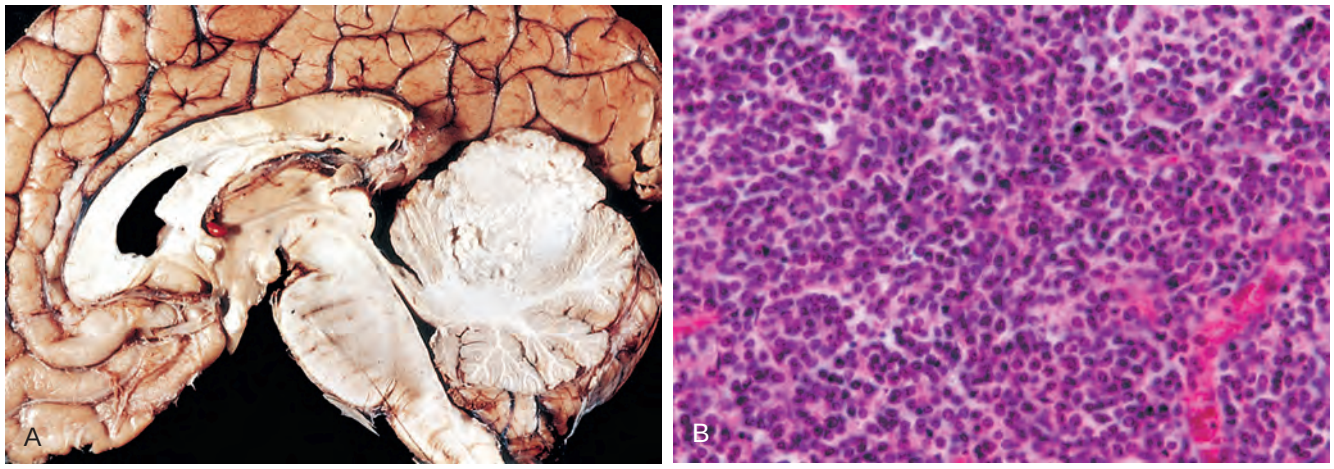

Figure 28-52 Medulloblastoma. **A,** Sagittal section of brain showing medulloblastoma destroying the superior midline cerebellum. **B,** Microscopic appearance of medulloblastoma.

Tumors of similar poorly differentiated histology and resembling medulloblastomas may occur in the cerebral hemispheres. These lesions are known as CNS supratentorial primitive neuroectodermal tumors (CNS PNET). This term unfortunately can lead to confusion with the peripheral lesion (peripheral neuroectodermal tumor), which shares a genetic alteration with Ewing sarcoma. In the CNS, PNET is distinct from medulloblastoma and from the peripheral tumor.

Atypical Teratoid/Rhabdoid Tumor

This highly malignant tumor of young children is a WHO grade IV tumor occurring in the posterior fossa and supratentorial compartments in nearly equal proportions. It is characterized by divergent differentiation with epithelial, mesenchymal, neuronal, and glial components, and often includes rhabdoid cells, resembling those of a rhabdomyosarcoma.

Molecular Genetics. Consistent genetic alterations in chromosome 22 (>90% of cases) are a hallmark of rhabdoid tumor. The relevant gene is *hSNF5/INI1*, which encodes a protein that is part of a large chromatin-remodeling complex; deletions of the locus and loss of nuclear staining for INI1 protein are seen in the majority of tumors.

MORPHOLOGY

Atypical teratoid/rhabdoid tumors tend to be large, with a soft consistency, and spread along the surface of the brain. The rhabdoid cells have eosinophilic cytoplasm, sharp cell borders and eccentrically located nuclei. When these cells are smaller, the cytoplasm can take on an elongated appearance that mimics a rhabdomyosarcoma cell. The cytoplasm of the rhabdoid cell contains intermediate filaments and is immunoreactive for epithelial membrane antigen and vimentin. Some other markers that may be positive include smooth muscle actin and keratins. Other muscle markers such as desmin and myoglobin are not present. Rhabdoid cells are rarely a major component of the tumor; instead, islands of tumor with this pattern of differentiation are mixed with a small-cell component, as well as other histologic patterns (including mesenchymal, epithelial, and neuroglial differentiation). Mitotic activity is extremely prominent.

Clinical Features. These are highly aggressive tumors of the very young. Nearly all tumors occur before the age of 5 and most patients live less than a year after diagnosis.

Other Parenchymal Tumors

Primary CNS Lymphoma

Primary CNS lymphoma accounts for 2% of extranodal lymphomas and 1% of intracranial tumors. It is the most common CNS neoplasm in immunosuppressed individuals, including those with AIDS and immunosuppression after transplantation. In non-immunosuppressed populations, the age spectrum is relatively wide, but the frequency increases after 60 years of age.

The term *primary* emphasizes the distinction between these lesions and secondary involvement of the CNS by lymphoma arising elsewhere in the body (Chapter 13). Primary brain lymphoma is often multifocal within the brain parenchyma, yet involvement outside of the CNS in lymph nodes or bone marrow is a rare and late complication. Conversely, lymphoma arising outside the CNS rarely involves the brain parenchyma; involvement of the nervous system, when it occurs in systemic lymphoma, usually occurs in the setting of significant disease burden outside of the CNS. In this situation, secondary involvement of the CNS is usually manifested by the presence of malignant cells within the CSF and around intradural nerve roots, and occasionally by the infiltration of superficial areas of the cerebrum or spinal cord by malignant cells.

The vast majority of primary brain lymphomas are of B-cell origin. Overall, primary lymphomas of the CNS are aggressive and have worse outcomes than tumors of comparable histology occurring at non-CNS sites. In the setting of immunosuppression, the cells in nearly all primary brain lymphomas are latently infected by Epstein-Barr virus, and in the setting of organ transplantation, may be associated with a systemic post-transplantation lymphoproliferative disorder. When not associated with immunosuppression, these lymphomas show a phenotype typical of postgerminal center B-cell differentiation.