15 Neurosurgical Complications in Brain Tumor Patients

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The surgical management of brain tumor patients has dramatically evolved over the last 20 years. Neurosurgical adjuncts, such as the operating microscope, neuronavigation, intraoperative neuromonitoring, tumor-fluorescence (5-ALA), tractography, and cortical mapping have been successfully incorporated into the neurosurgical theater. These modalities have enhanced the safety profile of neurosurgical intervention. These technologies have allowed for improved preservation of neurologic function as well as mitigation of potential morbidities. Despite the continued advancement of radiation, chemotherapy, and immunotherapy, surgery remains the initial treatment modality in the majority of patients with brain tumors. The main objective of neuro-oncological surgery is to provide maximal cytoreduction, decrease the mass effect and associated complications, and establish the pathologic diagnosis. Studies have repeatedly shown the benefit of gross total resection of brain lesions, including most common high and low grade gliomas, solitary brain metastasis and meningiomas. This chapter will review the complications related to neurosurgical treatment of brain tumors and provide guidance on the management of those patients from pre- to post-operative care.

The original version of the chapter has been revised. A correction to this chapter can be found at https://doi.org/10.1007/978-3-031-41413-8_18

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N. A. Mohile, A. A. Thomas (eds.), *Brain Tumors*,
https://doi.org/10.1007/978-3-031-41413-8_15

There are generally two groups of complications related to brain tumor surgery—surgical and systemic [1]. Surgical complications arise as a direct result of the surgery and are usually specific to the neurosurgical site and procedure. They include neurologic complications, such as postoperative seizures and neurologic deficits, as well as postoperative cerebral edema, cerebral hemorrhage, infarction, hydrocephalus, and regional complications, such as CSF leak, wound infection or dehiscence. Systemic complications are not directly related to the neurosurgical site and procedure and include the following: pulmonary complications (e.g. pulmonary embolism, pneumonia, atelectasis), cardiac complications (e.g. myocardial infarction, arrhythmias, hypo/hypertension), renal complications (e.g. urinary tract infections, acute kidney injury) and others. The risk of both surgical and systemic complications can be reduced with preoperative planning, meticulous surgical technique and use of intra-operative adjuncts as well as proper post-operative management.

Preoperative Management

Every preoperative assessment should begin with obtaining thorough medical history and performing careful physical examination in order to identify any comorbidities that might affect the outcome of the tumor resection procedure. Common medical comorbidities to screen for include hypertension, diabetes, atrial fibrillation as well as other cardiac conditions which require anticoagulation and antiplatelet therapy. Therefore, all current medications need to be reviewed and adjusted according to the patient's status.

Perioperative Antiepileptic Therapy

There is little to no evidence on the efficacy of antiepileptic drugs (AED) in prevention of postoperative seizures in patients with brain tumors and no history of seizures [2, 3]. Thus, they should not be routinely prescribed unless a documented seizure has occurred. The patients who present with single or multiple seizures are at higher risk for recurrence in the presence of intracranial pathology. In these patients, AED therapy should be continued or initiated before surgery. Potential interactions between AED and other medications (especially chemotherapy) need to be considered before choosing a specific AED. Levetiracetam at the loading dose of 20 mg/kg intravenously followed by 500–1000 mg twice a day is commonly prescribed for seizure prophylaxis due to its low side effect profile.

Steroids

Steroids in patients with both primary and metastatic brain tumors significantly alleviate the symptoms occurring due to vasogenic edema and increased intracranial pressure both pre- and postoperatively. Dexamethasone is a corticosteroid of choice in neurooncological patients and has been shown to improve outcomes postoperatively in those patients. The initial IV bolus of 10 mg is followed by administration of 16 mg/day in 2–4 divided doses. The initiation of therapy should occur at least 3 days before surgery for maximal effect. Dexamethasone may be tapered off gradually in 2–3 weeks after surgery or quickly—3 days after surgery, depending on the individual benefit and the duration of preoperative steroid therapy. In general, lowest possible doses and early taper are recommended to avoid unnecessary side-effects and comorbidities due to steroid use. Prevention of steroid-induced ulcers requires gastrointestinal prophylaxis, such as proton pump inhibitors. Monitoring of blood glucose levels is also recommended while on steroid therapy. Prophylaxis against Pneumocystis jirovecii should be considered for patients requiring prolonged used of steroids.

