher risk of infection [2, 17, 18].

Mannitol is used for rapid reduction of ICP. Mannitol at a dose of 1 g/kg I.V. is effective in reducing ICP with a peak effect at 15 to 35 min after infusion. This drug induces osmotic diuresis leading to hyperosmolarity which in turn draws water out of the brain. Fluid and electrolyte balance should be routinely monitored after mannitol administration. Complications from mannitol include hypokalemia, alkalosis, and a hyperosmolar hyperglycemic state in patients with diabetes mellitus and in the elderly. Alternatively, by adding solute to the circulation, hypertonic saline can be administered to maintain hyperosmolarity without diuresis [2].

Steroids for the management of tumor-associated edema have been widely used since the early 1960s [19–23].. A large dose (10–20 mg) of dexamethasone is given intravenously for patients presenting acutely, followed by a maintenance dose of 4–6 mg every 4–6 h [2]. Dexamethasone reduces tumor cell viability, lowers CSF production, and suppresses VEGF (which has been implicated in the mechanism of tumor-associated edema) [1, 23]. Steroids have also been shown in vitro to modulate the expression and distribution of tight junction proteins including occludin, claudin-5, and ZO-1 in endothelial cells in the BBB. This functional and anatomic barrier is a cornerstone of the pathophysiology of cerebral edema [23].

If cerebral edema goes uncontrolled, it can lead to refractory intracranial hypertension (RICH). RICH can also occur postoperatively due to residual tumor or to postoperative complications such as hemorrhage, infarction, and increased edema [24]. A rise in ICP in tandem with a rise in MAP indicates a total loss of cerebral autoregulation and a poor prognosis. Timely management of RICH is crucial for better neurological outcomes. Barbiturate coma therapy (BCT), hypothermia, or decompressive craniotomy can be considered [25]. In a study assessing neurologic outcomes and survival in patients undergoing BCT after brain tumor surgery, it was shown in patients with RICH that ICP after BCT was significantly decreased as compared with ICP before BCT, all while having a low incidence of complications. Further, uncontrolled RICH (ICP ≥ 22 mmHg within 6 h of BCT) was an important predictor of mortality after BCT, and ICP ≥ 15 mmHg within 6 h of BCT was associated with poor neurological outcome [24]. Complications of BCT include hypotension, hepatic or renal dysfunction, respiratory depression, and rarely, severe refractory hypokalemia with a subsequent hyperkalemia after stopping BCT. The loss of neurologic examination entails relying on ICP, hemodynamic readings, and electroencephalography (EEG) monitoring to guide therapy [26, 27].

Surgical management Surgical management involves (1) external ventricular drain (EVD) placement to monitor ICP, lower CSF volume, and temporarily treat intracranial hypertension, (2) surgical resection of the space-occupying mass (usually a tumor or hematoma) responsible for the rise in ICP, and (3) in some patients, decompressive craniectomy (DC).

Patients with a GCS score ≤ 8 with signs of high ICP on CT need ICP monitoring. Invasive devices such as an EVD placed in the frontal horn of the lateral ventricle, or intra-parenchymal fiber-optic or microstrain gauge devices, are most commonly used for that purpose (Fig. 6). Guillaume and Janny first introduced ICP monitoring using intraventricular catheters in the 1950s [28, 29]. They have the ability to measure the ICP and drain CSF to temporarily relieve intracranial hypertension, and are considered the gold standard approach. They are, however, contraindicated in patients with coagulopathy and their function can be impaired when used in patients with highly compressed and anatomically distorted ventricles [30–32]. It is also worth noting more recent advances in non-invasive modalities of ICP monitoring. Such techniques include assessment of (1) cerebral hemodynamics by transcranial Doppler ultrasonography [33]; (2) tympanic membrane displacement measured by impedance audiometry whereby increased ICP transmits a pressure wave to the tympanic membrane via the cochlear perilymph [34–36]; (3) assessment of optic nerve sheath diameter by ocular ultrasound [37]; and by (4) devices that produce an acoustic signal transferred through the cranium [38], or more recently (5) that utilize the ophthalmic artery to measure ICP using Doppler ultrasound [32].

