

# Frozen Section Discrepancy in the Evaluation of Central Nervous System Tumors

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● **Context.**—Frozen section (FS) evaluation of central nervous system (CNS) lesions provides an assessment of specimen adequacy and facilitates triage for ancillary studies. Frozen section also provides an accurate preliminary diagnosis; however, certain lesions are recognized to cause diagnostic challenges at FS.

**Objective.**—To identify cases in which there was a discrepancy between the FS diagnosis and final diagnosis in the case to heighten awareness of common diagnostic pitfalls in surgical neuropathology.

**Design.**—All CNS FS cases involving a tumor diagnosis at FS or permanent section (N = 2156) from September 1997 until June 2005 were retrospectively reviewed. Discrepancies between the FS and final diagnoses were identified.

**Results.**—Of the 2156 cases identified, 57 (2.7%) discrepant diagnoses were found. Twelve (21.1%) of 57 discrepancies involved errors in classification of spindle cell lesions, most commonly confusing schwannomas or me-

ningiomas with other lesions. Twelve (21.1%) of 57 cases involved errors in differentiating oligodendrogliomas from astrocytomas. Nine (15.8%) of 57 discrepancies involved errors in the diagnosis of CNS lymphoma. Eight (14.0%) of 57 cases involved errors in differentiating reactive from neoplastic processes, most frequently gliosis versus glioma. Four (7.0%) of 57 discrepancies involved errors in the overgrading of tumors. The remaining 12 (21.1%) of 57 cases included an assortment of other discrepancies.

**Conclusions.**—Frozen section of CNS neoplastic processes can be highly accurate. Less than 3% of FS diagnoses in 1 institution's experience were discrepant with the final diagnoses. Approximately 80% of the discrepant cases were classified into 5 categories: spindle cell lesions, astrocytoma versus oligodendroglioma, differential diagnosis of CNS lymphoma, reactive versus neoplastic process, and tumor overgrading. Awareness of these pitfalls may help in further increasing diagnostic accuracy.

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In the setting of stereotactic biopsies, the primary goal of frozen section (FS) evaluation of a suspected central nervous system (CNS) neoplasm is to evaluate the submitted tissue for adequacy.<sup>1,2</sup> An adequate sample best equips the pathologist to provide an accurate final diagnosis of the sampled lesion. The rapid diagnostic evaluation at FS may guide intraoperative management, which may be particularly important during open craniotomy.<sup>1,2</sup> In addition, FS allows for the appropriate triage of tissue for ancillary studies such as electron microscopy, microbiologic cultures, and frozen tissue storage.<sup>1–6</sup> The role of the neuropathologist in interpreting CNS FS is to assist the neurosurgeon, along with clinicoradiologic correlation, in making the most accurate judgment regarding the nature of the CNS lesion in addition to determining the adequacy of the submitted tissue for diagnosis.<sup>1,2</sup>

Studies have reported the diagnostic accuracy of CNS intraoperative consultation to be generally greater than 85% to 90%.<sup>1,5,7,8–12</sup> Conversely, few studies have attempted

to systematically address the diagnostic inaccuracies of CNS intraoperative consultation. One such study retrospectively examined more than 4100 cases for the accuracy of cytologic preparations at intraoperative consultation and found that, in decreasing order, ependymomas, glioblastomas, metastatic carcinomas, oligodendrogliomas, meningiomas, and astrocytomas were the most frequently misdiagnosed lesions.<sup>10</sup> They noted a 95% accuracy rate in diagnosis (excluding grading deviations).<sup>10</sup> To our knowledge, no study of similar magnitude has examined misdiagnosed cases encountered in the setting of FS. This study sought to identify some of those difficult cases to heighten awareness of common diagnostic pitfalls in the assessment of CNS FS neoplastic lesions.

