118 Primary and Metastatic Tumors of the Nervous System

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Primary brain tumors are diagnosed in approximately 52,000 people each year in the United States. At least one-half of these tumors are malignant and associated with a high mortality. Glial tumors account for about 30% of all primary brain tumors, and 80% of those are malignant. Meningiomas account for 35%, vestibular schwannomas 10%, and central nervous system (CNS) lymphomas about 2%. Brain metastases are three times more common than all primary brain tumors combined and are diagnosed in approximately 150,000 people each year. Metastases to the leptomeninges and epidural space of the spinal cord each occur in approximately 3–5% of patients with systemic cancer and are also a major cause of neurologic disability.

APPROACH TO THE PATIENT: Primary and Metastatic Tumors of the Nervous System

CLINICAL FEATURES

Brain tumors of any type can present with a variety of symptoms and signs that fall into two categories: general and focal; patients often have a combination of the two (Table 118-1). General or nonspecific symptoms include headache, with or without nausea or vomiting, cognitive difficulties, personality change, and gait disorder. Generalized symptoms arise when the enlarging tumor and its surrounding edema cause an increase in intracranial pressure or direct compression of cerebrospinal fluid (CSF) circulation leading to hydrocephalus. The classic headache associated with a brain tumor is most evident in the morning and improves during the day, but this particular pattern is actually seen in a minority of patients. Headaches are often holocephalic but can be ipsilateral to the side of a tumor. Occasionally, headaches have features of a typical migraine with unilateral throbbing pain associated with visual scotoma. Personality changes may include apathy and withdrawal from social circumstances, mimicking depression. Focal or lateralizing findings include hemiparesis, aphasia, or visual field defect. Lateralizing symptoms are typically subacute and progressive. A visual field defect is often unnoticed by the patient; its presence may only be revealed after it leads to an injury such as an automobile accident occurring in the blind visual field. Language difficulties may be mistaken for confusion. Seizures are a common presentation of brain tumors, occurring in about 25% of patients with brain metastases or malignant gliomas but can be the presenting symptom in up to 90% of patients with a low-grade glioma. All seizures that arise from a brain tumor will have a focal onset whether or not it is apparent clinically.

TABLE 118-1 SYMPTOMS AND SIGNS AT PRESENTATION OF BRAIN TUMORS

	High-Grade Glioma (%)	Low-Grade Glioma (%)	Meningioma (%)	Metastases (%)
Generalized				
Impaired cognitive function	50	10	30	60
Hemiparesis	40	10	36	60
Headache	50	40	37	50
Lateralizing				
Seizures	20	70+	17	18
Aphasia	20	<5	—	18
Visual field deficit	—	—	—	7

NEUROIMAGING

Cranial MRI is the preferred diagnostic test for any patient suspected of having a brain tumor and should be performed with gadolinium contrast administration. Computed tomography (CT) scan should be reserved for those patients unable to undergo magnetic resonance imaging (MRI; e.g., pacemaker). Malignant brain tumors—whether primary or metastatic—typically enhance with gadolinium and may have central areas of necrosis; they are characteristically surrounded by edema of the neighboring white matter. Low-grade gliomas usually do not enhance with gadolinium and are best appreciated on fluid-attenuated inversion recovery (FLAIR) MRIs. Meningiomas have a characteristic appearance on MRI because they are dural-based with a dural tail and compress but do not invade the brain. Dural metastases or a dural lymphoma can have a similar appearance. Imaging is characteristic for many primary and metastatic tumors and sometimes will suffice to establish a diagnosis when the location precludes surgical intervention (e.g., brainstem glioma). Functional MRI is useful in presurgical planning to define eloquent sensory, motor, or language cortex. Positron emission tomography (PET) is useful in determining the metabolic activity of the lesions seen on MRI; MR perfusion and spectroscopy can provide information on blood flow or tissue composition. These techniques may help distinguish tumor progression from necrotic tissue as a consequence of treatment with radiation and chemotherapy or identify foci of high-grade tumor in an otherwise low-grade-appearing glioma.

Neuroimaging is the only test necessary to diagnose a brain tumor. Laboratory tests are rarely useful, although patients with metastatic disease may have elevation of a tumor marker in their serum that reflects the presence of brain metastases (e.g., β human chorionic gonadotropin [β-hCG] from testicular cancer). Additional testing such as cerebral angiogram, electroencephalogram (EEG), or lumbar puncture is rarely indicated or helpful.

TREATMENT BRAIN TUMORS

Therapy of any intracranial malignancy requires both symptomatic and definitive treatments. Definitive treatment is based on the specific tumor type and includes surgery, radiotherapy, and chemotherapy. However, symptomatic treatments apply to brain tumors of any type. Most high-grade malignancies are accompanied by substantial surrounding edema, which contributes to neurologic disability and raised intracranial pressure. Glucocorticoids are highly effective at reducing perilesional edema and improving neurologic function, often within hours of administration. Dexamethasone has been the glucocorticoid of choice because of its relatively low mineralocorticoid activity. Initial doses are typically 12–16 mg/d in divided doses given orally or IV (both are equivalent). Although glucocorticoids rapidly ameliorate symptoms and signs, their long-term use causes substantial toxicity including insomnia, weight gain, diabetes mellitus, steroid myopathy, and personality changes. Consequently, a taper is indicated as definitive treatment is administered and the patient improves.

Patients with brain tumors who present with seizures require antiepileptic drug therapy. There is no role for prophylactic antiepileptic drugs in patients who have not had a seizure. The agents of choice are those drugs that do not induce the hepatic microsomal enzyme system. These include levetiracetam, topiramate, lamotrigine, valproic acid, and lacosamide (Chap. 445). Other drugs, such as phenytoin and carbamazepine, are used less frequently because they are potent enzyme inducers that can interfere with both glucocorticoid metabolism and the metabolism of chemotherapeutic agents needed to treat the underlying systemic malignancy or the primary brain tumor. Venous thromboembolic disease occurs in 20–30% of patients with high-grade gliomas and brain metastases. Therefore, prophylactic anticoagulants should be used during hospitalization and in nonambulatory patients. Those who have had either a deep vein thrombosis or pulmonary embolus can receive therapeutic doses of anticoagulation safely and without increasing