To relieve increased pressure inside a rigid box, one can either reduce the volume of its contents, expand the

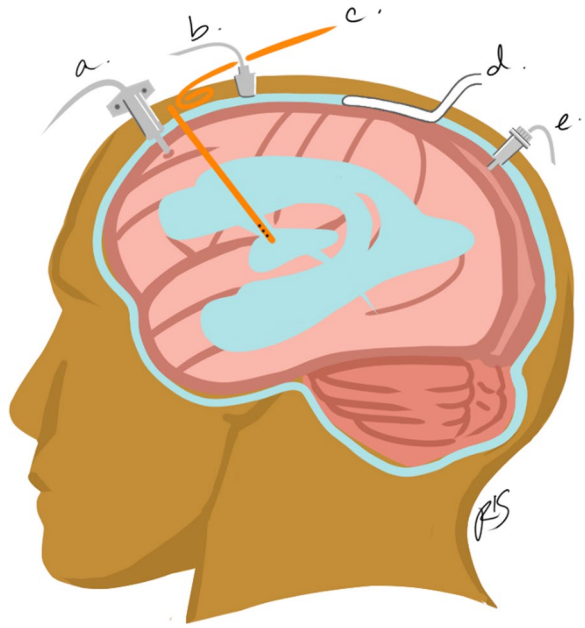

Fig. 6 Various methods of monitoring ICP. **a** intraparenchymal fiberoptic catheter, **b** epidural transducer, **c** ventriculostomy, **d** subdural catheter, **e** subdural bolt. Ventriculostomy offers the ability to monitor ICP as well as drain CSF to achieve temporary relief of intracranial hypertension. An EVD is a small catheter inserted through the skull usually into the lateral ventricle; it is connected to a closed collecting device to allow for CSF drainage. The loop is most often set at 10–20 cm H_2O. CSF drains when ICP exceeds drainage resistance. The EVD can also be connected to a transducer that records ICP. Ventricular catheters cannot be placed if cerebral edema has obliterated or significantly compressed the ventricles. In contrast to EVD, subdural and intraparenchymal monitors cannot be used to drain CSF, but can be placed in patients with ventricles of any size

volume of the box, or increase the compliance of the box by removing a portion of it. Surgical resection of the tumor offers the most effective and definitive method of relieving elevated ICP caused by a space-occupying lesion [2, 30]. Gaining such a safety valve by DC, which involves removing part of the skull vault and opening the dura mater to make more space as the brain contents swell, is one essential component of modern neurocritical care [39].

Theodor Kocher (1901) and Harvey Cushing (1905) were the first to report surgical decompression techniques as a measure to reduce intracranial hypertension [40, 41]. Generally, a larger unilateral DC near the location of the lesion offers a more favorable outcome [30, 42, 43]. Its importance in emergency care relates to its use in patients with intractable cerebral edema and intracranial hypertension [41]. In the particular case of posterior fossa lesions causing intracranial hypertension, it is recommended not to place an EVD without suboccipital DC as it could lead to upward herniation, a phenomenon seen infrequently in practice [16, 44–46]. The importance of DC stems from its ability to restore normal ICP and CSF flow in the CNS. In fact, CBF and cerebral metabolism, and thereby neurologic and cognitive functions, were improved after DC, an observation which in turn proves the importance of the Monro-Kellie doctrine and the role of the rigid skull in that doctrine [39].

On rare occasions when the patient is herniating, all other treatments have proved insufficient, the operating room is unavailable, and air or ground medical transport is delayed, a technique called trephination is needed. Trephination is the drilling of a hole through the patient's skull to decompress an extra-axial (subdural or epidural) hematoma; it has been in use since the Neolithic era. Hippocrates discussed this technique extensively as a treatment in head injury. Hippocratic physicians believed that it allowed blood to flow out from the cranium before it decayed into pus. By Galen's time, trephining was commonly used to treat skull fractures by relieving pressure, removing skull fragments, or draining blood [47]. In modern times, it can be life-saving, and typically works best for comatose patients with a unilateral pupillary dilation caused by an epidural hematoma after head trauma. In that situation, the scalp incision and burr hole are placed on the same side of the head as the enlarged pupil, usually in the temporal squama anterior and superior to the ear.

Hydrocephalus

Classical CSF circulatory theory states that CSF is initially produced in the lateral ventricles by the choroid plexus. It flows thence through the right and left foramina of Monro to enter the third ventricle. From there, it goes through the aqueduct of Sylvius into the fourth ventricle. CSF can then flow through one or both of the foramina of Luschka laterally to end up in the subarachnoid space of the cisterns and overlying the cerebellar cortex, or through the foramen of Magendie at the midline to begin its passage through the spinal subarachnoid space. Ultimately, it re-enters the intracranial compartment and is absorbed through the arachnoid granulations into the superior sagittal sinus. Hydrocephalus is caused by blockage along this classical pathway, overproduction of CSF, or lack of absorption thereof [48]. CNS tumors, especially intraventricular tumors, can when large enough block CSF flow and cause obstructive hydrocephalus. Not only obstruction by tumor but also infection, meningitis, trauma, and subarachnoid hemorrhage can each alter the integrity of the arachnoid granulations and thereby interfere with CSF absorption, leading to hydrocephalus (Fig. 7) [48]. Hydrocephalus can also occur postoperatively, even after resection of the tumor.

