Surgical management of brain and spinal tumors (CNS tumors)

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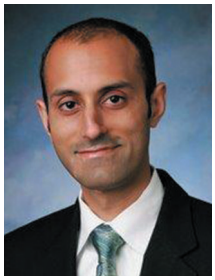
In the United States, an estimated 1.7 million new diagnoses of cancer are expected in 2019. Central Nervous System (CNS) tumors range from benign to malignant and can occur in the brain or spinal cord. Estimates for 2019 for new brain metastasis, spine metastasis and primary brain tumors are approximately 200,000, 125,000 and 24,000, respectively (Figure 5).



The American Cancer Society estimates that approximately 18,000 people in the United States will die of primary brain cancer, and that the number of deaths will be higher when including deaths from metastatic brain and spine cancer are included (Figure 5). Interestingly, primary brain tumors account for only 1% of new cancer diagnoses, but 3% of all cancer deaths, underscoring the poor prognosis of primary brain tumors. In general, brain tumors present with seizure, headache and neurologic deficit, whereas spine tumors present with back pain, ataxia and/or paraparesis.

All brain and spinal tumors share a common goal of surgical management — to balance the extent of resection with the avoidance of permanent neurologic deficit. The phrase "safe maximal resection" was coined to convey this balancing act between tumor removal and neurologic deficit. For brain tumors, the general surgical indications are described as the four Ds: Diagnosis; improve or prevent neurologic Deficit; prevent Death; and obtain necessary tissue for clinical Drug trials.

For spine metastases, the four Ds remain surgical indications, but there is additionally consideration of spine stability, which is guided by the principles of decompressing the spinal cord and stabilizing the spine. The risk of surgical neurologic deficit increases with tumors in or near the spinal cord and those in regions of the brain that control language (left temporal lobe), motor (posterior frontal lobe), vision (occipital cortex) and neurocognitive (hippocampal and deep brain structures) function. Other challenges of treating CNS tumors include the blood–brain barrier (BBB), which chemotherapies have difficulty crossing, and radiotherapy has limitations due to brain and spinal cord radiation damage.

This article reviews the surgical management of the top four cancerous tumors encountered in the brain and spinal column: metastatic brain, metastatic spine, meningiomas and high-grade gliomas (Figures 5 and 6).

Metastatic tumors are the most common CNS tumor type. Metastatic cancer to the brain may be slightly more common than that to the spine. The number of cancer patients developing brain metastasis is estimated to be between ~200,000–300,000 annually. Autopsy studies show that 25% of cancer patients have brain metastasis at death. Eighty percent of all cancers can metastasize to the brain, with lung, breast, melanoma and colorectal accounting for approximately 45%, 15%, 10% and 5% of brain metastases, respectively (Figure 8).

More than 80% of brain metastases are located in the cerebral hemispheres, at the gray matter-white matter junction, where small tumor cells can get trapped in intracranial arteries of decreasing diameter (Figure 8B). At presentation, over 50% of patients have multiple brain metastases. Trials from the Radiation Therapy Oncology Group (RTOG) show median survivals ranging from 2.3 to 7.1 months, depending on age, Karnofsky Performance Status (KPS) and systemic disease. Once diagnosed, brain metastases are usually the life-limiting component of the patient's overall cancer burden.

Treatment options for brain metastases include glucocorticoids, chemotherapy, whole-brain radiation, stereotactic radiosurgery and/or surgical excision. Without treatment, survival can be as little as four weeks, increasing to eight weeks with high-dose glucocorticoids (e.g., dexamethasone). Radiation treatment can improve survival for three to six months with radiosensitive tumors responding quickly enough to negate surgery (e.g., small cell cancer of the lung, germ cell tumors, multiple myeloma, leukemia, and lymphoma). For others, surgical excision followed by radiation therapy for both single and multiple metastases can lead to a median 10 to 14 months of survival. Stereotactic radiosurgery appears to have similar results.

The surgical indications for brain metastasis are individualized but usually fall within the 4Ds. Large metastatic lesions (>2.5 cm) are more likely to be symptomatic by causing mass effect and mid-line shift (Figure 8). Some metastases incite peritumoral cerebral edema that may worsen with radiation, causing increased symptoms or even become life-threatening. In general, solitary and multiple metastases can be safely excised in patients who are good surgical candidates (e.g., no bleeding dyscrasias, no significant cardiac disease, no significant respiratory disease). Finally, surgical excision may be necessary after failure of radiation therapy or stereotactic radiosurgery.

