Molecular Genetics. Molecular abnormalities as well as histologic appearance distinguish oligodendrogliomas from astrocytic tumors. The most common genetic alterations in oligodendrogliomas are mutations of the isocitrate dehydrogenase genes (*IDH1* and *IDH2*), which occur in up to 90% of oligodendrogliomas and portend a better prognosis, as they do for astrocytic tumors. Deletions of portions of chromosomes 1p and 19q, typically occurring together as a co-deletion, are seen in up to 80% of cases. Additional genetic alterations occur with progression to anaplastic oligodendroglioma. The more common of these include loss of 9p, loss of 10q, and mutations in *CDKN2A*. In contrast to high-grade astrocytic tumors, *EGFR* gene amplification is not seen, but a significant proportion do show increased EGFR protein levels.

In addition to having implications for the biology of the tumors, the molecular alterations in anaplastic oligodendrogliomas have relevance to the choice of treatment modalities. Tumors with co-deletion of 1p/19q have consistent, long-lasting responses to chemotherapy and radiation, whereas those without loss of 1p or 19q appear to be resistant to chemotherapy regimens.

MORPHOLOGY

Oligodendrogliomas are well circumscribed, gelatinous, gray masses, often with cysts, focal hemorrhage, and calcification. The tumors are composed of sheets of regular cells with spherical nuclei containing finely granular chromatin (similar to normal oligodendrocytes) surrounded by a clear halo of vacuolated cytoplasm (Fig. 28-50). The tumor typically contains a delicate network of anastomosing capillaries. Calcification, present in as many as 90% of these tumors, ranges from microscopic foci to massive depositions. Tumor cells infiltrating the cerebral cortex often collect around neurons (perineuronal satellitosis). Mitotic activity is minimal or absent, and proliferation indices are low. Oligodendrogliomas are considered to be WHO grade II/IV lesions.

Anaplastic oligodendrogliomas (WHO grade III/IV) are characterized by a higher cell density, nuclear anaplasia, detectable mitotic activity, and necrosis. These changes can often be found in nodules within an otherwise typical grade II oligodendroglioma. Some of these high-grade oligodendroglial tumors also show patterns that are indistinguishable from glioblastoma. Because several studies have shown that such appearance correlates with worse behavior, these tumors are grouped with glioblastoma.

Clinical Features. In general, individuals with oligodendrogliomas have a better prognosis than do those with astrocytomas. Current treatment with surgery, chemotherapy, and radiation therapy has yielded an average survival of 5 to 10 years. Individuals with anaplastic oligodendroglioma have an overall worse prognosis. Progression from low to higher grade lesions occurs, typically over about 6 years.

Ependymoma and Related Paraventricular Mass Lesions

Ependymomas are tumors that most often arise next to the ependyma-lined ventricular system, including the oft-obliterated central canal of the spinal cord. In the first two decades of life they typically occur near the fourth ventricle and constitute 5% to 10% of the primary brain tumors in this age group. In adults the spinal cord is the most common location; tumors in this site are particularly frequent in the setting of neurofibromatosis type 2 (NF2).

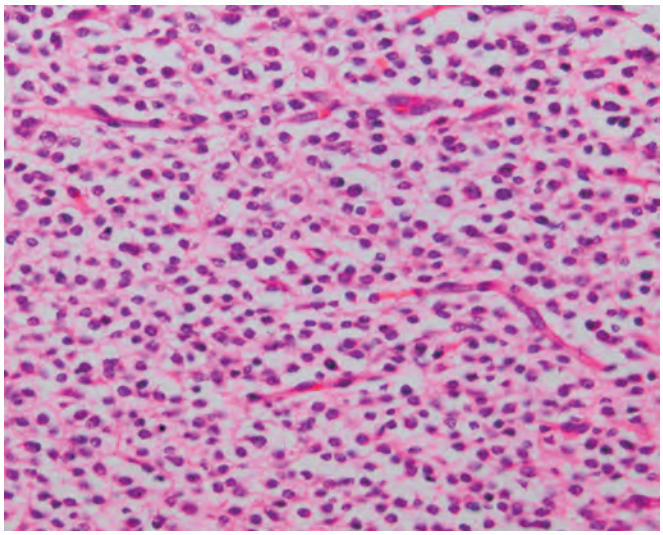

Figure 28-50 Oligodendroglioma. Tumor nuclei are round, with cleared cytoplasm forming "halos" and vasculature composed of thin-walled capillaries.

Molecular Genetics. Given the association of spinal ependymomas with NF2, it is not surprising that the *NF2* gene on chromosome 22 is commonly mutated in ependymomas in the spinal cord but not at other sites. Ependymomas do not share the genetic alterations that are found in infiltrating gliomas, such as mutations in *TP53*. There appear to be at least two separate subtypes, one expressing a mesenchymal phenotype, typically in younger patients with a higher propensity to develop metastases, and a second with aberrations of large regions of chromosomes or whole chromosomes that tends to have a better overall prognosis.

MORPHOLOGY

In the fourth ventricle, ependymomas are typically solid or papillary masses arising from the floor of the ventricle (Fig. 28-51*A*). Although ependymomas are moderately well demarcated from adjacent brain, the proximity of vital pontine and medullary nuclei usually makes complete extirpation impossible. In the intraspinal tumors, the sharp demarcation sometimes makes total removal feasible. Ependymomas are composed of cells with regular, round to oval nuclei and abundant granular chromatin. Between the nuclei there is a variably dense fibrillary background. Tumor cells may form gland-like round or elongated structures (rosettes, canals) that resemble the embryologic ependymal canal, with long, delicate processes extending into a lumen (Fig. 28-51*B*); more frequently present are **perivascular pseudorosettes** (Fig. 28-51*B*), in which tumor cells are arranged around vessels with an intervening zone consisting of thin ependymal processes directed toward the wall of the vessel. GFAP expression is found in most ependymomas. While most ependymomas are well differentiated and behave as WHO grade II/IV lesions, anaplastic ependymomas (WHO grade III/IV) reveal increased cell density, high mitotic rates, areas of necrosis, and less evident ependymal differentiation.