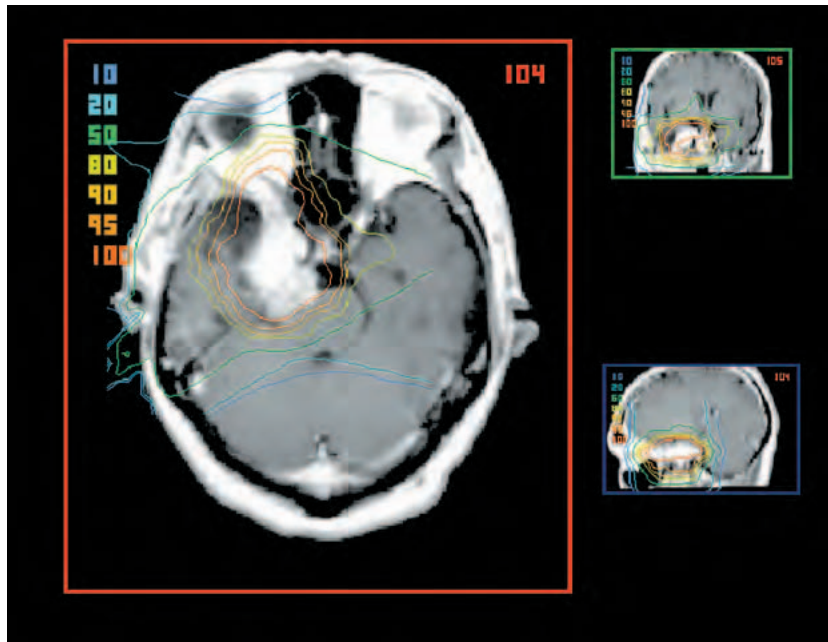




Fast Facts: Brain Tumors

Lauren E Abrey and Warren P Mason
Second edition





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Declaration of Independence

This book is as balanced and as practical as we can make it.
Ideas for improvement are always welcome: feedback@fastfacts.com

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Introduction

The term ‘brain tumor’ encompasses a wide range of tumor types, including malignant tumors arising from the brain parenchyma, low-grade tumors arising from the meninges or pituitary gland, and a variety of other rare tumors. The approach to managing patients is truly multidisciplinary, involving primary care physicians, neurologists, radiologists, neurosurgeons, pathologists, radiation oncologists and neurooncologists. Provision of optimal care for an individual patient requires adequate input from each specialty in order to synthesize an appropriate diagnostic and therapeutic plan.

Advances in radiology and pathology allow more precise and detailed diagnoses than ever before. Similarly, developments in molecular biology and imaging techniques are constantly improving available diagnostic modalities. Increasingly, pathologists are using molecular genetic features to supplement classic histological classifications. Furthermore, advances in neurosurgical techniques enable us to operate on tumors previously considered inoperable, and novel delivery systems allow various treatments to reach tumors otherwise protected by the blood–brain barrier.

Chemotherapy is now being used successfully to treat patients with primary brain tumors, and the use of temozolomide chemotherapy with irradiation has become the standard of care for most newly diagnosed patients. Additionally, various targeted therapies under investigation in glioma hold great promise for the future. Bevacizumab, a new antiangiogenic agent, is effective in the treatment of recurrent malignant glioma and is, at the time of writing, approved in the USA and 28 other countries.

In this book, we summarize the salient features of the various brain tumors and treatment modalities in a way that will be useful to the practicing clinician. Perhaps the most important message is that there are currently a variety of effective therapies available to a brain tumor patient. Therefore, it is critically important to select the best initial approach for an individual patient in order to achieve the best overall outcome, both in terms of survival and quality of life.

Classification

Intracranial tumors can be classified in several different ways. The most fundamental differentiation is between primary intracranial lesions and metastatic tumors. Primary tumors can be further subdivided according to whether they arise from the brain parenchyma, meninges, pituitary region, pineal region or skull base.

Neurological symptoms and neuroimaging provide information about tumor location, which is useful in developing a differential diagnosis (Table 1.1). However, definitive diagnosis of primary brain tumors is based on the cell of origin and requires histopathological assessment. The World Health Organization (WHO) classification of tumors of the central nervous system is used widely (see Key references).

Most intracranial tumors arise from the brain parenchyma, primarily from glial cells (astrocytes or oligodendrocytes). Primary neuronal tumors are uncommon. Meningeal tumors are the second most common type of intracranial tumor. Tumors also arise from a variety of other cell types, including some not ordinarily found in the brain (e.g. germ cells, lymphocytes and embryonic rests) (Figure 1.1).

Incidence and epidemiology

Brain metastases are much more common than primary intracranial tumors. Approximately 170 000 people in the USA are diagnosed with brain metastases every year, while 62 930 are diagnosed with a primary benign or malignant brain tumor. More than 13 000 die each year as a result of a primary malignant brain tumor. In children and in men aged 20–39 years, brain tumors are the second leading cause of cancer-related death in the USA.

Data from several studies suggest an increase in the incidence of both primary brain tumors, particularly primary central nervous system (CNS) lymphoma, and brain metastases since the 1970s. This may be partly due to a true increase in incidence, but it is also a consequence of greater access to and improvements in neuroimaging techniques.