Spinal epidural and vertebral body metastases are found in 5–10% of all patients with cancer, giving an annual estimated number of cases between approximately 90,000 and 175,000 (Figure 5). The cancers that mostly commonly metastasize to the spine are breast, prostate, lung and renal cell cancer, of which 73%, 68%, 36%, and 35% of cases will experience spine metastasis, respectively. The majority of metastatic spine cancers start in the vertebral body and expand to compress the epidural space, explaining why 20% of patients present with symptoms of back pain and/or motor weakness (e.g., paraplegia). Previous studies have shown that surgery to restore the ability to walk improves survival and pain control in such patients (median survival time 126 days vs.100 days, pain control 90% vs. 70%).

Surgery for metastatic spine disease involves circumferential spinal cord decompression with or without spine stabilization to alleviate pain and/or prevent or restore neurologic deficit (Figure 9). It is hampered by a potential for high blood loss requiring transfusion, a long hospital stay, and up to eight weeks of recovery from surgery-related pain. In general, the goals of surgical intervention are to decompress the spinal cord to restore neurologic function and to stabilize pathologic fractures with instrumentation or vertebroplasty (i.e., methylmethacrylate bone cement) (Figures 9E, 9F). However, surgical morbidity can be as high as 50%.

When faced with a patient with metastatic spine disease, surgeons must weigh surgical morbidity, mortality and recovery time with the chances of improving neurologic function, decreasing pain and restoring spine stability. Surgical decision-making is done in the context of a patient who may not survive surgery or whose life expectancy may be shorter than the expected recovery time. The authors favor using the Spine Instability Neoplastic Score (SINS) to aid in surgical decisions. This scoring system gives an idea of spine stability, aiding in overall surgical decision-making.

Meningiomas are the most common primary central nervous system tumor, accounting for roughly 36% of all primary adult intracranial tumors (Figures 5 and 10). These tumors arise from cells within the dural covering of the brain and usually grow in an extrinsic fashion. Most meningiomas occur in patients 50–60 years of age, with a twofold higher incidence in females.

The biological behavior of meningiomas is one of continued growth, leading to compression of neuronal structures. Surgery is the treatment of choice and is frequently unsuccessful in treating these tumors. There are usually two reasons that this is not possible. First, the tumor location or its proximity to neurovascular structures may make complete resection impossible. Secondly, the inherent biology of the tumor may give a particular meningioma an increased chance of recurrence despite complete resection. Fortunately, histologically "atypical" or "malignant" tumors comprise of less than 10% of meningiomas. These two types of tumors are especially disposed to recurrence.

Surgery is favored for symptomatic meningiomas, whereas asymptomatic meningiomas may be monitored with serial imaging. The Simpson Classification is the most well-known scale used for the prediction of tumor recurrence after resection. The extent of resection, according to the Simpson Classification system, ranges from Grade 1 (complete resection) to Grade 5 (decompression only). After a macroscopically complete resection (Simpson Grade 1), the 5-, 10- and 15-year recurrence-free rates were 93%, 80% and 68%, respectively. For incompletely resected lesions (Grade 2–5), the progression-free rates at the same postoperative intervals were expectedly lower, at 63%, 45% and 9%, respectively.

Treatment options for recurrence or incomplete resection include further surgery, conventional external beam irradiation, stereotactic radiosurgery and systemic therapies. Most patients with malignant meningiomas will receive radiation therapy after surgery; however, radiation therapy or stereotactic radiosurgery are limited by radiation neurotoxicity, tumor size and injury to adjacent vascular or cranial nerves. To date, adjuvant chemotherapies have proven to be ineffective in controlling recurrent meningiomas.

High-grade gliomas (i.e., astrocytoma WHO grades III and IV, oligodendroglioma WHO grade III) represent approximately 25% of all primary brain tumors and are the most common intrinsic brain tumor (Figure 7, Figure 10B). These tumors are among the most difficult to treat. Despite advances in surgery, radiation and chemotherapy, the median survival after diagnosis of the most aggressive astrocytoma, glioblastoma (WHO grade IV), remains poor at approximately 12–14 months, with only 3–5% of patients surviving longer than five years. Glioblastoma can occur as the result of progression from lower-grade astrocytomas (i.e., WHO Grade II or III) or can arise de novo. Initial neurologic symptoms are seizure, headache and new neurologic deficit. Without treatment, survival is typically three months. Treatment involves a combination of surgery for "safe maximal resection," radiation therapy and the oral chemotherapy, temozolomide.