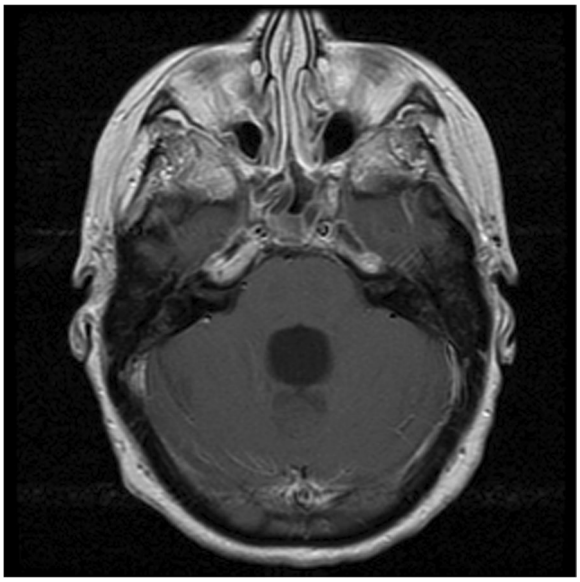

Fig. 7 Fourth ventricle hydrocephalus. This is a patient with lymphoma and associated leptomeningeal dissemination who presented first with headache, followed by apnea, coma, and quadriplegia (after resuscitation). The patient was treated with a ventriculoperitoneal shunt to drain the fourth ventricle and relieve pontomedullary compression

Such an event is in accordance with theories that blood and high protein content in the CSF affect the arachnoid granulations and reduce the absorption of CSF [49].

Depending on the rate and severity at which hydrocephalus develops, it can cause intracranial hypertension as discussed in a prior section. Hydrocephalus can serve as a determining factor for ICP management, surgical approach, and the decision to deal first with either hydrocephalus or the tumor [49]. Ventricular dilation in such cases provides an excellent space in which to maneuver the endoscope, a tool widely used in the resection of intraventricular tumors. In the transventricular approach, blood supply to the tumor is interrupted allowing a piecemeal resection. In some cases, the lesion is peeled off surrounding normal tissue. When one foramen of Monro is obstructed by the tumor, unilateral hydrocephalus can develop. In such cases, the burr hole is placed more laterally to obtain good access to the foramen for biopsy and to the septum for septostomy to restore CSF circulation. If the tumor arises in the anterior part of the third ventricle, the burr hole is placed at the coronal suture; the burr hole is placed more anteriorly if the tumor is in the posterior part of the ventricle. In pineal region tumors, hydrocephalus occurs due to aqueductal compression. In some patients with such tumors, third ventriculostomy and tumor biopsy are needed; others will require tumor resection through a posterior fossa or transtentorial approach [50].

Epilepsy and status epilepticus (SE)

Seizures are common in patients with primary or secondary brain tumors and are described as tumor-associated epilepsy (TAE). They mostly present as the initial clinical manifestation of the tumor or occur later in the course of the disease. The risk of TAE varies among different neoplasms and depends primarily on the tumor's type and location. In fact, TAE is more common with frontal and temporal tumors and less common with occipital and infratentorial tumors [51, 52]. Although frontal and temporal tumors are more amenable to resection, TAE is more challenging to treat in frontal lesions than in those found elsewhere in the brain [52, 53]. TAE risk is higher in tumors of lower grade [51, 52]. This can be explained by tumor growth rate and genetic biomarkers. Slow-growing tumors (low-grade tumors) gradually induce epileptogenic changes in brain parenchyma, whereas in fast-growing tumors (high-grade tumors), epilepsy is mostly caused by acute or subacute tissue damage such as necrosis and hemosiderin deposition [51, 54, 55].

Tumor-associated status epilepticus (TASE) is a life-threatening medical emergency that can be convulsive or non-convulsive in its manifestation. TASE can present as an unexplained decrease in level of consciousness, or as an abnormally prolonged generalized seizure (or a chain of multiple seizures) without recovery of consciousness to baseline. It can create such long-term consequences as neuronal death or injury and alteration of neuronal networks, depending on the type and duration of seizures [13, 56]. Brain tumors account for 3–12% of the cases of status epilepticus (SE) [51, 57]. Status epilepticus appears to be less common in patients with TAE (15–22%) than in patients with epilepsy from the general population (30–40%) [52, 57, 58]. Convulsive TASE presents with partial tonic-clonic, generalized tonic-clonic, or predominant tonic posturing or clonic movements. Partial convulsive or non-convulsive seizures do not have overt clinical manifestations and usually require EEG for a diagnosis [13]. Unfortunately, non-convulsive TASE is underdiagnosed and can hold a poor outcome at 2 months in patients with progressing brain tumors, tumor recurrence, or metastatic lesions [59]. Just as occurs with TAE, the incidence of TASE is higher in frontal lobe lesions. In contrast to TAE, however, TASE is more likely to occur later in the course of the disease or as a sign of tumor progression [51, 52, 60, 61]. Furthermore, TASE risk is directly proportional to tumor grade, and high-grade glioma patients are more predisposed to TASE. This observation can be explained by a myriad of