## MATERIALS AND METHODS

After receiving institutional review board approval, a computer search was performed to identify all CNS FS cases from September 1997 until June 2005 with a tumor diagnosis on FS or final diagnosis (N = 2156). The FS diagnoses were compared with the final diagnoses as indicated on the pathology report, and discrepancies between the diagnoses were identified: confusing benign with malignant processes (and vice versa), misclassifying 2 different neoplastic conditions, and overgrading. Differences between FS or final diagnoses because of possible sampling error (ie, undergrading of tumors or composite tumors such as oligoastrocytoma in which only 1 component may have been sampled) were not considered discrepant as long as the general tumor cell type was consistent between FS and final diagnosis. A group of blindly selected, nondiscrepant cases was

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Category	No.	M/F	Mean Age, y	Mean No. of FS Slides*	Mean No. of Permanent Sections
Discrepant	57	29/28	46.6	1.39	2.16
Nondiscrepant	109	57/52	48.1	1.39	2.45

\* FS indicates frozen section.

used to compare the mean numbers of frozen and permanent sections in each group. The majority of the FS diagnoses were rendered by 1 of 3 staff neuropathologists, as were all of the final diagnoses. Three of the discrepant cases were reviewed by a general pathologist at the time of FS.

## RESULTS

Of the 2156 cases identified, 57 (2.7%) discrepant diagnoses were identified. The mean age of the patients in the discrepant diagnosis group (29 males, 28 females) was 46.6 years (range, 5–83 years). Within the randomly selected nondiscrepant cases (n = 109), the mean age (48.1 years; range, 5–81 years) and gender distribution (57 males, 52 females) did not differ significantly from the discrepant group, nor did the mean number of FS or permanent sections examined (Table 1).

Review of the discrepant cases revealed 5 general categories of discrepancies (Tables 2 and 3). Twelve (21.1%) discrepancies involved errors in classification of spindle cell lesions of the CNS (Figure 1, A through D; Figure 2, A through D), most commonly confusing schwannomas and meningiomas with each other and with other lesions. Twelve (21.1%) cases involved errors in differentiating oligodendroglioma from astrocytoma (Figure 3, A through D). Nine (15.8%) discrepancies involved errors in the diagnosis of CNS lymphoma (Figure 4, A through F). Eight (14.0%) cases involved errors in differentiating reactive from neoplastic processes, most frequently gliosis versus low-grade glioma (Figure 5, A through D). Four (7.0%) discrepancies involved errors in the overgrading of tumors. The remaining 12 (21.1%) cases included an assortment of other discrepancies (Figure 6, A and B). The discrepancies did not significantly impact patient management in any of the cases because postoperative management was predicated on the final diagnosis.

## COMMENT

It is well recognized that discrepancies can occur at intraoperative consultation because of sampling error, incorrect assignment of tumor grade, or error in recognition of the histologic cell type.<sup>13</sup> Inaccuracies because of sampling error are an unavoidable trade-off in satisfying the surgeon's need for a rapid intraoperative consultation; most gliomas are morphologically heterogeneous and

therefore sampling dependent. Only overgrading or misdiagnosis of tumors can be realistically improved on. Recent studies<sup>9,11</sup> have advocated the addition of cytologic touch imprints or smear preparations to traditional FS to improve diagnostic accuracy of CNS lesions in some instances. Cytology can be particularly helpful in situations in which the quality of FS is suboptimal because of freezing artifact or simply the soft and edematous nature of neurosurgical specimens. Cytology preparations are much simpler and quicker to generate, have smaller tissue requirements than FS, and can provide improved cellular details, all of which may be especially valuable in cases of stereotactic biopsies.<sup>13,14</sup> Frozen section proponents cite an increased diagnostic accuracy because of a similarity to permanent sections and preservation of tissue architecture.<sup>10</sup> The literature is mixed with respect to the single most useful method, and in reality, they are complementary procedures. Some studies<sup>15,16</sup> suggest that FS is more accurate, whereas more recent studies<sup>5,10</sup> suggest cytologic preparations are at least as accurate as FS. Regardless of which approach one decides to use, knowledge of pertinent clinical and radiologic information at the time of intraoperative consultation are critical in arriving at an accurate diagnosis.<sup>13,17</sup> This underscores the importance of communication with the neurosurgeon at the time of surgery in ensuring that adequate and representative tissue has been sampled. Given the practice of neuropathology intraoperative consultation at the institution in which the study was performed and the good quality of FS slides, FS was the sole means of evaluation used in the majority of cases in this study.

