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Brain Tumors

J. Ricardo McFaline-Figueroa, MD, PhD,[a,b,c,d] Eudocia Q. Lee, MD, MPH[a,b,c]

[a]Center for Neuro-Oncology, Dana-Farber Cancer Institute, Boston, Mass; [b]Department of Neurology, Brigham and Women's Hospital, Boston, Mass; [c]Harvard Medical School, Boston, Mass; [d]Department of Neurology, Massachusetts General Hospital, Boston.

ABSTRACT

Brain tumors are common, requiring general medical providers to have a basic understanding of their diagnosis and management. The most prevalent brain tumors are intracranial metastases from systemic cancers, meningiomas, and gliomas, specifically, glioblastoma. Central nervous system metastases may occur anywhere along the neuroaxis, and require complex multidisciplinary care with neurosurgery, radiation oncology, and medical oncology. Meningiomas are tumors of the meninges, mostly benign and often managed by surgical resection, with radiation therapy and chemotherapy reserved for high-risk or refractory disease. Glioblastoma is the most common and aggressive malignant primary brain tumor, with a limited response to standard-of-care concurrent chemoradiation. The new classification of gliomas relies on molecular features, as well as histology, to arrive at an "integrated diagnosis" that better captures prognosis. This manuscript will review the most common brain tumors with an emphasis on their diagnosis, oncologic management, and management of medical complications.

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KEYWORDS: Brain metastases; Brain tumor; Cerebral edema; Glioblastoma; Meningioma; Seizures

INTRODUCTION

The complexity in caring for patients with brain tumors poses a challenge to primary care providers, although they play a vital role in their timely diagnosis and coordination of care. Furthermore, the incidence of brain tumors is increasing in certain groups, possibly due to advances in the diagnosis of primary brain tumors, or in the treatment and improved survival from systemic cancer.[1,2] Thus, it is important for primary care providers to be familiar with their management. This article will review the 3 most common types of brain tumors, with an emphasis on their clinical presentation, diagnosis, basic oncological management, and most common medical complications.

INTRACRANIAL METASTASES

Most systemic malignancies can spread to the nervous system, and the site of involvement has important implications for treatment and prognosis. The brain parenchyma is the most commonly involved site and is the focus of this section, hereafter referred to as brain metastases (**Figure 1**). Leptomeningeal metastases refer to the malignant invasion of cerebrospinal fluid and leptomeninges (ie, the inner membranes covering the brain and spinal cord) (**Figure 2**). It is important to distinguish leptomeningeal disease from dural metastases (ie, the outer membrane covering the brain and spinal cord), as the latter lie outside of the blood–brain barrier and are amenable to systemic therapies. Cancer may also metastasize to the spinal cord as intramedullary tumors; to the leptomeninges overlying the spinal cord, the conus medullaris, or the cauda equina; to the epidural spaces and compress the spinal cord; to the nerve plexuses; and even to individual nerves.

Brain metastases comprise the majority of brain tumors, with their incidence estimated to be 10 times more common than primary brain tumors,[1] although comprehensive data on their epidemiology are lacking. The most common systemic malignancies to metastasize to the brain are lung cancer, breast cancer, and melanoma.[3] Recent studies shed light on the epidemiology of brain metastases at the time of systemic cancer diagnosis (ie, synchronous brain metastases) using the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database. Cagney et al[4] estimate the

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Requests for reprints should be addressed to Eudocia Q. Lee, MD, MPH, Dana-Farber Cancer Institute, Center for Neuro-Oncology, 450 Brookline Avenue, D-2110, Boston, MA 02115.

E-mail address: eqlee@partners.org

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overall annual incidence of synchronous brain metastases at 23,598 patients per year in the United States, based on SEER data from 2010 to 2013. The incidence per tumor type for all stages of disease was highest in small cell lung cancer, lung adenocarcinoma, and non-small cell lung cancer not otherwise specified, with a prevalence of over 10%. Considering only patients with metastatic disease at the time of diagnosis, metastatic melanoma was the most likely to present with synchronous brain metastases (28.2%), followed by lung adenocarcinoma, non-small cell lung cancer not otherwise specified, small cell lung cancer, squamous cell carcinoma of the lung, bronchioalveolar carcinoma, and renal cancer, all with a prevalence of over 10%. Analysis of SEER data by Kromer et al[5] revealed similar results. The exact prevalence of brain metastases in all cancer patients remains unknown, although 2 large autopsy series of patients who died from cancer showed a prevalence of brain metastases between 15% and 17%.[6,7]