factors including those imposed by the tumor itself (such as cerebral edema, necrosis, BBB disruption, etc.), by the molecular or immune pathology of the tumor microenvironment, or by the treatment used for high grade tumors (e.g., chemotherapeutic drugs can decrease the level of anti-epileptic drugs [AED] in blood) [52]. In a study by Urban and colleagues, it was shown that immune checkpoint inhibitors in patients with brain metastasis also increase the risk of TASE [62].

Management of TAE and TASE

Time is of the essence in managing TAE and TASE. AED refractoriness is higher in TAE than in the epilepsies noted in the general population and is directly related to the tumor grade in TAE. Thus, patients with high grade tumors should be treated more aggressively, particularly in starting AED polytherapy, to avoid the progression of TAE to TASE. Furthermore, as noted previously, TAE in frontal lesions poses a challenge in treatment, the reason for which has yet to be explained [52]. AED refractoriness in TAE has been explained by sub-therapeutic AED levels, reduced AED efficacy, tumor progression, and expression of multi-drug resistant proteins [52]. Quick administration of abortive AEDs in TAE can prevent progression into TASE which often has deleterious side effects on patient outcomes [13]. In contrast to TAE, TASE is more responsive to AED therapy and is managed by first-line AEDs like phenytoin and benzodiazepines [52]. It was also shown that TASE is as responsive to drug therapy as is status epilepticus occurring in the general population [51, 63]. One recent study showed that the independent predictors of an unfavorable outcome 1 year after TASE onset were longer TASE duration, evidence of tumor progression at TASE onset, and absence of surgical treatment before onset. TASE duration was the main modifiable factor associated with poor prognosis. Accordingly, patients with TASE should receive early aggressive treatment [57].

Electrocorticography (ECoG) during surgery shows that on average, two-thirds of the mapped-out region of epileptogenicity is located in or near the tumor [64]. In addition, low-grade tumors can occasionally have active brain tissue within them, in which chronic epileptogenic changes can provoke clinical seizures. Thus, surgical intervention can be curative in TAE [64, 65]. Surgical resection also offers seizure control in patients with TAE who failed medical management with two first-line AEDs. The extent of tumor removal directly correlates with subsequent freedom from seizures. Gross total resection is most predictive of seizure absence in TAE associated with low-grade tumors [66–69]. However, subtotal resection may be of benefit if the epileptogenic focus was identified prior to resection, or can be mapped out by ECoG done at the time of surgery for tumor removal [70]. Surgical planning for TAE starts with obtaining a scalp EEG to localize the epileptogenic focus. In addition, intracranial EEG with subdural grids, strip electrodes, and depth electrodes can accurately localize this focus. ECoG and stereoencephalography are also used to supplement scalp EEG [64].

Cerebrovascular complications

Patients with metastatic and primary CNS tumors have an increased risk of ischemic stroke, intracerebral hemorrhage, and cerebral venous sinus thrombosis. These complications can be caused by the tumor itself or by its treatment.

Ischemic stroke

Primary brain tumors, particularly glioma, meningioma, and primary CNS lymphoma, are the second leading causing of cancer-associated ischemic stroke [71, 72]. Such associated strokes are most frequently cardioembolic or postoperative in nature, the latter being the result of sacrificing the vasculature involved by the tumor and rendering immediate postoperative neurological deficits, postsurgical patient immobility leading to an enhanced thromboembolic state, or having an underlying stroke risk exacerbated by surgery [72]. Ischemic stroke can be due to the tumor's directly compressing or infiltrating nearby vasculature, tumor embolism, tumor microenvironment, direct involvement of vessels such as in intravascular lymphoma, or treatment-related factors such as vascular sequalae from radiation and chemotherapy or surgical resection. Leptomeningeal disease can provoke diffuse cerebral vasculopathy and may infiltrate into perivascular spaces to cause small-vessel stroke [73]. Treatment complications from surgery and radiotherapy account for the majority of ischemic strokes in patients with primary brain tumors [72]. Radiation can induce vasculopathy, thereby accelerating endothelial injury and atherosclerosis, and causing a stroke [74]. The use of bevacizumab or other therapies blocking VEGF is associated with ischemic stroke and intracranial hemorrhage in patients with glioma [75, 76]. In patients taking anti-angiogenic therapy, the most common ischemic stroke subtype is the lacunar variety. Such strokes occur in the setting of prolonged therapy, while by contrast the majority of ICHs are asymptomatic, intra-tumoral, and occur in the context of tumor progression [76]. Spontaneous ischemic infarcts are a rare occurrence in patients with glioma with few cases reported in the literature [74, 77, 78]. More commonly such occlusive

strokes occur after interruption of a critical artery during tumor resection, with neurologic sequelae evident when the patient awakens from anesthesia. It is interesting to note that ischemic stroke can predispose to the development of brain tumor, and most specifically glioma. Ischemic tissue overproduces hypoxia-inducible factor 1α (HIF-1α) which activates tissue survival pathways in the brain by inducing VEGF production, thereby predisposing to the development of gliomas [79].