Despite the validated accuracy of intraoperative consultation for CNS lesions, several pitfalls are well recognized. Roessler et al<sup>10</sup> retrospectively reviewed more than 4100 cases and found that, in decreasing order, ependymomas, glioblastomas, metastatic carcinomas, oligodendrogliomas, meningiomas, and astrocytomas were the most frequently misdiagnosed lesions with the use of cytologic preparations. A French study<sup>12</sup> of 1315 FS cases found concordance between intraoperative and permanent diagnoses to be 96.6% in classifying lesions as neoplastic or nonneoplastic, 92.6% for tumor malignancy or benignity, and 87.6% for exact histologic concordance. The authors found the most frequent errors in histologic typing involved gliomas, hemangioblastomas, and metastases. Oneson et al<sup>3</sup> reported their study of 1000 consecutive intraoperative consultation cases, of which 91 cases were from the central or peripheral nervous system. They found 13 diagnostic errors at intraoperative consultation, 11 of which were deferred to permanent section without a specific diagnosis rendered. Although not enumerated, the most common diagnostic difficulty was in differentiating low-grade glioma from gliosis. Another discrepant case

Category	No.	M/F	Mean Age, y	Most Common Discrepancy
Spindle cell lesion	12	5/7	52.5	Meningioma vs other spindle cell lesion
Astrocytoma vs oligodendroglioma	12	7/5	44.9	Not applicable
Lymphoma	9	5/4	58.9	Glioma vs lymphoma
Reactive vs neoplastic	8	4/4	40.6	Gliosis vs glioma
Tumor overgrading	4	2/2	44.0	Gliomas
Miscellaneous	12	6/6	38.0	
<b>Total</b>	<b>57</b>	<b>29/28</b>	<b>46.6</b>	

**Table 3. Summary of Discrepant Diagnoses**

Frozen Diagnosis	Permanent Diagnosis	No. of Cases
Spindle cell lesions		
Meningioma	Schwannoma	3
Meningioma	Sarcoma	2
Neurofibroma	Schwannoma	1
Low-grade glioma	Schwannoma	1
Schwannoma	Hemangioma	1
Meningioma	Hemangioblastoma	1
Schwannoma	Sarcoma	1
Benign spindle cell proliferation	Choristoma	1
Meningioma	Paranglioma	1
Astrocytoma vs oligodendroglioma		
Low-grade astrocytoma	Low-grade oligodendroglioma	9
High-grade astrocytoma	High-grade oligodendroglioma	3
Reactive vs neoplastic		
Low-grade glioma	Gliosis	4
Necrotic tumor	Fibrin and hemosiderin	1
Vascular malformation	Gliosis	1
Radiation gliosis	Recurrent glioma	1
Low-grade neuroectodermal neoplasm	Choroid plexus and cerebellum	1
CNS lymphoma*		
Astrocytoma	Diffuse large B-cell lymphoma	3
Lymphoma	Primitive neuroectodermal tumor	1
Lymphoma	Oligodendroglioma	1
Progressive multifocal leukoencephalopathy	Diffuse large B-cell lymphoma	1
Lymphoma	Reactive astrocytes and chronic inflammation	1
Lymphoma	Glioblastoma	1
Chronic inflammation and astrocytosis	Diffuse large B-cell lymphoma	1
Tumor overgrading		
High-grade glioma	Low-grade glioma	2
High-grade glioma	Cellular ependymoma	1
Chordoid meningioma	Microcystic meningioma	1
Miscellaneous		
Pilocytic astrocytoma	Ganglioglioma	2
Glioblastoma	Metastatic carcinoma	1
Epidermoid cyst	Craniopharyngioma	1
Ependymoma	Medulloblastoma	1
Metastatic carcinoma	Metastatic melanoma	1
Low-grade glioma	Epidermoid cyst	1
Ependymoma	Subependymoma	1
Myxopapillary ependymoma	Paranglioma	1
Dysembryoplastic neuroepithelial tumor	Ganglioglioma	1
Pleomorphic xanthoastrocytoma	Low-grade neoplasm	1
Benign vessels with calcification	Pituitary adenoma with prominent vascularity	1

\* CNS indicates central nervous system.