CLINICAL SIGNIFICANCE

- Brain tumors are common in the general population and can present with focal neurological symptoms, seizures, or headaches, while some are asymptomatic and found incidentally.
- The most prevalent brain tumors are brain metastases, meningiomas, and gliomas, specifically glioblastoma.
- The management of brain tumors and their complications requires complex coordination of care among medical oncologists, radiation oncologists, neurosurgeons, and primary care providers.

Clinical Presentation and Diagnosis

The clinical presentation of brain metastases is variable. Headache is common, but is neither sensitive nor specific for the diagnosis. The classic headache is mild at onset, begins when the patient awakens in the morning, disappears shortly after arising, and returns the following morning, but is present in only one-quarter to one-third of patients.[8] The question of when to image those without the classic "brain tumor headache" or those with chronic headache is a difficult one. The US Headache Consortium recommends neuroimaging to rule out a secondary cause of headaches for patients with an abnormal neurological examination, atypical headache features, or headaches that do not fit the strict definition of migraine or other primary headache disorder.[9] Atypical features include rapidly increasing headache frequency, history of lack of coordination, history of localized neurological signs, and history of headache causing awakening from sleep.

Seizures are another common symptom in patients with brain metastases and can occur at any time of the disease course. Neuroimaging should be considered for all adults presenting with a first unprovoked seizure.[10] Patients may also present with focal neurological symptoms, for example, aphasia, weakness, sensory loss, visual disturbances, and ataxia. Cognitive or behavioral impairment is likewise common and may be the result of focal structure disease (eg, frontal or right parietal injury) or secondary to increased intracranial pressure.

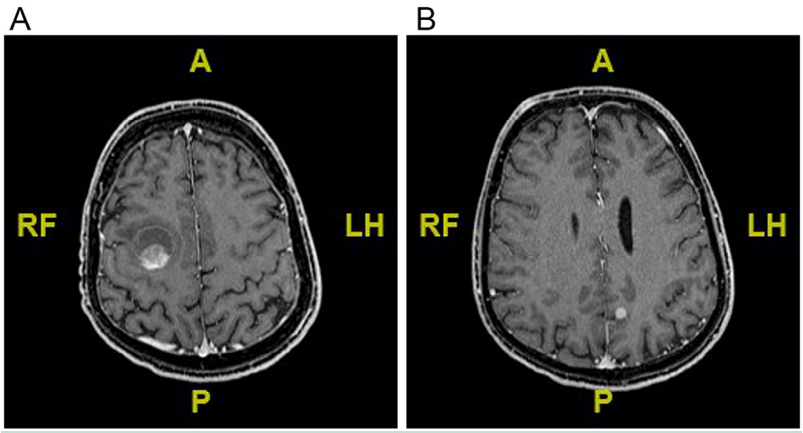

Figure 1 A 36-year-old man with a history of skin melanoma presents with a first-time seizure. Brain magnetic resonance imaging (MRI) revealed a dominant right frontal hemorrhagic metastasis (**A**) as well as additional smaller metastases (**B**). Body positron emission tomography/computed tomography revealed lung metastases as well. The right frontal lesion was resected to relieve symptoms; pathology confirming metastatic melanoma. As molecular testing revealed a BRAF V600E mutation, he was treated in combination with the BRAF inhibitor dabrafenib and the MEK inhibitor trametinib. His systemic disease responded and his brain metastases stabilized. Unfortunately, his disease progressed 8 months later.