Management of ischemic stroke in primary brain tumors can be challenging. Tumor complications pose restrictions on the use of the mainstay treatment modalities used for ischemic stroke in the general population [80]. IV tissue plasminogen activator (IV-tPA) can be administered in patients with systemic malignancy under the right conditions. However, its use is contraindicated in patients with CNS tumor, coagulopathy, or thrombocytopenia. In fact, intracranial mass lesions are considered a relative contraindication to IV-tPA. Since glioblastoma has an inherent tendency to bleed, hence utilizing thrombolysis can further increase such risk. IV-tPA may be given in patients with extra-axial tumors at low risk of hemorrhage, such as meningiomas [81]. Endovascular treatment should be considered in patients with large-vessel occlusion [82].

Intracerebral hemorrhage (ICH)

Just as is true for ischemic stroke, ICH can be due to the tumor itself or to its treatment. Intra-tumoral hemorrhage (ITH) causes expansion of tumor volume and thus increases local mass effect. ITH poses a substantial risk to patients with particular CNS tumors, especially when combined with anticoagulation. Bleeding increases with tumor size and patient age. ITH is present in 5–10% of intracranial tumors on presentation, sometimes causing significant neurologic decline, but in some it may be minor and thus not symptomatic [83].

Highly malignant gliomas like glioblastoma, and brain metastases, tend to bleed the most. However, low-grade tumors like pilocytic astrocytoma, meningioma, pituitary adenoma, or hemangioblastoma can also bleed [83]. ITH in brain metastasis is an indicator of poor prognosis [84]. Brain metastasis from melanoma, choriocarcinoma, thyroid carcinoma, hepatocellular carcinoma, and renal cell carcinoma are at a particularly high risk of spontaneous bleeding (20–50% risk) [85].

Causes of tumor-associated bleeding include radiation therapy, hypertension, anticoagulation, advanced age, malignant pathology, and traumatic brain injury [83]. The mechanism behind ITH is unclear, but inherent abnormalities in tumor blood vessels are likely to play a role. Particularly, VEGF and matrix metalloproteinase 2 may promote bleeding associated with metastatic brain tumors, because of their ability to remodel the nearby vasculature and provoke loss of vascular integrity [83, 86]. Furthermore, invasion of tumor cells into nearby vessels and the tumor necrosis that results also contribute to ITH [83]. Stereotactic radiosurgery is an effective form of treatment with acceptably low rates of complications for patients with brain tumors, particularly metastases [87]. However, it carries a small increased risk of intra-tumoral hemorrhage [88–90]. Finally, chemotherapy can lead to coagulopathy and thrombocytopenia which further predisposes to intracranial bleeding, especially in a setting of trauma wherein

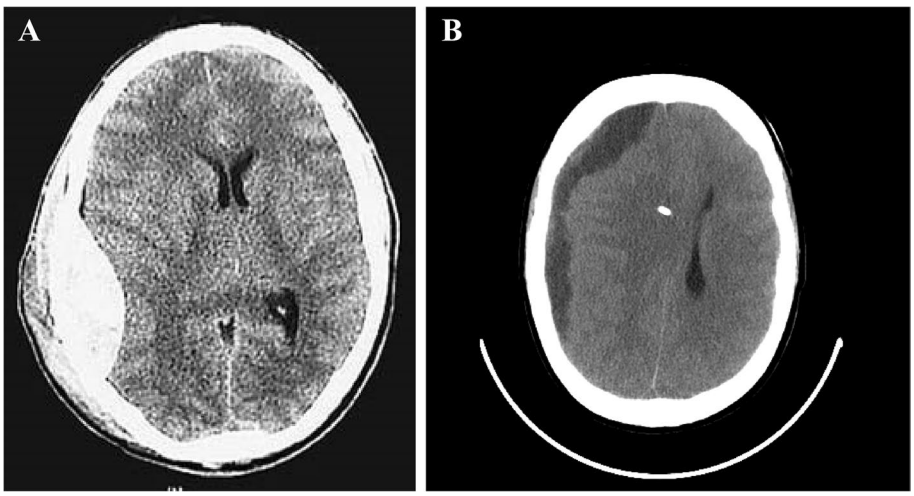

Fig. 8 CT scans showing epidural (**A**) and subdural (**B**) hematoma causing ICP elevation, brain compression, and midline shift