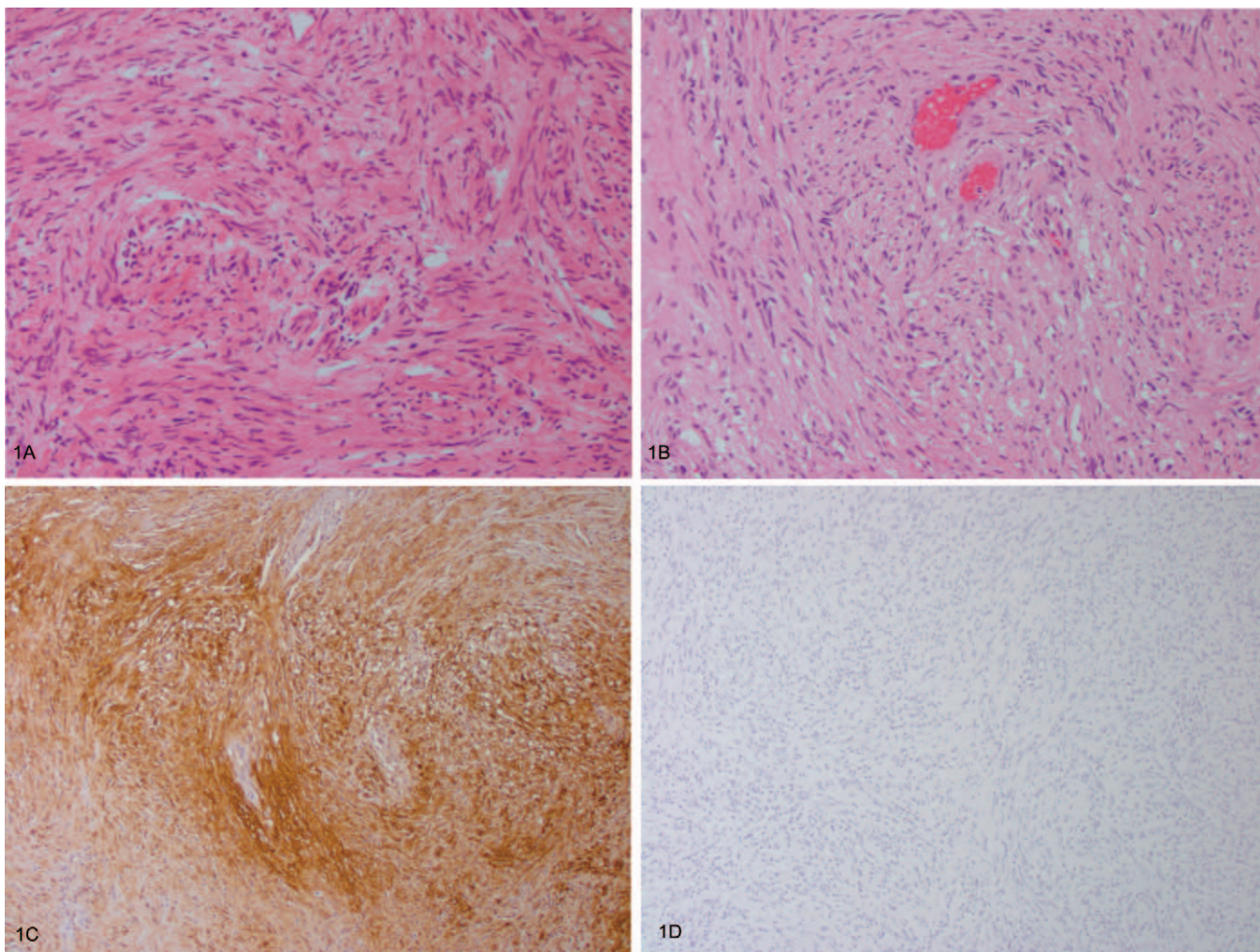
was clearly due to sampling error with only necrotic tissue from a glioblastoma seen at frozen intraoperative consultation. Our study took a different approach by examining only rendered diagnoses at intraoperative consultation and eliminating those cases that were discrepant chiefly because of sampling error. Because of the design of the study, interobserver variability may account for some of the discrepancies observed. However, certain common problematic categories emerged and are discussed in the following.