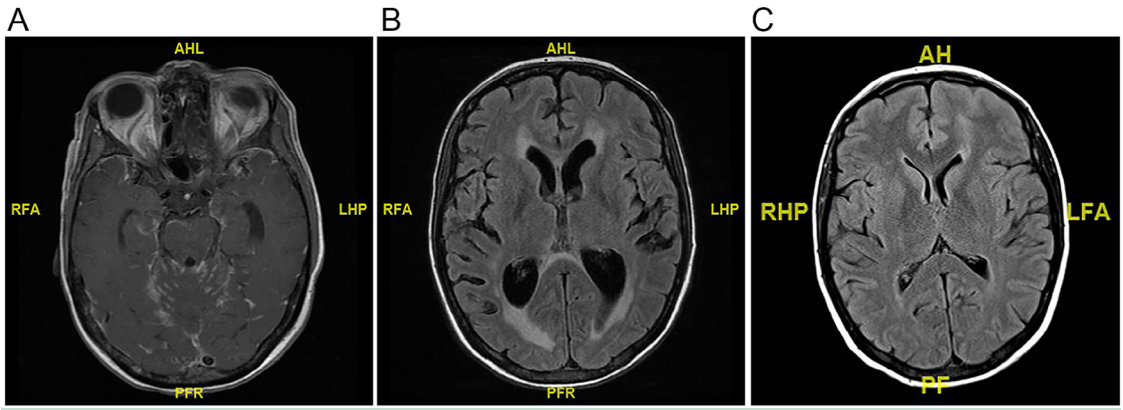

Figure 2 A 47-year-old woman with metastatic breast cancer presented with confusion, headache, and vomiting. Brain magnetic resonance imaging (MRI) with contrast demonstrated (**A**) new leptomeningeal enhancement on T1 post contrast image, most notable by the enhancement of cerebellar folia, as well as (**B**) new hydrocephalus in comparison with (**C**) a brain MRI from 1 year prior. A ventriculoperitoneal shunt was placed to relieve symptoms from hydrocephalus.

Classically, leptomeningeal metastases present with signs and symptoms of increased intracranial pressure due to decreased cerebrospinal fluid reabsorption and poor ventricular outflow leading to hydrocephalus or focal neurologic deficits involving multiple sites within the neuroaxis.[8] Clinical manifestations include headache worsened in the recumbent position, cognitive changes, focal cortical or cerebellar dysfunction, incontinence, and gait disorders. Malignant invasion of the leptomeninges can also lead to multiple cranial neuropathies and radiculopathies.

The National Comprehensive Cancer Network guidelines for central nervous system cancers provide an algorithm for establishing the diagnosis of brain metastases.[11] Magnetic resonance imaging (MRI) of the brain with and without contrast is the gold standard for neuroimaging, although computed tomography (CT) with and without contrast is reasonable for those that cannot undergo MRI. In patients with a known history of cancer and little concern for alternative diagnoses, neuroimaging may be sufficient for diagnosis. In those without known cancer, CT imaging of the chest/abdomen/pelvis or whole-body positron emission tomography-CT may reveal other sites of involvement outside the central nervous system that may be biopsied for tissue confirmation. In those without evidence of systemic malignancy or those with concern for an alternative diagnosis, a stereotactic or open biopsy, or surgical resection of the brain mass is recommended to further direct care.

Leptomeningeal metastases can present a diagnostic challenge. Cerebrospinal fluid cytology is the gold standard for diagnosis, but poor sampling, inadequate sample volume (<10.5 mL), and inefficient handling may lead to false-negative results.[12] Serial sampling and collection at the site of symptoms (ie, ventricular for cranial disease and lumbar for spinal disease) increases the diagnostic yield. Flow cytometry increases sensitivity to leptomeningeal spread of hematologic malignancies.[13] MRI is less specific than cytology, but may provide supportive information for those with negative cytology.[14] In those with a clinical suspicion, physical examination to look for evidence of cranial neuropathies or radiculopathies, brain and spine MRI, and cerebrospinal fluid examination are indicated.[11]

Oncological Management

There is no universal standard of care for brain metastases, and response to therapy varies per tumor type. As most patients with brain metastases have advanced systemic disease, the prognosis remains generally poor. Graded Prognostic Assessment indices estimate survival in brain metastasis patients according to tumor subtype and prognostic factors.[15] In general, management is aimed at palliation in patients with poor prognoses. More aggressive management is reserved for patients with good prognoses (such as a young patient with excellent performance status and brain metastasis from hormone receptor/HER2 positive breast cancer with estimated median survival time of 25.3 months per Graded Prognostic Assessment).

The role of surgery depends on the diagnostic need and extent of disease. Surgery may be necessary to establish a diagnosis. In patients with good functional status, controlled or absent systemic disease, and a single, surgically accessible brain metastasis, surgical resection may be indicated and associated with improved survival and lengthened functional independence.[16,17] In those with multiple brain metastases, palliative surgical resection may be considered for the removal of a large, dominant, symptomatic lesion.

