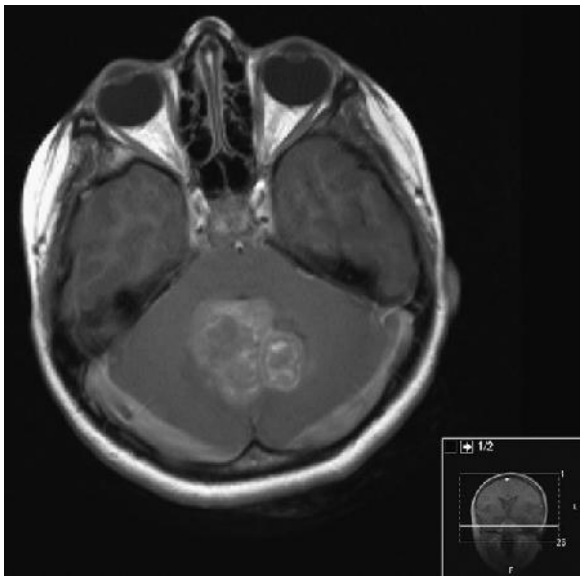

FIGURE 119-3 Contrast-enhanced T1-weighted MRI shows a large enhancing tumor in the midline of the cerebellum with compression of the fourth ventricle.

ventricle location (Fig. 119-3). They are often accompanied by hydrocephalus. The desmoplastic variant of medulloblastomas can be located lateral to the fourth ventricle.

The differential diagnosis of contrast-enhancing lesions includes brain abscess, but infection is a consideration only in rare clinical situations. Diffusion-weighted magnetic resonance images can be useful in distinguishing tumor from infection. Low-grade gliomas can be misdiagnosed as cerebral infarction, especially on brain CT. Periventricular enhancement in PCNSL can sometimes be confused with active multiple sclerosis lesions or with brain metastasis. Dural pathologies such as sarcoidosis, meningeal infection, or dural metastasis can mimic a meningioma. Posterior fossa ependymomas in children can mimic medulloblastomas.

Biopsy or resection is the preferred method to establish the histology and grade of primary brain tumors. Exceptions include PCNSL in which malignant cells are identified in the CSF or by vitreous biopsy to establish the diagnosis, and brainstem gliomas in which the MRI appearance is characteristic and biopsy is considered dangerous.

TREATMENT

Maximal surgical resection is the goal for patients with benign and malignant primary brain tumors with the exception of PCNSL in which clinical deterioration can result from resection, and biopsy alone is recommended for diagnosis. Surgical resection provides tissue for analysis and often relieves neurological symptoms; maximal surgical resection improves outcome. Surgical resection is also indicated in patients with a single brain metastasis and who have limited systemic disease with a prognosis of at least 3 months. Small patient series also indicate that resection of up to three brain metastases can be beneficial in extending overall survival and improving quality of life. More than three metastases are typically treated with radiation therapy without surgery.

Standard therapy for newly diagnosed glioblastoma is maximal resection and external beam radiation of 60Gy over 6 weeks in combination with daily temozolomide followed by temozolomide for 6 months. In a prospective randomized trial of newly diagnosed glioblastoma patients, the median survival with radiation and temozolomide was 14.6 months versus 12.1 months with radiation alone. In addition, the 2-year survival rate was superior with the combined regimen (26.5%) versus radiation alone (10.4%). O-6-methylguanine DNA methyltransferase (MGMT) is a DNA repair gene that reduces the efficacy of temozolomide and other DNA-damaging treatments for cancer. Methylation of the MGMT promoter in tumor tissue silences this gene and results in improved survival in glioblastoma. Determination of the promoter status of MGMT is often obtained as a part of clinical research trials but is rarely used in clinical practice.

The introduction of "targeted agents" that are designed to deactivate oncogenic pathways is a major advance in cancer treatment, including glioblastoma. Bevacizumab, a monoclonal antibody to vascular endothelial growth factor, is associated with a high response rate (6 month progression-free survival of 46%) in recurrent glioblastoma, although the effect on overall survival is not significant. Molecular markers in glioblastoma that are predictive and prognostic of outcome have not yet been identified. There is some evidence that tissues harboring IDH1 mutations are correlated with a superior outcome compared with wild type IDH1. The discovery of molecular "drivers" may lead to identification of targets for therapy.

Anaplastic gliomas are treated by maximal surgical resection, followed by external beam radiation. Despite the overall better prognosis for anaplastic gliomas, chemotherapy is frequently recommended but of uncertain benefit. One anaplastic glioma exquisitely sensitive to chemotherapy is the AO with codeletions of 1p and 19q. Small clinical trials have evaluated the benefit of chemotherapy alone in these patients. Deferring radiation until the time of tumor progression may reduce the CNS toxicity associated with brain radiation.

The long-term progression-free survival and overall survival of low-grade glioma patients is better than those with glioblastoma or anaplastic glioma, but malignant transformation occurs in up to 50% of such patients and close monitoring is required. Patients with low-grade gliomas should be treated initially with surgical resection. Postsurgical management of low-grade gliomas remains controversial, specifically whether radiation should be administered at diagnosis or delayed until the time of progression. The only prospective clinical trial to compare early versus delayed radiation therapy demonstrated that early radiation does not improve survival but does delay the time to tumor progression. In general, radiation therapy is deferred for patients younger than 40 years of age who have undergone complete resection. An ongoing cooperative group trial seeks to determine if temozolomide chemotherapy added to radiation offers a survival advantage over radiation alone.

Maximal surgical resection is important in patients with meningioma to reduce the risk of relapse. When complete removal is not possible, radiation therapy should be considered, depending upon the location of the tumor and regardless of grade. Radiation therapy is recommended regardless of the