of such patients are alive after 2 years. Survival is substantially shorter in older patients and in patients with lower performance status or with large unresectable lesions. Most of the molecular characteristics of gliomas do not have specific prognostic significance, apart from the beneficial effects of the presence of *IDH1* mutations. Nevertheless, identification of molecular aberrations may provide targets for therapies.

Pilocytic Astrocytoma

Pilocytic astrocytomas (grade I/IV) are distinguished from the other types by their gross and microscopic appearance and relatively benign behavior. They typically occur in children and young adults, and are usually located in the cerebellum but may also appear in the floor and walls of the third ventricle, the optic nerves, and occasionally the cerebral hemispheres. The histologic separation of these tumors from other astrocytomas is supported by the rarity of *TP53* mutations or molecular signatures of infiltrating astrocytomas. Those pilocytic astrocytomas that occur in patients with neurofibromatosis type 1 show functional loss of neurofibromin; this genetic alteration is not observed in sporadic forms. Two types of alterations in the BRAF signaling athway have been found in pilocytic astrocytoma: translocations which serve to separate the kinase domain from the inhibitory domain, and an activating point mutation (V600E) that is also found in an increasing number of other tumor types (Chapter 7). These findings suggest that targeted therapy with BRAF inhibitors might play a role in the treatment of pilocytic astrocytomas, particularly for lesions in regions not suitable for resection.

MORPHOLOGY

Pilocytic astrocytoma is often cystic (Fig. 28-49); if solid, it may be well circumscribed or, less frequently, infiltrative. The tumor is composed of bipolar cells with long, thin "hairlike" processes that are GFAP-positive and form dense fibrillary meshworks; Rosenthal fibers and eosinophilic granular bodies, are characteristic findings. Tumors are often biphasic, with both loose "microcystic" and fibrillary areas. An increase in the number of blood vessels, often with thickened walls or vascular cell proliferation, is seen but does not imply an unfavorable prognosis. Necrosis and brisk mitotic activity is uncommon. Unlike diffuse fibrillary astrocytomas of any grade, pilocytic astrocytomas show limited infiltration of the surrounding brain.

These tumors grow very slowly, and, in the cerebellum particularly, may be treated by resection. Symptomatic recurrence of incompletely resected lesions is often associated with cyst enlargement rather than growth of the solid component. Tumors that extend into the hypothalamic region from the optic tract can have a more ominous clinical course because of their location.

Pleomorphic Xanthoastrocytoma

This tumor occurs most often in the temporal lobe in children and young adults, usually with a history of seizures. The tumor consists of neoplastic, occasionally bizarre, astrocytes, which are sometimes filled with lipids; these cells can express neuronal and glial markers. The degree of nuclear atypia can be extreme and may suggest a high-grade astrocytoma, but the presence of abundant reticulin deposits, relative circumscription, and chronic inflammatory cell infiltrates, along with the absence of necrosis and mitotic activity, distinguish this tumor from more malignant types. The pleomorphic xanthoastrocytoma is usually a low-grade tumor (WHO grade II/IV) with a 5-year survival rate estimated at 80%. Necrosis and mitotic activity are indicative of higher grade tumors and predict a more aggressive course.

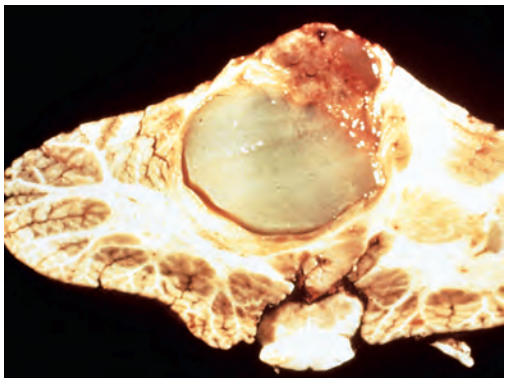

Figure 28-49 Pilocytic astrocytoma in the cerebellum with a nodule of tumor in a cyst.

Brainstem Glioma

A clinical subgroup of astrocytomas, brainstem gliomas, occur most often in the first 2 decades of life and make up 10% to 20% of all brain tumors in this age group. Several distinct anatomic patterns have been defined in the pediatric age group, each differing in clinical course: intrinsic pontine gliomas (the most common), with an aggressive course and short survival; cervicomedullary junction tumors, often exophytic, with a less aggressive course; and dorsally exophytic gliomas, with an even more benign course which may arise in the tectum of the midbrain, pons, or medulla. Among the rarer brainstem gliomas affecting adults, most are intrinsic pontine gliomas. These can be separated into low-grade diffuse fibrillary astrocytomas and glioblastoma, with the expected differences in clinical course and survival.

The concept that these are a distinct type of glioma is supported by sequencing the genomes of childhood pontine gliomas. Surprisingly, this has revealed that most tumors of this type have a lysine to methionine mutation at position 27 (K27M) in histone H3.1 or H3.3. Of note, H3K27 is a position that is subject to acetylation and methylation events that regulate chromatin structure and gene expression, yet another example of oncogenic mutations that directly impact the epigenome.

Oligodendroglioma

These are infiltrating gliomas comprised of cells that resemble oligodendrocytes. These tumors constitute 5% to 15% of gliomas and are most common in the fourth and fifth decades. Patients may have had several years of neurologic complaints, often including seizures. The lesions are found mostly in the cerebral hemispheres, with a predilection for white matter.

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