Whole-brain radiotherapy is the historic standard for radiotherapy in brain metastases and results in improved neurologic function.[18] However, it is associated with neurotoxicity, particularly fatigue and neurocognitive dysfunction.[19] This limitation created an interest in studying focused forms of radiotherapy, like stereotactic radiosurgery or stereotactic radiotherapy. Multiple studies failed to identify a survival advantage to combination stereotactic radiosurgery and

whole-brain radiotherapy, compared with stereotactic radiosurgery alone, despite improved local and distant brain recurrence rates.[19-21] Thus, stereotactic radiosurgery alone is preferred for patients with a limited number and small volume of brain metastases, while multiple brain metastases (>3) and large lesions are treated with whole-brain radiotherapy.[11]

Historically, systemic therapies played little role in direct treatment of brain metastases, but rather for control of systemic disease. However, advances in immunotherapy and the development of agents that cross the blood–brain barrier are shifting this paradigm.[1,22] New studies about the treatment of brain metastases from metastatic melanoma are a perfect example. Initial results from the COMBI-MB trial of dabrafenib plus trametinib in $BRAF^{V600}$-mutant metastatic melanoma showed an intracranial response of 76% in patients without prior radiotherapy.[23] In another recent study, treatment with pembrolizumab elicited an intracranial response in 22% of patients with metastatic melanoma, albeit in a small cohort.[24] There are other examples of systemic therapies undergoing active research reviewed elsewhere.[1]

MENINGIOMAS

Meningiomas are mostly benign, slow-growing neoplasms derived from the meningothelial cells of the arachnoid mater and are the most common primary brain tumor (**Figure 3**).[2,25] According to 2008-2012 data from the Central Brain Tumor Registry of the United States, meningiomas account for 35% of all primary brain tumors, with an incidence rate of 7.75 per 100,000 and a median age at diagnosis of 65 years.[2] The World Health Organization (WHO) classification scheme grades meningiomas as grade I to III, based on histology. Grade I meningiomas, also called benign meningiomas, are the most common and carry a favorable prognosis. However, WHO grade II and III meningiomas are more aggressive and associated with a 78% and a 44% survival at 5 years, respectively.[26]

Clinical Presentation and Diagnosis

Meningiomas may present with headaches, seizures, or focal neurological symptoms due to compression or invasion of adjacent structures. Oftentimes, they are incidentally found on neuroimaging. A radiographic diagnosis can be made in the absence of tissue confirmation when there is evidence of a homogeneously enhancing, dural-based mass with a dural tail and cerebrospinal fluid cleft.[11] However, dural-based intracranial metastases and central nervous system lymphoma may have a similar appearance. In cases of diagnostic uncertainty or concern for high-grade features, biopsy or resection can establish the diagnosis.

Oncological Management

Meningioma management depends on the presence of symptoms, the histologic grade of surgically confirmed meningiomas, and for high-grade meningiomas, the extent of resection. Patients with incidentally found, asymptomatic meningiomas may be observed radiographically, given their often slow or absent growth.[27] In symptomatic patients, or in patients with rapidly growing tumors, surgery is indicated for both therapeutic and diagnostic purposes.[11] Adjuvant radiotherapy is reserved for those with grade II and grade III meningiomas or subtotal resection, given the high risk of recurrence and high mortality rate.[11,25,28] Chemotherapy plays a limited role in management, mostly as salvage therapy for refractory disease. However, recent studies identified novel oncogenic mutations in a subset of meningiomas that may prove useful therapeutic targets.[29,30]

