2 Pathology of CNS Tumors

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2.1 Introduction

The incidence of CNS tumors is 7–10 per 100,000 (Parkin and Muir 1992). These include parenchymal tumors as well as other non-CNS intracranial lesions like meningioma. CNS tumors can be organized according to the cell of origin, location, or behavior. Consideration of metastatic lesions provides an additional criterion for organization into primary and secondary lesions. Most presentations and classifications are based on the cell of origin, including the recent classification protocols established by the World Health Organization (WHO) (Kleihues et al. 1993; Burger 1995). The bulk of this chapter is organized according to the cell of origin. The cell of origin is not known for all CNS tumors. The identity of the hemangioblastoma stromal cell, for example, is not known. The bulk of the mature central nervous system cellular population consists of neurons, astrocytes, oligodendrocytes, and ependymal cells. These are all derivatives of the primitive embryonal neuroectoderm. The most common intraparenchymal neoplasms arise from the astrocyte and will be discussed first.

2.2 Astrocytic Neoplasms

The astrocyte is a glial derivative of the neuroectoderm. Its functions include supportive, reactive, and metabolic activity. The astrocyte provides support for other cells in the CNS and can react during injury by providing an intertwining meshwork of long cytoplasmic processes, a procedure known as gliosis. This characteristic gives the astrocyte a star-like appearance, resulting in its name. The astrocyte is also thought to play an important role in microenvironment potassium levels (Paulson et al. 1987), neurotransmitter uptake (Norenberg and Martinez-Hernandez 1979), and ion exchange (Langley 1990). It may also play an important role in blood–brain barrier formation (Abbott et al. 1992). Neoplastic transformation of an astrocyte results in the formation of an astrocytoma. Astrocytomas occur throughout the CNS and are associated with a progressive spectrum of biological activity and aggressiveness. This spectrum has been dealt with in a number of ways. A four-tiered grading protocol has become standard although other grading systems still exist (Coons and Johnson 1991; Daumas-Duport et al. 1988). The grade I astrocytoma refers to a benign astrocytic neoplasm that does not show significant pleomorphism, mitotic activity, endothelial proliferation, or necrosis. From a behavioral perspective, a grade I astrocytoma should not recur if completely resected and implies a corresponding
lack of tumor infiltration. The grade II, III, and IV astrocytomas are more infiltrative and will show varying combinations of pleomorphism, mitotic activity, endothelial proliferation, and necrosis. Beginning with a baseline grade of I, one additional grading unit is added for the presence of each additional criterion. For example, an astrocytoma (one point) demonstrating pleomorphism (second point) and mitotic activity (third point) is considered to be grade III. This grading system roughly corresponds to the older three-tiered nomenclature of “low grade astrocytoma”, “anaplastic astrocytoma”, and “glioblastoma multiforme”. In most cases these correspond to astrocytoma grades II, III, and IV, respectively. Small sample sizes such as those provided during stereotactic biopsy can provide significant problematic sampling error and result in undergrading. Effective communication between the surgeon, radiologist, and pathologist is important in providing a diagnosis in problematic cases.

The grade II or low-grade astrocytoma is very infiltrative as seen by the lack of grossly identifiable margins. This tumor is typically solid although degeneration can result in cyst formation. The consistency and color will vary. The microscopic features can be subtle with cellularity only minimally above that seen in the normal brain (Fig. 2.1). The pleomorphism may also overlap that seen in reactive gliosis, the nemesis of the surgical neuropathologist. Intraoperative cytologic preparations yield a mild to moderately dense population of neoplastic astrocytes with prominent but delicate cytoplasmic processes. Reactive gliosis around a high-grade lesion can mimic the histology of a low-grade astrocytoma. Non-neoplastic gliotic processes can be similarly misdiagnosed. Helpful criteria seen in paraffin sections include microcystic change, irregular cell distribution, perineuronal satellitosis, and linear filling. Some low-grade astrocytomas show more extensive pleomorphism and are easier to diagnose (Fig. 2.2A). A moderate degree of variation in nuclear size and shape is a welcome feature.

An immunohistochemical stain for the glial-fibrillary acidic protein (GFAP), an intermediate filament protein specific for astrocytes, delineates the cytoplasm of both neoplastic and non-neoplastic astrocytes. The presence of reactivity within the cytoplasm of tumor cells confirms the astrocytic nature of the lesion. Immunostains specific for the proliferation associated antigen Ki-67 (MIB-1) can be helpful in distinguishing between a low-grade astrocytoma and reactive gliosis. It can also be helpful in determining whether a higher-grade lesion is present in a small biopsy specimen with prominent pleomorphism but no additional grading criteria (Hsa et al. 1997). Some grade II astrocytomas contain sufficient components of other glial elements (Cooper 1935; Hart 1974) and justify a diagnosis of mixed glioma. The oligoastrocytoma is a common example. The use of this mixed terminology should only be reserved for clear examples of mixed lesions. A long survival is possible if a low-grade astrocytoma retains its low grade. They can, however, undergo malignant transformation and become a more aggressive higher-grade lesion.

The grade III astrocytoma is usually analogous to an anaplastic astrocytoma. The cerebral hemispheres are the usual site of occurrence. The gross appearance is soft and it shows moderate delineation.