Five general categories of discrepant diagnoses (accounting for nearly 80% of discrepant cases) emerged on review of the 57 discrepant cases in our current series of 2156 FS cases: spindle cell lesions (most commonly involving schwannoma or meningioma), astrocytoma versus oligodendroglioma, differential diagnosis of lymphoma, reactive versus neoplastic processes, and tumor overgrading. The following is intended as a practical review of the salient points helpful in discriminating some of the more

common difficult differential diagnoses encountered at intraoperative consultation of CNS lesions.

### Spindle Cell Lesions

Distinguishing meningiomas, peripheral nerve sheath tumors, and other spindled cell proliferations can be challenging at FS, particularly with limited submitted tissue or tissue distorted by crush artifact or cautery. Both meningiomas and schwannomas commonly arise in the cerebellopontine angle region and can show a predominantly benign, spindled cell appearance, thick-walled vessels, abundant collagen, and perivascular whorling. Although degenerative atypia ("ancient" change) is classically characteristic of schwannomas, meningiomas can demonstrate prominent nuclear pleomorphism at times. In addition, some meningiomas lack whorling, psammoma bodies, or cytoplasmic protrusions,<sup>14,18</sup> features that are typically used in making the diagnosis. In most instances, the neurosurgeon, based on imaging studies and intraoperative



**Figure 1.** A 58-year-old woman with an intradural extramedullary tumor of the lumbar spine. A, Frozen section demonstrates bland spindle cells arranged in a storiform pattern, diagnosed as meningioma (hematoxylin-eosin, original magnification  $\times 200$ ). B, Paraffin-embedded sections reveal areas of variable cellularity and wavy nuclei with pointed ends (hematoxylin-eosin, original magnification  $\times 200$ ). C, An S100 protein immunostain reveals diffuse positivity as well as hypercellular and hypocellular zones. The final diagnosis was schwannoma (immunoperoxidase, original magnification  $\times 100$ ). D, Epithelial membrane antigen immunostain (positive in many meningiomas) is negative (immunoperoxidase, original magnification  $\times 100$ ).