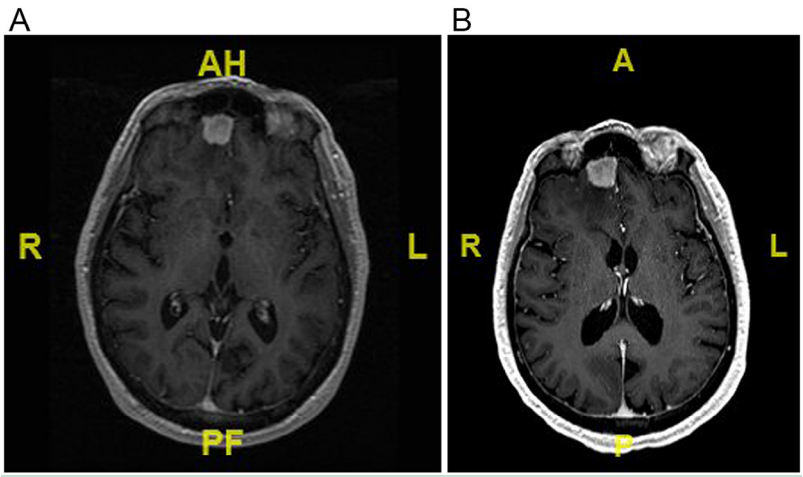

Figure 3 (**A**) A dural-based enhancing mass was found incidentally on T1-post contrast magnetic resonance imaging sequences in an 82-year-old man after experiencing a mechanical fall. (**B**) Four years later, the mass has slowly grown, consistent with a benign meningioma. Given his age, lack of symptoms, and patient preference, he remains on observation with serial imaging.

GLIOBLASTOMA

Gliomas are the most common malignant tumors of the central nervous system and include astrocytomas, oligodendrogliomas, ependymomas, and a variety of rare histologies (**Table 1**).[25] Glioblastoma, a grade IV astrocytoma, is the most common and the most aggressive (**Figure 4**). Glioblastoma makes up 15% of all primary brain tumors and 45% of malignant primary brain tumors, with an incidence of 3.2 per 100,000 and a median age at diagnosis of 64 years.[2]

Clinical Presentation and Diagnosis

Glioblastoma may present with headaches, seizures, or focal neurological symptoms. Due to its aggressive nature, symptoms may develop rapidly. MRI brain with and without contrast is the modality of choice for neuroimaging. The appearance can vary, but most often shows a supratentorial, heterogeneously enhancing mass lesion with central necrosis and surrounding white matter signal that may be due to edema or infiltrating tumor.[31]

Diagnosis requires pathological confirmation through biopsy or surgical resection. The 2016 WHO classification of central nervous system tumors relies on a mixture of histological appearance and molecular information to arrive at an "integrated diagnosis."[25] Isocitrate dehydrogenase (IDH) mutational status is at the forefront of this re-classification for gliomas, and glioblastoma is now re-classified as IDH-mutant or IDH-wildtype. Mutations in IDH1, most commonly a histidine-to-arginine substitution at codon 132 (R132H), or IDH2 is inversely correlated with grade and associated with better outcomes. For example, in one study, IDH1 R132H mutation was associated with a 27.4-month median survival, compared with 14 months for IDH-wildtype glioblastoma patients.[32] IDH mutational status is the most prominent single prognostic factor in high-grade gliomas, and IDH-mutant glioblastoma, a grade IV tumor, has a more favorable prognosis than IDH-wildtype anaplastic astrocytoma, a grade III glioma.[33]

O^6-methylguanine-DNA methyltransferase (MGMT) promoter methylation status is another important molecular marker in glioblastoma. The MGMT protein reverses DNA

Table 1 Primary Central Nervous System Tumors[25]

Diffuse astrocytic and oligodendroglial tumors
Diffuse astrocytoma, IDH-mutant
Diffuse astrocytoma, IDH-wild type
Diffuse astrocytoma, NOS
Anaplastic astrocytoma, IDH-mutant
Anaplastic astrocytoma, IDH-wild type
Anaplastic astrocytoma, NOS
Glioblastoma, IDH-wild type
Glioblastoma, IDH-mutant
Glioblastoma, NOS
Diffuse midline glioma, H3 K27M-mutant
Oligodendroglioma, IDH-mutant and 1p/19q co-deleted
Oligodendroglioma, NOS
Anaplastic oligodendroglioma, IDH-mutant and 1p/19q co-deleted
Anaplastic oligodendroglioma, NOS
Oligoastrocytoma*, NOS
Anaplastic oligoastrocytoma*, NOS
Other astrocytic tumors
eg, Pilocytic astrocytoma
Ependymal tumors
eg, Ependymoma
Other gliomas
Choroid plexus tumors
Neuronal and mixed neuronal-glial tumors
Tumors of the pineal region
eg, Pineocytoma, pineoblastoma
Histiocytic tumors
Embryonal tumors
Medulloblastomas, genetically defined
- WNT-activated
- SHH-activated and TP53 mutant
- SHH-activated and TP53-wildtype
- Non-WNT/Non-SHH