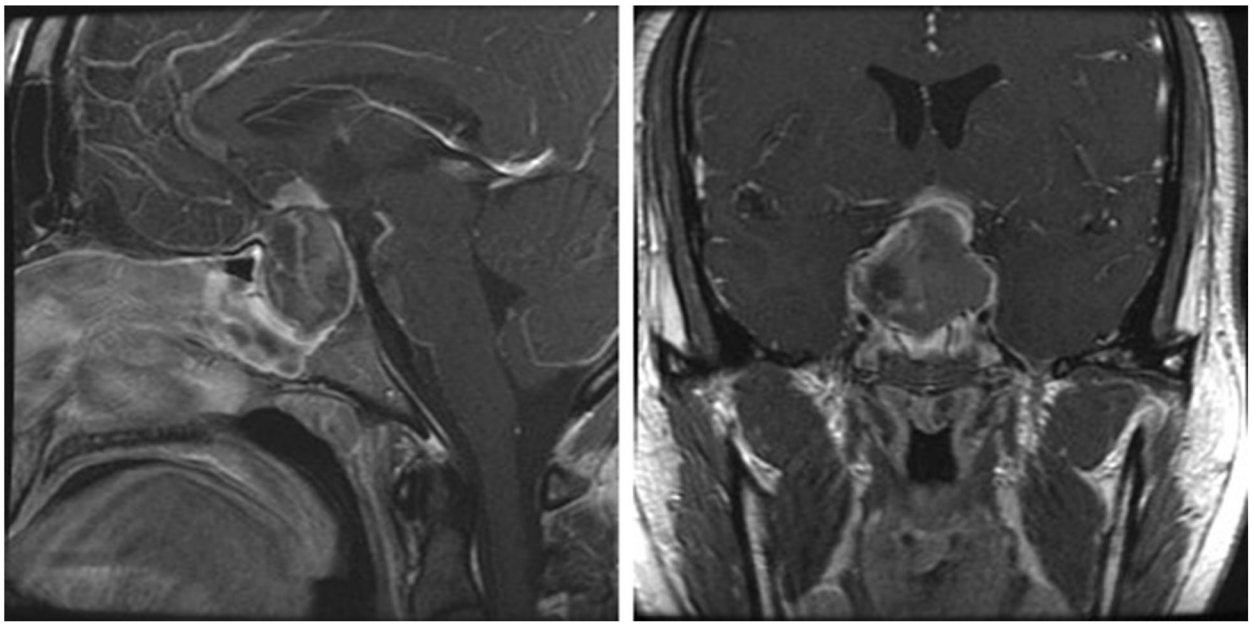

Fig. 9 Sagittal and coronal T1-weighted MRI showing evidence of pituitary apoplexy. A pituitary tumor fills the sella and extes into the suprasellar space, where it compresses the optic chiasm and the pituitary gland, causing sudden severe headache, loss of vision, and low levels of anterior pituitary hormones causing asthenia. A subarachnoid component of bleeding is seen at the upper pole of this tumor, as occasionally in pituitary apoplexy blood leaks into the subarachnoid space and intensifies the patient's symptoms

patients may endure a subdural, epidural, or intraparenchymal hemorrhage (Fig. 8).

Non-enhanced CT scan is primarily used in an emergency setting to diagnose ITH, other forms of intracranial bleeding, or hydrocephalus. Since bleeding can sometimes mask the tumor inciting it, especially if it is the first sign of that tumor, CT densitometry has been proposed to improve detection of hidden solid neoplasms [83]. Most commonly, the tumor causing the overlying hematoma is resected along with the hematoma. Minimally invasive surgery can be used for this purpose. When the hematoma is small, conservative treatment is applied. After the hematoma is absorbed, tumor detection becomes easier, and surgical resection of the underlying tumor can be done with greater precision. Since ICH can present with signs of increased ICP, the aforementioned therapies for ICP control may be necessary in addition to surgical resection [83].

Pituitary apoplexy

Hemorrhagic infarction of a pituitary tumor leading to rapid expansion of the sellar region and acute pituitary gland dysfunction is the hallmark of pituitary apoplexy (Fig. 9). Patients typically (but not invariably) present in their fifth or sixth decade of life with headache, visual disturbance, ophthalmoplegia, cranial neuropathies, endocrine dysfunction (mainly acute adrenal insufficiency), and altered mental status. In subclinical apoplexy, a small hemorrhage is detected radiographically within the pituitary adenoma while the patient is asymptomatic. In contrast, large hemorrhages can be life-threatening by causing subarachnoid bleeding and vasospasm, and by altering mental status and cardiovascular function [91]. Pituitary apoplexy paves the way to the discovery of the pituitary adenoma in the majority of patients who show intrasellar hemorrhage [92]. An increased risk of pituitary apoplexy is seen in patients with hypertension, anticoagulant use, estrogen therapy, dopamine agonists, or dynamic testing of pituitary function. Furthermore, larger tumor size is associated with a higher incidence of intra-tumoral bleeding [91].