The goals of surgery are to obtain diagnostic tissue for both diagnosis and prognostication, to alleviate symptoms related to mass effect, to diminish tumor burden via cytoreduction and to decrease long-term steroid use. Surgery for high-grade gliomas involves balancing our goal of "safe maximal resection" of the tumor and avoiding a new neurologic deficit. Surgical techniques for increasing extent of resection involve the use of advanced magnetic resonance imaging (e.g., functional MRI), intraoperative microscope, stereotactic navigated instruments for resection, intraoperative imaging, intraoperative mapping and monitoring of language and motor pathways, and awake craniotomy for speech preservation in cooperative patients. Although studies have shown improved survival with >98% resection (median survival 13 months vs. 8.8 months), patient death may be hastened if patients are left with a profound neurologic deficit and reduced quality of life. After surgery, patients will undergo radiation and chemotherapy (i.e., temozolomide). Future hope also lies in individualized cancer care with new targeted therapies (e.g., molecules inhibitors, immunotherapy, conjugated antibody chemotherapy).

The surgical management of CNS tumors revolves around the concept of "safe maximal resection." Surgical indications are defined by the need for diagnosis; improvement or prevention of neurologic deficit, prevention of death and/or the need to obtain tissue for clinical drug trials, as well as consideration of spine stability in the case of spinal tumors. The risk of surgical neurologic deficit increases with tumors in or near the spinal cord for language (left temporal lobe, usually), motor (posterior frontal lobe), vision (occipital cortex) and neurocognitive (hippocampal and deep brain structures) centers.

Acknowledgements

We thank Kristin Kraus for editorial assistance in preparing this article.

FIGURE 5, Estimated cancer statistics in the United States (U.S.) for 2019

Cancer cases	Estimated new 2019 (%)	Estimated deaths 2019 (%)
All sites cancer	1,762,450	606,880
Brain and other nervous system	23,820 (1%)	17,760 (3%)
Brain metastases occur in 6–14% of cancer patients	105,747–246,743 (1,762,450 × 6 and × 14%)	
Spine metastases occur in 5–10% of cancer patients	88,123–176,245 (1,762,450 × 5 and × 10%)	
Meningiomas occur in 37% of all primary SPINAL tumors	8,813 (23,820 × 37%)	
Malignant, High-grade Glioma occur in 24% of all primary SPINAL tumors.	5,716 (23,820 × 24%)	

Primary brain tumor estimates from American Cancer Society.1 Metastatic brain, metastatic spine, meningiomas, and malignant high-grade glioma estimates extrapolated from published rates of occurence.3,4,7

FIGURE 6, Top 4 primary central nervous system tumors for 2011–2015

CNS tumor	%
Non-malignant meningioma	36.7%
Malignant high-grade glioma (e.g., glioblastoma, oligodendroglioma)	24.9%
Non-malignant pituitary tumors	16.4%
Non-malignant nerve sheath tumors (e.g., acoustic neuroma)	8.5%

(Note: Includes both non-malignant and malignant tumors, n = 392,982).3

FIGURE 7, Low and high-grade gliomas based on World Health Organization (WHO) classification 2,3,12–14

Pathology	WHO grade	Mean age (yr)	M:F ratio	Mean survival (yr)	Mean time progression (yr)	Notes:
Diffuse astrocytoma	II (LGG)	34	1.18 : 1	6–8	4–5	
Anaplastic astrocytoma	III (HGG)	51	1.31 : 1		2	
Glioblastoma	IV (HGG	61	1.26 : 1	1		MGMT silencing and mutated IDH-1 associated with longer survival12–14
Oligodendroglioma	II (LGG)	40–45	1.1 : 1	11–15		1p/19q loss is associated with longer survival11
Anaplastic oligodendroglioma	III (HGG)	45–50	1.1 : 1	3.5		1p/19q loss is associated with longer survival11