Medulloblastomas, histologically defined
- Classic
- Desmoplastic/nodular
- With extensive nodularity
- Large cell/anaplastic

Medulloblastoma, NOS
Other embryonal tumors
Tumors of the cranial and spinal nerves
eg, Schwannoma, neurofibroma
Meningiomas
Mesenchymal, nonmeningothelial tumors
eg, Solitary fibrous tumor/hemangiopericytoma, hemangioblastoma
Melanocytic tumors
Lymphomas
Diffuse large B-cell lymphoma of the central nervous system
Immunodeficiency-associated central nervous system lymphomas
- AIDS-related diffuse large B-cell lymphoma
- EBV-positive diffuse large B-cell lymphoma, NOS

Intravascular large B-cell lymphoma
Other CNS lymphomas
Germ cell tumors
Tumors of the sellar region
Craniopharyngioma
Granular cell tumor of the sellar region
Pituicytoma
Spindle cell oncocytoma

AIDS = acquired immunodeficiency syndrome; CNS = central nervous system; EBV = Epstein-Barr virus; H3 K27M = Histone H3 variant with lysine to methionine substitution at codon 27; IDH = isocitrate dehydrogenase; NOS = not otherwise specified, denotes a histological diagnosis in the absence of molecular information; SHH = Sonic hedgehog gene; TP = Tumor protein p53; WNT = Wnt signaling pathway; 1p/19q co-deleted = Co-deletion of the short arm of chromosome 1 and the long arm of chromosome 19.

*Oligoastrocytoma is a histological diagnosis. In the presence of molecular information, these tumors are re-classified as astrocytomas or oligodendrogliomas.

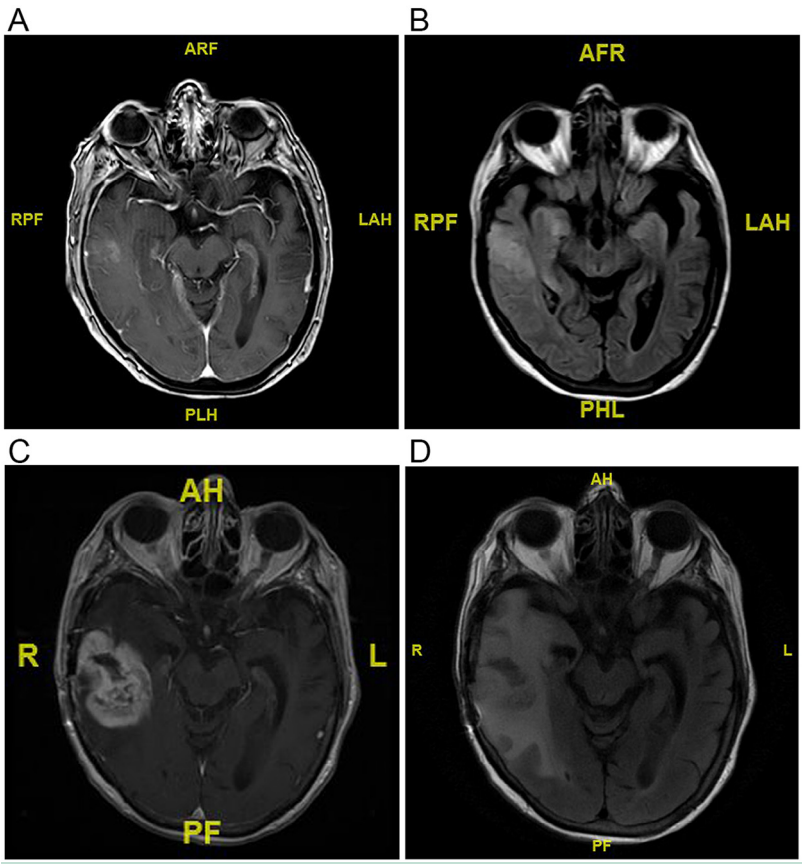

Figure 4 A 73-year-old woman presented following her first seizure. (**A**) T1 post-contrast and (**B**) fluid-attenuated inversion recovery sequences reveal a small enhancing lesion with surrounding edema in the right temporal lobe. She underwent resection and pathology demonstrated an isocitrate dehydrogenase-wildtype, O^6-methylguanine-DNA methyltransferase unmethylated glioblastoma. She received radiation and temozolomide, but subsequently progressed as demonstrated by increasing enhancement (**C**) and surrounding edema (**D**). Ultimately, patient succumbed to her disease 14 months after initial diagnosis.