Antiplatelet and Anticoagulation Medications

The risk of hemorrhage for intracranial surgery is high. Antiplatelet and anticoagulation therapy, including chemical DVT prophylaxis, should be withheld before surgery unless there are specific circumstances that are discussed with the surgical team. In general antiplatelet/anticoagulant medications should be stopped 5–7 days before elective surgery. Patients with drug-eluting stents

(DES) need to be administered dual antiplatelet therapy for up to 12 months after DES surgery. Even brief cessation of the therapy drastically increases the chances of life-threatening stent thrombosis. Therefore, the decision concerning the continuation of therapy through brain tumor surgery should be based on consultation between the patient's neurosurgeon and cardiologist and the consensus should be balanced between risks and benefits. Anticoagulation drugs are stopped preoperatively (unfractionated heparin: stop full IV anticoagulation 4–6 hours before surgery, subcutanoueous dosig, stop 12 hours before surgery; low molecular weight heparin (LMW heparin): stop prophylactic dose 12 hours before surgery, stop full anticoagulation 24 hours before surgery; fondaparinux: stop 2 to 4 days prior to surgery; rivaroxaban: stop 48 hours before; apixaban: stop 48 hours before surgery). Patients who require constant anticoagulation therapy with vitamin K antagonists (VKA) (e.g. mechanical heart valves) need to be bridged with LMW heparin. VKA (warfarin, acenocoumarol) are stopped 5 days before surgery and LMW heparin is started, with the last dose administered subcutaneously no later than 12 h before surgery.

Hyperglycemia

Perioperative hyperglycemia is significantly associated with adverse effects in patients undergoing brain tumor resection [4]. Glucose levels should be maintained at <180 mg/dL and hypoglycemia should be avoided in all patients. Close surveillance for hyperglycemia is especially warranted in patients that receive corticosteroids. The target level of glycosylated hemoglobin (HbA1C) should be <7.0% before surgery in patients with diabetes. Antidiabetic drugs are withheld preoperatively (metformin and short-acting sulfonylureas: 24 hours before surgery; thiazolidinediones: 24 to 36 hours before surgery; long-acting sulfonylureas: 48 to 72 hours before surgery) and substituted with intravenous insulin infusion or sliding scale insulin. Postoperatively, IV or subcutaneous insulin is administered as appropriate with careful attention as corticosteroids are weaned and pre-procedure diabetic medications are restarted to prevent hypoglycemia.

Optimizing Other Medical Conditions

Decision to withhold or administer antihypertensives and other cardiac medications perioperatively needs to be determined after consultation with a cardiologist and/or anesthesiologist. Fluid status should be addressed and optimized accordingly to prevent post induction hypotension and acute kidney injury. Patients with a history of pulmonary disease are at greater risk for perioperative respiratory complications, therefore optimization of lung function should be completed preoperatively.

Preoperative Imaging

There are several neurosurgical adjuncts that aid the neurosurgeon with preoperative planning and intraoperative approaches that optimize the extent of resection and safety profile. Moreover, additional imaging technologies are used for tumors located in eloquent areas to mitigate potential neurologic deficits related to resection. Neuronavigation utilizes thin-sliced MRI and CT scans to form a 3D reconstruction of the lesion and its relationship with adjacent anatomy. It can be further supplemented with functional data, such as functional MRI (fMRI) or diffusion tensor imaging (DTI). fMRI data is particularly useful for preoperative planning of surgical approach and surgical corridor as well as intraoperative navigation for intra-axial lesions located in eloquent areas. DTI tractography allows for a visualization of white matter fibers, such as the visual pathway, arcuate fasciculus, corticospinal tract and others. Despite the usefulness of intraoperative MRI (iMRI), fMRI, and DTI tractography in identification of crucial anatomical structures and their relationship to the lesion, current research shows low quality evidence on their efficacy in maximizing the extent of resection, postoperative neurological status, progression-free survival and overall survival in patients with gliomas, when compared to traditional neuronavigation [5–7]. However further research is ongoing as these new techniques are integrated into the neurosurgical workflow.