One theory of the pathophysiological origin of pituitary apoplexy suggests that the inciting tumor grows enough to compress its vascular supply leading to ischemia and hemorrhage. Another theory weighs the importance of stripping the tumor of its blood supply and triggering a necrotic area that can bleed more easily than intact tumor [93]. Moreover, the uniquely rich and complex blood supply to the pituitary system—the hypophyseal-portal system—exposes the pituitary to systemic blood pressure spikes which increase the risk of bleeding [94]. Finally, inherent tumor characteristics may also be at the heart of bleeding risk. As pituitary adenomas are highly active metabolically, express low levels of VEGF, and have

Table 9 Management of pituitary apoplexy

1) Support the patient's hemodynamic status IV fluid administration (normal saline or Ringer's lactate) BP support Watch the rate of sodium correction (should increase by 12 mEq/L or less in 24 h) ➔ minimizes the risk of central pontine myelinolysis
2) Obtain CT scan of brain when possible, to visualize hemorrhage
3) Draw blood for baseline serum cortisol level
4) Give stress dose of 100 mg IV of hydrocortisone in patients with suspected adrenal insufficiency. This is followed by a short course of high-dose hydrocortisone (50 mg IV at 6 h intervals) with a subsequent slow taper based on response ➔ glucocorticoids treat adrenal insufficiency and reduce the swelling associated with the tumor and hemorrhage
5) Surgical management • Endoscopic or microsurgical transsphenoidal decompression • When is it done? o Usually done in patients with acute vision loss, worsening visual field deficit, or ophthalmoplegia *OR* o Calculate "Pituitary Apoplexy Score." A PAS score of 4 or more, or a worsening score while the patient is under observation warrants surgery *OR* o If no improvement in the patient's symptoms after 1 week of steroid administration

IV intravenous, *BP* blood pressure

very low blood flow, an interruption of blood supply may lead to infarction [95, 96].

When pituitary apoplexy is suspected, visualization of hemorrhage within the sellar region is necessary to make a definitive diagnosis. Initially, non-contrast CT scan is performed to detect acute blood, and a hyperdense lesion in the sellar region usually indicates hemorrhage within three days of the clinical event. Because a CT scan is sensitive but not specific for hemorrhage, an MRI T2-weighted gradient echo sequence is obtained. This modality detects small hemorrhages, allows better anatomical visualization of the pituitary gland, and delineates the tumor and its relationship to the optic apparatus and cavernous sinus. Moreover, pituitary apoplexy often leads to acute adrenal insufficiency which can cause hyponatremia or cardiovascular collapse. Hence, the workup also includes measurement of serum electrolytes and fluid balance. Symptoms of adrenal insufficiency include nausea/vomiting, abdominal pain, myalgia, arthralgia, and a severe drop in blood pressure leading to a hypovolemic shock. Anterior pituitary function should also be assessed with a hormone panel that includes random serum cortisol, free T4, TSH, IGF-1, FSH, LH, total testosterone, and prolactin levels [91].

Management of pituitary apoplexy in an emergency setting involves supporting the patient's hemodynamic status and treating adrenal insufficiency (Table 9). After obtaining blood for baseline measurement of serum cortisol, glucocorticoid is given as a stress dose of 100 mg IV of hydrocortisone if adrenal insufficiency is suspected. This initial bolus dose is followed by a short course of 50 mg of hydrocortisone at 6-h intervals with a subsequent slow taper. Glucocorticoid helps to treat adrenal insufficiency and reduces the swelling associated with the tumor thereby reducing the intrasellar pressure. IV fluids should also be administered to sustain hemodynamic stability. When hyponatremia is present, serum sodium must be corrected at a rate of 12 mEq/L or less in 24 h to avoid central pontine myelinolysis [91].

Patients with minor symptoms, or those with clinical improvement after the apoplectic event, can be treated conservatively with excellent outcomes [91]. When patients present with acute and significant visual symptoms and/or ophthalmoplegia, surgery is indicated [97]. Surgery is also indicated in patients with a "Pituitary Apoplexy Score"—used for monitoring such patients for signs of deterioration—of ≥ 4 or an increasing score if the patient was managed conservatively [97, 98]. In addition, surgery is indicated if there is no improvement in symptoms after a week of steroid administration. An endoscopic or microsurgical transsphenoidal approach is used to decompress the hemorrhage into pituitary adenomas and to address the adenoma itself. This approach offers low morbidity and mortality with proper access to the contents of the sellar region [91, 93].