Key: LGG = low-grade glioma, HGG = high-grade glioma, IDH-1 = isocitrate dehydrogenase 1 gene, MGMT = methyl-guanine-methyl-transferase

Figure 8A Figure 8B

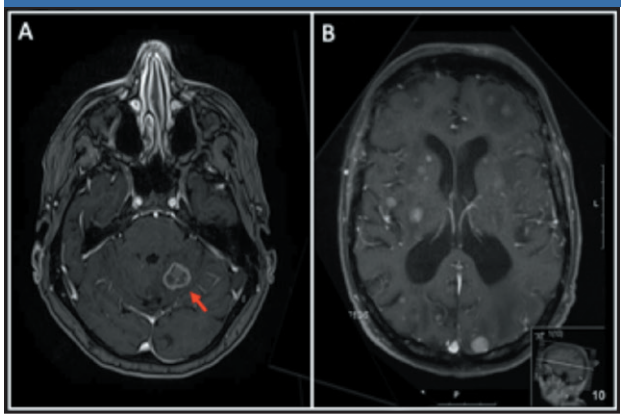


Figure 8: Brain metastases are the most common brain tumor. A. Axial T1-weighted magnetic resonance imaging (MRI) scan with contrast of patient with colorectal cancer and solitary metastasis to the left cerebellar brain (arrow). Mild edema causing mass effect on the fourth ventricle noted. B. Axial T1-weighted MRI scan with contrast of patient with lung cancer and multiple brain metastases scattered throughout the frontal, parietal and occipital lobes.

Figure 9A, B, C, D, E, F

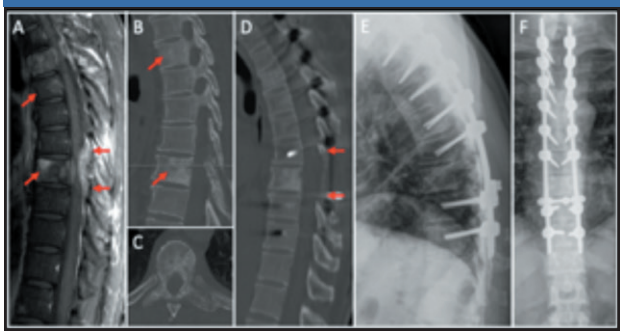


Figure 9: Imaging of a 52-year-old male patient presenting with paraplegia from metastatic prostate cancer to the thoracic spine with epidural spinal cord compression (A–C) treated with thoracic laminectomy and stabilization (D–F). A. Sagittal T1-weighted magnetic resonance imaging (MRI) scan with contrast. Arrows identify metastatic cancer to vertebral bodies and epidural space. B–C. Sagittal (B) and axial (C) computed tomography (CT) scans depicting osteoblastic response to metastatic prostate cancer. D. Postoperative sagittal CT with arrows indicating extent of laminectomy bone removal. E–F. Lateral (E) and anteroposterior (F) X-rays showing long-segment pedicle screw–rod construct for stabilization.

Figure 10A Figure 10B

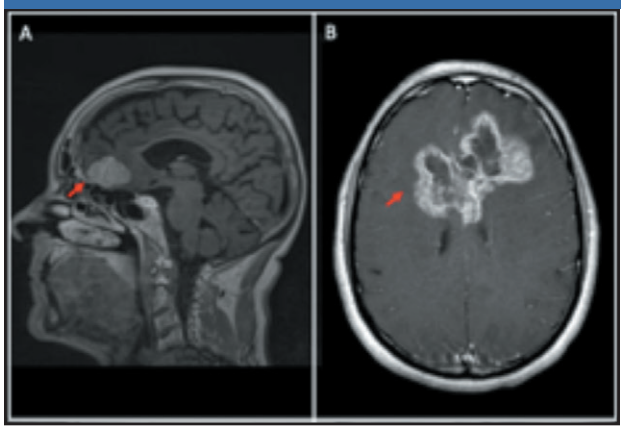


Figure 10: Magnetic resonance imaging (MRI) showing the two most common primary SPINAL tumors: meningioma and glioblastoma (GBM). A. Sagittal T1-weighted MRI scan with contrast with arrow showing a dural-based, extrinsic to the brain. The imaging is consistent with olfactory groove meningioma. B. Axial T1-weighted MRI scan with contrast of GBM (astrocytoma, WHO Grade IV).