TABLE 1.1

Brain tumor classification by location

Cerebral hemisphere

- Glioma
- Primary central nervous system lymphoma
- Meningioma
- Ependymoma
- Metastases

Intraventricular

- Ependymoma/subependymoma
- Subependymal giant cell astrocytoma (tuberous sclerosis)
- Central neurocytoma
- Colloid cyst of the third ventricle
- Meningioma
- Choroid plexus papilloma/carcinoma

Cerebellum

- Medulloblastoma
- Hemangioblastoma
- Dermoid/epidermoid tumor
- Pilocytic astrocytoma
- Astrocytoma
- Dysplastic gangliocytoma (Lhermitte–Duclos disease)
- Metastases

Cerebellopontine angle

- Vestibular schwannoma
- Meningioma
- Epidermoid tumor
- Choroid plexus papilloma
- Metastases

Sellar region

- Pituitary adenoma
- Germ cell tumor
- Craniopharyngioma
- Meningioma
- Rathke cleft cyst
- Lymphoma
- Metastases

Pineal region

- Pineal parenchymal tumor
- Germ cell tumor
- Meningioma
- Tectal glioma
- Dermoid/epidermoid tumor

Skull base

- Meningioma
- Cranial nerve schwannoma
- Paraganglioma
- Chordoma
- Esthesioneuroblastoma
- Primary sarcoma or carcinoma
- Metastases

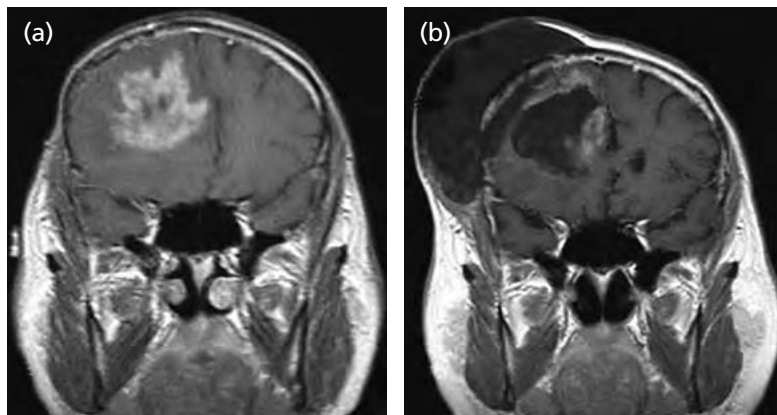


Figure 3.4 (a) T1-weighted magnetic resonance scans with contrast reveal a recurrent right frontal glioma. (b) Following resection, the patient developed a massive subgaleal effusion at the craniotomy site. Decompression was achieved by the insertion of a ventriculoperitoneal shunt.

prophylaxis. Risk factors for postoperative seizures include a history of seizures, surgery adjacent to motor cortex, and postoperative hemorrhage or edema. Although prophylactic anticonvulsants are routinely used in patients undergoing craniotomy for tumor resection, there are no data from randomized trials to support this practice.

Postoperative infections occur in 1–2% of patients undergoing supratentorial craniotomy, and can range from superficial cellulitis to deep infections of bone, surgical cavity and meninges. Most craniotomy infections result from contamination by skin pathogens and the risk can be greatly reduced by use of prophylactic antibiotics.

Systemic complications following craniotomy occur in 5–10% of patients, and commonly include deep venous thrombosis without or with pulmonary embolism, systemic infections, myocardial infarction and electrolyte disturbance. Elderly infirm patients are most susceptible to these morbidities.

Mortality associated with craniotomy for resection of intrinsic brain tumors has declined steadily and is presently in the range 1.7–2.7%. Most deaths occur in the elderly with neurological impairment, and

are usually due to neurological complications such as intracranial hematoma, edema with cerebral herniation, and early tumor progression.

Radiotherapy

Radiotherapy targets actively dividing cells, with tumor cell death being achieved via induction of DNA damage. The goal of radiotherapy is to achieve maximal tumor control while sparing normal structures from the toxicities of irradiation. The efficacy of radiotherapy depends on the delivery of adequate doses of radiation to the target tissue within the brain. The safety of radiotherapy depends on the relative exclusion of normal brain tissues and other critical structures from exposure to ionizing irradiation.

Modern conventional external-beam megavoltage radiotherapy administers irradiation in fractionated doses, thereby allowing normal tissues adequate time to recover from radiation damage. Furthermore, the use of image-guided conformal techniques has enabled radiation oncologists to target the tumor with unprecedented accuracy, so as to minimize the exposure of surrounding normal tissues to ionizing radiation.

Radiotherapy is one of the most effective treatments for brain tumors. It can be curative for some types of brain tumor, such as germinoma, and has a central role in the management of most primary brain tumors, including low-grade and malignant gliomas, where it can reduce the rate of tumor progression and prolong patient survival. Radiotherapy is also the primary palliative modality for the treatment of brain metastases from systemic cancers.

Basic principles. Radiotherapy induces cellular damage by ionizing molecules in DNA, organelles and membranes. The generation of these free radicals can be accentuated by the presence of oxygen, or reversed by naturally occurring free-radical scavengers. The most important cellular target of radiotherapy is DNA, as ionizing irradiation can cause DNA crosslinks and breaks, as well as molecular damage to nucleotides. Although the cell is capable of repairing much of this damage using a variety of ‘housekeeping’