Cerebral venous sinus thrombosis

Cerebral venous sinus thrombosis (CVST) is associated with dehydration and oral contraceptive use, but may also result from direct tumor invasion or compression of the nearby venous sinuses. Such thrombosis can be seen in dural or calvarial metastases as well as meningiomas. As a result of sinus occlusion, CSF absorption decreases, causing an increase in ICP. This is followed by vasogenic and cytotoxic edema as a result of BBB disruption. Parenchymal hemorrhagic and hemorrhagic venous infarction are then encountered. The most common presentation

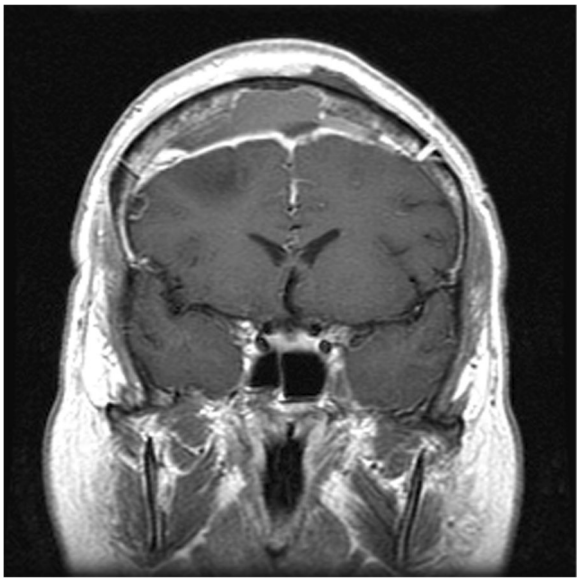

Fig. 10 Post-operative epidural and subdural abscess. This patient with a history of vertex meningioma presented to the emergency department with fever and wound drainage. One month prior to presentation, this patient had undergone meningioma resection, craniectomy, and insertion of a methylmethacrylate cranioplasty plate

is that of intracranial hypertension. Moreover, presentations such as subarachnoid hemorrhage, thunderclap headache, recurrent transient ischemic attacks, tinnitus, isolated headache, and multiple cranial nerve palsies as seen in cavernous sinus thrombosis are also encountered albeit rarely. Symptomatic treatment to manage seizures and elevated ICP is indicated in patients with CVST. Anticoagulant therapy is also needed to promote clot resolution and prevent clot expansion. However, in patients who do not improve, or who clinically deteriorate despite treatment, endovascular thrombolysis should be performed in advanced centers to open the occluded sinus or veins [99].

CNS infections

CNS infections are an important cause of morbidity and mortality. They are more commonly seen with hematologic malignancies but can also occur in patients with CNS tumors. They occur as a result of immunologic compromise caused by the tumor itself or by its treatment. Infection is also seen as a post-operative complication. The specific pathogen depends on a myriad of factors particularly the type and duration of immunosuppression. Patients with immunocompromise pose a diagnostic challenge because they do not display the typical signs and symptoms of a CNS infection such as fever, nuchal rigidity, or headache. However, they can present with altered mental status, and patients with brain abscess can present with seizures or focal neurologic deficits. Infectious agents usually make their way to the brain via hematogenous spread (i.e., metastasis from an infection elsewhere), or by direct spread from a surrounding location [100].

CT or MRI can be helpful in identifying a brain abscess or meningeal enhancement as seen in meningitis (Fig. 10). CSF analysis as well as gram stain and culture are done in patients with suspected CNS infection. In such cases, neuroimaging is indicated to rule out mass effect prior to a lumbar puncture. Empiric treatment is thus initiated based on the patient's presentation, suspected pathogen, and initial lab findings. Patients with a brain abscess, increased ICP, and focal deficit(s) should be taken to the operating room for resection and reduction of local pressure [100].

Summary

In summary, our review of cranial neurosurgical oncologic emergencies highlights the various tumor and treatment-related complications encountered in patients with intracranial tumors. Cerebral edema, hydrocephalus, intracranial hemorrhage, cerebral venous sinus thrombosis, and CNS infections all cause an increase in ICP that presents with a myriad of symptoms and signs that should be detected and treated promptly in an emergency setting. Conservative management, if adequate, may be applied when mass effect is absent and the patient is neurologically intact. However, in severe and rapidly progressing cases in which the patient presents with altered mental status and neurologic deficits, an emergency neurosurgical procedure is indicated for removal of the cause(s) of the excess ICP, protection of brain function, and monitoring of ICP.

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