Intraoperative Management

Patient Positioning

Proper patient positioning is essential in providing surgical corridor visualization while minimizing iatrogenic pressure or traction injury due to the lengthy nature of some neurosurgical procedures. Prevention of pressure ulcers relies both on crafted positioning and ample use of gel and foam padding. The patient should be placed in a physiological position to prevent brachial plexus and other peripheral nerve injuries. The position of the patient can also affect the risk of developing venous air embolism (VAE).

Venous Air Embolism

The incidence of VAE during intracranial procedures has been reported in up to 76% of cases [8], the majority of which are asymptomatic. The risk of VAE increases when the surgery is done in close proximity to dural sinuses. Elevation of the patients head above the heart (e.g. sitting position for posterior fossa tumors) creates an additional gravitational gradient. Other risk factors include blood loss and dehydration. In patients with preoperatively detected patent foramen ovale, decision to avoid sitting or semi-sitting position should be considered.

Any unexplained hypotension, decreases in end-tidal carbon dioxide, arterial oxygen saturation, hypercapnia, and/or increase in end-tidal nitrogen should immediately suggest the possibility of VAE during surgery. Precordial Doppler and transesophageal echocardiography can be used to screen for air emboli. Surgeons should immediately soak the surgical field with saline to prevent further emboli by blocking venous channels. The patient is then placed in partial left lateral decubitus position (Durant maneuver), nitrogen dioxide is discontinued (if being utilized) and the patient should receive 100% oxygen. Catheter aspiration can be considered in severe cases. Hemodynamic instability should be treated immediately and if not effective, the surgery should be aborted.

Skin Incision and Tissue Handling

Planning of the scalp incision parallel to the major scalp vessels allows for better perfused skin flaps than U-shaped incisions. The base of the flap should be wider than the height to maintain adequate blood supply. The initial skin incision should be well optimized for possible salvage opportunities in case of postoperative infection, treatment induced dehiscence, or possible reoperation for disease recurrence. Meticulous dissection and gentle tissue handling prevent maceration of tissues that can lead to infection or delayed wound healing.

Ensuring Gross Total Resection and Preventing New Neurologic Deficits

Ensuring gross total resection (GTR) relies on meticulous surgical technique and visualization of the tumor. Intraoperative microscope and intraoperative imaging modalities, such as traditional neuronavigation, DTI tractography, fMRI and iMRI allow for preservation of crucial adjacent anatomical structures and deep white matter tracts, and as such, prevention of new neurological deficits (see Sect. 2.3). Moreover, fluorescence guided surgery with 5-aminolevulinic acid (5-ALA) or sodium fluorescein can additionally aid in visualization of the tumor margins and in maximizing GTR. Studies on the 5-ALA guided resections with and without addition of iMRI showed significantly higher rates of GTR and progression-free survival than those using white light alone [9, 10]. Utilization of 5-ALA requires low light conditions for 48 hours postoperatively to prevent photosensitivity reactions. Other techniques and modalities, such as neuro-endoscopy or BrainPath allow for minimally-invasive transsulcal approaches to subcortical lesions sparing transcortical injury. Preservation of en-passage vessels to adjacent functional cortex is of utmost importance during tumor dissection.