alkylation at guanine sites, and silencing of its promoter via DNA methylation leads to decreased expression. MGMT promoter methylation is associated with tumor regression and prolonged overall and progression-free survival in patients treated with an alkylating agent or radiotherapy.[34,35]

Oncological Management

Management of glioblastoma includes a combination of neurosurgery, radiotherapy, and chemotherapy. Referral to an experienced brain tumor neurosurgeon for maximum safe resection is imperative, as the extent of resection impacts survival.[36,37] In 2005, Stupp et al[38] reported on the results of the European Organisation for Research and Treatment of Cancer (EORTC) and National Cancer Institute of Canada Clinical Trials Group (NCIC) trial and established the current standard of care for postoperative management of newly diagnosed glioblastoma. The "Stupp protocol" consists of 6 weeks of concurrent focal irradiation (60 Gy divided into 2 Gy fractions per day) with continuous daily temozolomide, followed by 6 cycles of adjuvant temozolomide. The regimen resulted in a median overall survival of 14.6 months, compared with 12.1 months for glioblastoma patients treated with radiation alone. The 5-year analysis of the EORTC-NCIC trial confirmed that the greatest benefit of adding temozolomide was seen in those with MGMT promoter methylation.[39]

A relatively new treatment option for glioblastoma is tumor-treating fields, which provides alternating electric field therapy and disrupts mitoses. The tumor-treating fields portable device received US Food and Drug Administration approval for treatment of newly diagnosed glioblastoma after interim analysis of a multicenter, prospective, randomized trial showed added survival benefit of tumor-treating fields with temozolomide compared with temozolomide alone.[40] The device is worn on the head and its main toxicity is skin irritation.

The potential toxicities of chemoradiation are of significant concern to neuro-oncologists and radiation oncologists treating elderly (age 65-70 years or older) patients with glioblastoma. Several studies have tried to address the question of what is the optimum regimen for these patients.[41-43] In

summary, options include "Stupp protocol" (standard radiation plus temozolomide), short-course (hypofractionated) radiotherapy alone, temozolomide alone, or hypofractionated radiation plus temozolomide. Although no randomized study compares "Stupp protocol" with hypofractionated radiation plus temozolomide, a recent phase III, randomized study of patients 65 years and older with a newly diagnosed glioblastoma and good performance status demonstrated increased survival with hypofractionated radiation plus temozolomide compared with hypofractionated radiation alone.[43] Treatment was well tolerated with chemoradiation, and quality of life was similar between the 2 treatment groups. The benefit from the addition of temozolomide was greatest in patients with MGMT promoter methylation. For patients in whom combined chemoradiation may not be tolerated (due to, eg, comorbid conditions, poor functional status, or patient preference), temozolomide monotherapy can be a reasonable treatment for elderly patients with MGMT promoter methylated tumors, whereas hypofractionated radiation therapy alone is a viable option for those with unmethylated tumors.[11]

Table 2 Work-Up and Management of Common Medical Complications in Brain Tumor Patients[44]