Intraoperative Neurophysiological Monitoring

Somatosensory evoked potentials (SSEP), motor evoked potentials (MEP) and intraoperative electromyography (EMG) can be used to evaluate the functioning of sensory and motor pathways. Cortical and subcortical mapping allows for navigation around those regions and tracts during resection of lesions in eloquent brain. Cortical mapping is particularly useful to maximize safe resection in motor, language, and cognition related lesions. Sleep mapping (during anesthesia) is usually performed for lesions that do not directly infiltrate eloquent regions, while awake mapping is preferred for more infiltrating lesions as they allow for real time feedback. All techniques have been shown to mitigate the risk of postoperative neurologic deficit and are utilized extensively in modern neurosurgical oncology.

Closure

Ensuring proper watertight dural and galeal closure decreases the risk of cerebrospinal fluid (CSF) leak, CSF fistula, pseudomeningocele, delayed wound healing, and infection. Skin approximation can be completed with surgical staples, absorbable, or non-absorbable suture with alignment of the dermal edges being critical for proper wound healing. The use of subgaleal closed drainage systems can minimize hematoma formation and improve healing.

Postoperative Complications and Management

Hemorrhage

Postoperative intracranial hemorrhage is one of the most feared complications of brain tumor surgery with high morbidity and mortality. However, small hematomas in the tumor cavity are found on postoperative imaging in up to 30% of patients [11]. Major hemorrhage requiring reoperation accounts for 2% of brain tumor cases [12]. Risk factors include subtotal resection, tumor type (hemangioblastoma, infratentorial tumors), older age, pre-existing conditions, such as hypertension or coagulopathy. Ensuring intraoperative hemostasis and perioperative normotension are essential in preventing postoperative hemorrhage.

Seizures

Seizures occur in up to 10% of patients after brain tumor surgery [13]. Seizures can result from the cortical irritation after tumor resection, idiopathic causes, brain manipulation, or prolonged retraction. In some cases, intracranial hemorrhage or cerebral edema can result in postoperative seizures. Therefore, early postoperative seizures warrant reimaging usually with a noncontrast CT head. In general, patients are managed with antiepileptic drugs (see Sect. 2.1).

Neurologic Deficit

There are a number of factors contributing to the risk of new neurologic deficit after brain tumor resection. Many of them might be anticipated secondary to location of the lesion and surgical corridor. Deep location of tumors, location in or near eloquent areas, and tumors encasing major vessels are risk factors for postoperative deficits. Arterial or venous infarcts due to vessel sacrifice or injury can lead to symptomatic deficits. Neurologic deficits are often transient and resolve over the ensuing days/weeks/months. Intraoperative imaging, neuronavigation, and neurophysiological monitoring can reduce the risk of iatrogenic injury and new neurologic deficits (see Sect. 3.4).

Patients with new neurologic deficits should be evaluated by a comprehensive therapy/rehab team consisting of physical, occupational, and speech therapy as clinically warranted. Modern rehabilitation techniques/devices improve the quality of life of patients with persistent deficits.

Postoperative delirium can occur. Environmental techniques that can improve or prevent postoperative delirium include orienting the patient towards time and surroundings (lights on during daytime, family members present), proper uninterrupted sleep protocol, proper nutrition, and early mobilization.

Hydrocephalus

The rates of postoperative hydrocephalus reach 6–8% [14] for the lesions located at the skull base in close proximity to the fourth ventricle. Other risk factors include metastatic disease, intraventricular lesions, and transventricular approaches. The etiology of postoperative hydrocephalus is multifactorial and case dependent, including obstructive hydrocephalus from obstruction of CSF flow pathways or nonobstructive hydrocephalus from protein or blood product buildup in the CSF inhibiting normal CSF reabsorption. In the cases of persistent hydrocephalus, permanent CSF diversion via shunt is necessary.

Infection

Infections after brain tumor resection occur in 2–4% of patients [15, 16]. Known risk factors include duration of surgery, male sex, postoperative CSF leak and length of preoperative stay of more than one day [15]. Presentation ranges from superficial skin infection to meningitis, subdural empyema, or abscess. Additional risk factors for meningitis include elderly age group, presence of lumbar drain, and enteral nutrition. Standard antibiotic therapy based on sensitivity patterns should be started if infection is suspected. Subdural empyema and abscess may require additional reoperation for source control. Preventive methods include administration of perioperative antibiotics before induction (cefazolin), meticulous technique, strict sterility practices, and proper dural, galeal, and skin closure.

Wound Healing Complications

Dehiscence and wound healing problems can be related to older age, frailty syndrome, diabetes, previous surgery, previous chemo and radiotherapy, angiogenesis inhibitor utilization (bevacizumab), and carmustine (Gliadel©) wafer use. In order to improve wound healing the management should include correcting hyperglycemia, optimizing nutrition, utilizing proper closure techniques, and decreasing the pressure on the incision.

Venous Thromboembolism

Patients who undergo surgery due to brain tumor are at increased risk for developing venous thromboembolism (VTE). Additional risk factors for VTE include presence of malignancy, leg weakness, duration of surgery, and absence of thromboprophylaxis. Previous studies have shown the efficacy of intra- and postoperative intermittent pneumatic compression (IPC) [17] and LMW heparin [18] in reducing the risk of VTE. The timing of the start of anticoagulation therapy seems to affect the risk of postoperative hemorrhage, with higher rates of bleeding detected if the therapy is started during or early after the craniotomy. Current ESA guidelines [19] recommend the initiation of IPC thromboprophylaxis before surgery in all patients undergoing intracranial procedures. Moreover, the addition of subcutaneous LMW heparin is advised no earlier than one day post-surgery in patients with evidence of postoperative intracranial hemorrhage [19].

Other Systemic Complications

Cardiac complications occur in 1.1% and 0.7% of patients undergoing surgery for benign tumors and gliomas, respectively [20]. The incidence of acute renal failure after tumor resection is between 1.3 and 1.5% [20]. The treatment of those patients requires a multidisciplinary approach and management. Malnutrition results in poor wound healing and worse outcomes. Nutrition consultation is advised in those patients.

References

1. Sawaya R, Hammoud M, Schoppa D, et al. Neurosurgical outcomes in a modern series of 400 craniotomies for treatment of parenchymal tumors. Neurosurgery. 1998;42(5):1044–55; discussion 1055–6. https://doi.org/10.1097/00006123-199805000-00054.
2. Greenhalgh J, Weston J, Dundar Y, Nevitt SJ, Marson AG. Antiepileptic drugs as prophylaxis for postcraniotomy seizures. Cochrane Database Syst Rev. 2020;4(4):CD007286. https://doi.org/10.1002/14651858.CD007286.pub5.
3. Chen CC, Rennert RC, Olson JJ. Congress of Neurological Surgeons systematic review and evidence-based guidelines on the role of prophylactic anticonvulsants in the treatment of adults with metastatic brain tumors. Neurosurgery. 2019;84(3):E195–7. https://doi.org/10.1093/neuros/nyy545.
4. Hagan K, Bhavsar S, Arunkumar R, et al. Association between perioperative hyperglycemia and survival in patients with glioblastoma. J Neurosurg Anesthesiol. 2017;29(1):21–9. https://doi.org/10.1097/ANA.0000000000000339.
5. Jenkinson MD, Barone DG, Bryant A, et al. Intraoperative imaging technology to maximise extent of resection for glioma. Cochrane Database Syst Rev. 2018;1(1):CD012788. https://doi.org/10.1002/14651858.CD012788.pub2.
6. Li P, Qian R, Niu C, Fu X. Impact of intraoperative MRI-guided resection on resection and survival in patients with gliomas: a meta-analysis. Curr Med Res Opin. 2017;33(4):621–30. https://doi.org/10.1080/03007995.2016.1275935.
7. Caras A, Mugge L, Miller WK, Mansour TR, Schroeder J, Medhkour A. Usefulness and impact of intraoperative imaging for glioma resection on patient outcome and extent of resection: a systematic review and meta-analysis. World Neurosurg. 2020;134:98–110. https://doi.org/10.1016/j.wneu.2019.10.072.
8. Papadopoulos G, Kuhly P, Brock M, Rudolph KH, Link J, Eyrich K. Venous and paradoxical air embolism in the sitting position. A prospective study with transoesophageal echocardiography. Acta Neurochir. 1994;126(2–4):140–3. https://doi.org/10.1007/BF01476424.
9. Eyüpoglu IY, Hore N, Savaskan NE, et al. Improving the extent of malignant glioma resection by dual intraoperative visualization approach. PLoS One. 2012;7(9):e44885. https://doi.org/10.1371/journal.pone.0044885.