Complication	Clinical Presentation	Diagnosis	Management
Cerebral edema	• Worsening of neurologic deficits arising from culprit brain mass • Significant increases in cerebral edema can cause increased ICP and present as confusion, headaches, nausea, vomiting, etc.	• Clinical diagnosis • Cerebral edema is visible on brain imaging (either head CT or brain MRI), but treatment should be based on symptoms, not imaging	• Corticosteroids (preferably dexamethasone)
Endocrinopathies	• Can be seen in patients who received brain radiation, particularly if the hypothalamus or pituitary was in the radiation field	• Standard laboratory testing for endocrinopathies based on symptoms, such as TSH, cortisol, testosterone, FSH, LH, GH, etc.	• Hormone replacement based on the endocrinopathy
Fatigue	• Patient self-reported	• Evaluation for treatable causes of fatigue, such as medications, depression, sleep disturbance, anemia, nutritional deficiencies, alcohol/substance abuse, endocrinopathies, etc.	• Limited data on beneficial interventions • Reported benefit from exercise and corticosteroids • Studies of psychostimulants in brain tumor patients have yielded mixed results
Mood and other psychiatric disorders, including depression	• Patient self-reported depression or reported by caregiver • Psychosis, mania or irritability secondary to steroid use	• Clinical diagnosis	• Antidepressants or mood stabilizers (preferably ones that do not decrease the seizure threshold) • Steroid wean
Neurocognitive Impairment	• May be a presenting symptom or due to tumor growth • Can be seen after radiation, particularly after WBRT	• Clinical diagnosis • Screening tests (MOCA, MMSE) • Neuropsychological evaluation	• Occupational and cognitive/speech therapy • Limited data for donepezil • Prophylactic memantine for patients undergoing WBRT
Seizures	• Depends on type of seizure (focal vs generalized) and location of the seizure nidus	• Clinical diagnosis based on description of event • EEG is often not required	• Antiepileptic drug (preferably non-enzyme-inducing agent)
Venous thromboembolism	• Deep venous thrombosis (DVT) involving the leg typically presents with unilateral calf pain/tenderness or leg swelling • Pulmonary embolism (PE) can present with shortness of breath, chest pain, or tachycardia	• Venous ultrasonography • Chest CT angiogram with contrast	• Management is guided by safety of anticoagulation. • Anticoagulation is preferred treatment, but may be contraindicated in patients with hemorrhagic brain tumors. • Available data suggest that low-molecular-weight heparin is preferred over coumadin.

CT = computed tomography; EEG = electroencephalogram; FSH = follicle-stimulating hormone; GH = growth hormone; ICP = intracranial pressure; LH = luteinizing hormone; MMSE = mini-mental status examination; MOCA = Montreal cognitive assessment; MRI = magnetic resonance imaging; TSH = thyroid stimulating hormone; WBRT = whole brain radiation.

There is no standard of care for the treatment of recurrent glioblastoma. Options include neurosurgery for resectable recurrence, re-irradiation, systemic therapies such as lomustine or bevacizumab, alternating electric field therapy, and clinical trials.[11]

MANAGEMENT OF MEDICAL COMPLICATIONS IN BRAIN TUMOR PATIENTS

The care of patients with brain tumors includes the management of medical and neurologic complications.[44] While this section will focus on seizures and cerebral edema, patients with brain tumors are also at risk for neurocognitive decline, depression, fatigue, endocrinopathies, and venous thromboembolism (**Table 2**). Management of these complications by primary care providers can significantly improve quality of life and perhaps impact mortality.

Seizure Management

Seizures occur in many brain tumor patients, and the frequency depends on the tumor type, location, and growth rate. Twenty to thirty-five percent of patients with brain metastases develop seizures, compared with 20%-50% of patients with meningioma and 25%-60% of patients with high-grade gliomas.[45] The incidence is higher in low-grade compared with high-grade gliomas, around 60%-75%. As most low-grade gliomas are IDH mutant, this higher incidence may be secondary to altered isocitrate metabolism producing higher levels of 2-alpha-ketoglutarate, a mimic of the excitatory neurotransmitter glutamate.[46]

Existing guidelines advise against the use of antiepileptic medications for primary seizure prophylaxis in patients with brain tumors.[47] For patients with seizures, there is no consensus on the optimal choice of antiepileptic drug. However, it is common practice to avoid enzyme-inducing agents that may interfere with drug metabolism, such as phenytoin, carbamazepine, and phenobarbital, in favor of other antiepileptics such as levetiracetam, lacosamide, lamotrigine, and valproate.[44]

Steroid Dosing

Peritumoral cerebral edema can cause significant morbidity in brain tumor patients, and steroids offer a powerful tool for palliation.[44] Dexamethasone is the steroid of choice, given a long half-life and lack of mineralocorticoid activity. Side effects of steroid use include myopathy, mood disorders, psychosis, and peptic ulcer disease. Steroids should be tapered to the lowest dose possible to minimize side effects and should be used only in symptomatic patients.

CONCLUSION

Brain tumors require specialized and complex care by neuro-oncologists, medical oncologists, radiation oncologists, and brain tumor neurosurgeons. Primary care providers should be acquainted with their management, as they are at the forefront of diagnosis, care coordination, and management of complications.

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