10. Stummer W, Pichlmeier U, Meinel T, et al. Fluorescence-guided surgery with 5-aminolevulinic acid for resection of malignant glioma: a randomised controlled multicentre phase III trial. Lancet Oncol. 2006;7(5):392–401. https://doi.org/10.1016/S1470-2045(06)70665-9.
11. Fukamachi A, Koizumi H, Nukui H. Postoperative intracerebral hemorrhages: a survey of computed tomographic findings after 1074 intracranial operations. Surg Neurol. 1985;23(6):575–80. https://doi.org/10.1016/0090-3019(85)90006-0.
12. Wang C, Niu X, Ren Y, Lan Z, Zhang Y. Risk factors for postoperative intracranial hemorrhage after resection of intracranial tumor in 2259 consecutive patients. World Neurosurg. 2019;129:e663–8. https://doi.org/10.1016/j.wneu.2019.05.239.
13. Wu AS, Trinh VT, Suki D, et al. A prospective randomized trial of perioperative seizure prophylaxis in patients with intraparenchymal brain tumors. J Neurosurg. 2013;118(4):873–83. https://doi.org/10.3171/2012.12.JNS111970.
14. Burkhardt J-K, Zinn PO, Graenicher M, et al. Predicting postoperative hydrocephalus in 227 patients with skull base meningioma. Neurosurg Focus. 2011;30(5):E9. https://doi.org/10.3171/2011.3.FOCUS117.
15. Schipmann S, Akalin E, Doods J, Ewelt C, Stummer W, Suero Molina E. When the infection hits the wound: matched case-control study in a neurosurgical patient collective including systematic literature review and risk factors analysis. World Neurosurg. 2016;95:178–89. https://doi.org/10.1016/j.wneu.2016.07.093.
16. Uzuka T, Takahashi H, Nakasu Y, et al. Surgical site infection after malignant brain tumor resection: a multicenter study for induction of a basic care bundle. Neurol Med Chir (Tokyo). 2017;57(10):542–7. https://doi.org/10.2176/nmc.oa.2017-0034.
17. Frisius J, Ebeling M, Karst M, et al. Prevention of venous thromboembolic complications with and without intermittent pneumatic compression in neurosurgical cranial procedures using intraoperative magnetic resonance imaging. A retrospective analysis. Clin Neurol Neurosurg. 2015;133:46–54. https://doi.org/10.1016/j.clineuro.2015.03.005.
18. Hamilton MG, Yee WH, Hull RD, Ghali WA. Venous thromboembolism prophylaxis in patients undergoing cranial neurosurgery: a systematic review and meta-analysis. Neurosurgery. 2011;68(3):571–81. https://doi.org/10.1227/NEU.0b013e3182093145.
19. Faraoni D, Comes RF, Geerts W, Wiles MD. European guidelines on perioperative venous thromboembolism prophylaxis. Eur J Anaesthesiol. 2018;35(2):90–5. https://doi.org/10.1097/EJA.0000000000000710.
20. Bekelis K, Kalakoti P, Nanda A, Missios S. A predictive model of unfavorable outcomes after benign intracranial tumor resection. World Neurosurg. 2015;84(1):82–9. https://doi.org/10.1016/j.wneu.2015.02.032.