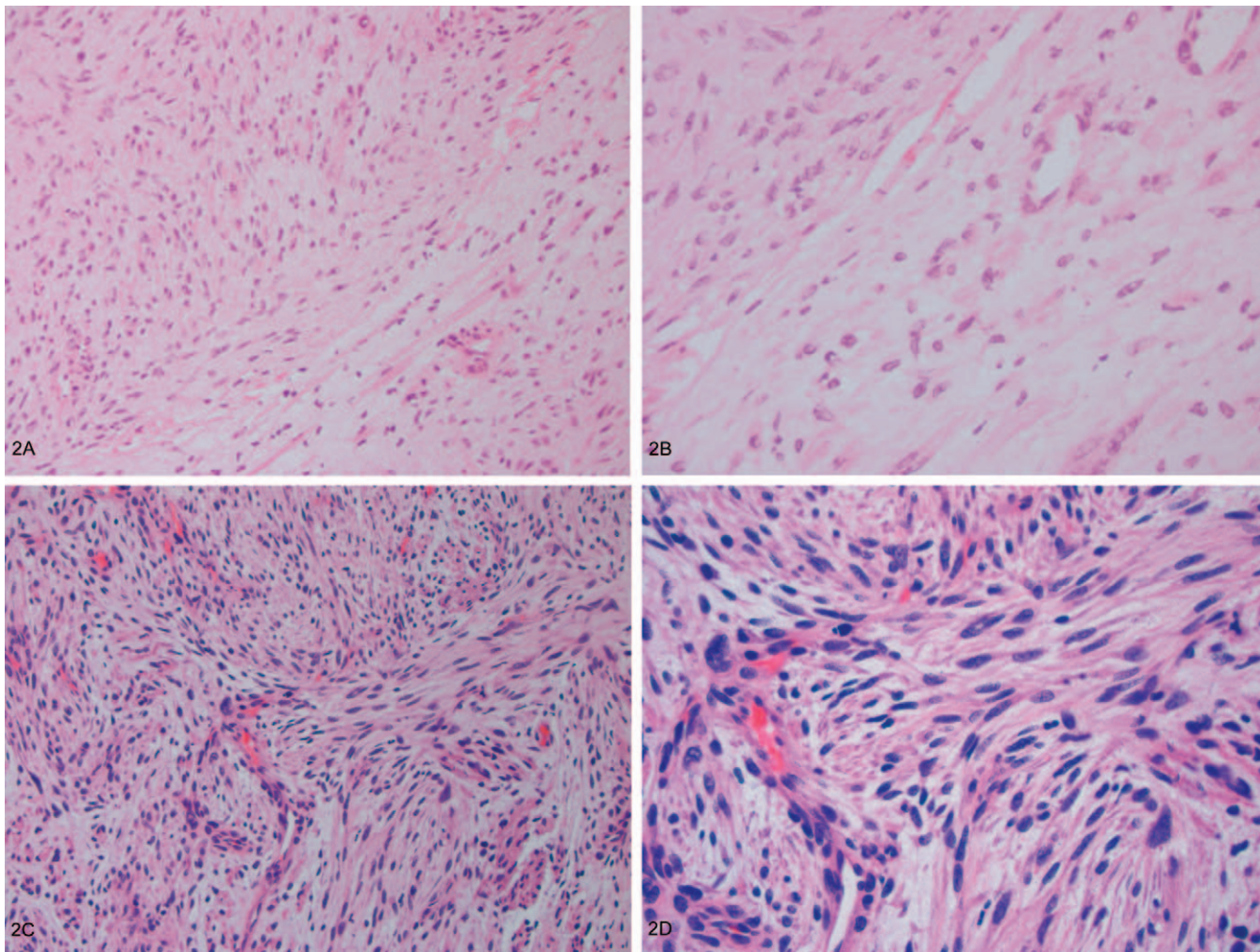
appearance, has a good idea which entity he or she is dealing with. Useful histologic clues suggesting schwannoma are perivascular hemosiderin deposition, mixtures of loose (Antoni B) and compact (Antoni A) patterns, and Verocay bodies. Cytologically, schwannoma nuclei are wavy with pointed ends. In contrast, meningiomas can have foci of more epithelioid syncytia, psammoma bodies, and uniform nuclei with blunted ends and intranuclear pseudoinclusions or cytoplasmic invaginations.<sup>14,18,19</sup> On occasion, the classic biphasic appearance of a schwannoma may not be evident in the sampled tissue. Freeze artifact can also induce changes in meningiomas that can mimic the Antoni B pattern of a schwannoma. In those instances in which the distinction cannot be made based on histology at FS with certainty, rather than overinterpreting and succumbing to pressures of providing a diagnosis, a diagnosis of benign spindled cell tumor with a suggestion of what the differential diagnosis may include is reasonable.

This category of discrepancies also included the final diagnoses of 3 sarcomas that had been diagnosed as be-

nign schwannoma or meningioma at FS. In all 3 instances, potentially useful clinical information (ie, history of prior radiation) was not provided or misinterpretation of imaging findings (favoring benign meningioma) may have led the pathologist astray at FS. In general, sarcomas are more uniformly cellular than most World Health Organization grade I meningiomas or schwannomas, although cellularity in a poorly cut FS slide may be difficult to assess, and occasional schwannomas and meningiomas with a fibroblastic pattern may be quite cellular. More reliable features for distinction include atypia, which is usually more uniformly widespread, more commonly encountered mitotic figures, and necrosis. Hemangiopericytoma, perhaps the most common primary CNS sarcoma, is also marked by a staghorn vascular pattern.

#### Astrocytoma Versus Oligodendroglioma

Differentiating a low-grade astrocytoma from a low-grade oligodendroglioma at FS is usually not critically important and has even been labeled as "adventuresome."<sup>14</sup> Because of potential treatment differences and prognosis,



**Figure 2.** A 77-year-old man with fifth cranial nerve mass, with a history of prior radiation for oral carcinoma. A and B, Frozen sections reveal spindle cells with minimal atypia and no mitotic activity, diagnosed as schwannoma (hematoxylin-eosin, original magnifications  $\times 200$  [A] and  $\times 400$  [B]). C and D, Paraffin-embedded sections demonstrate significant hypercellularity and atypia. The final diagnosis was sarcoma (hematoxylin-eosin, original magnifications  $\times 200$  [C] and  $\times 400$  [D]).

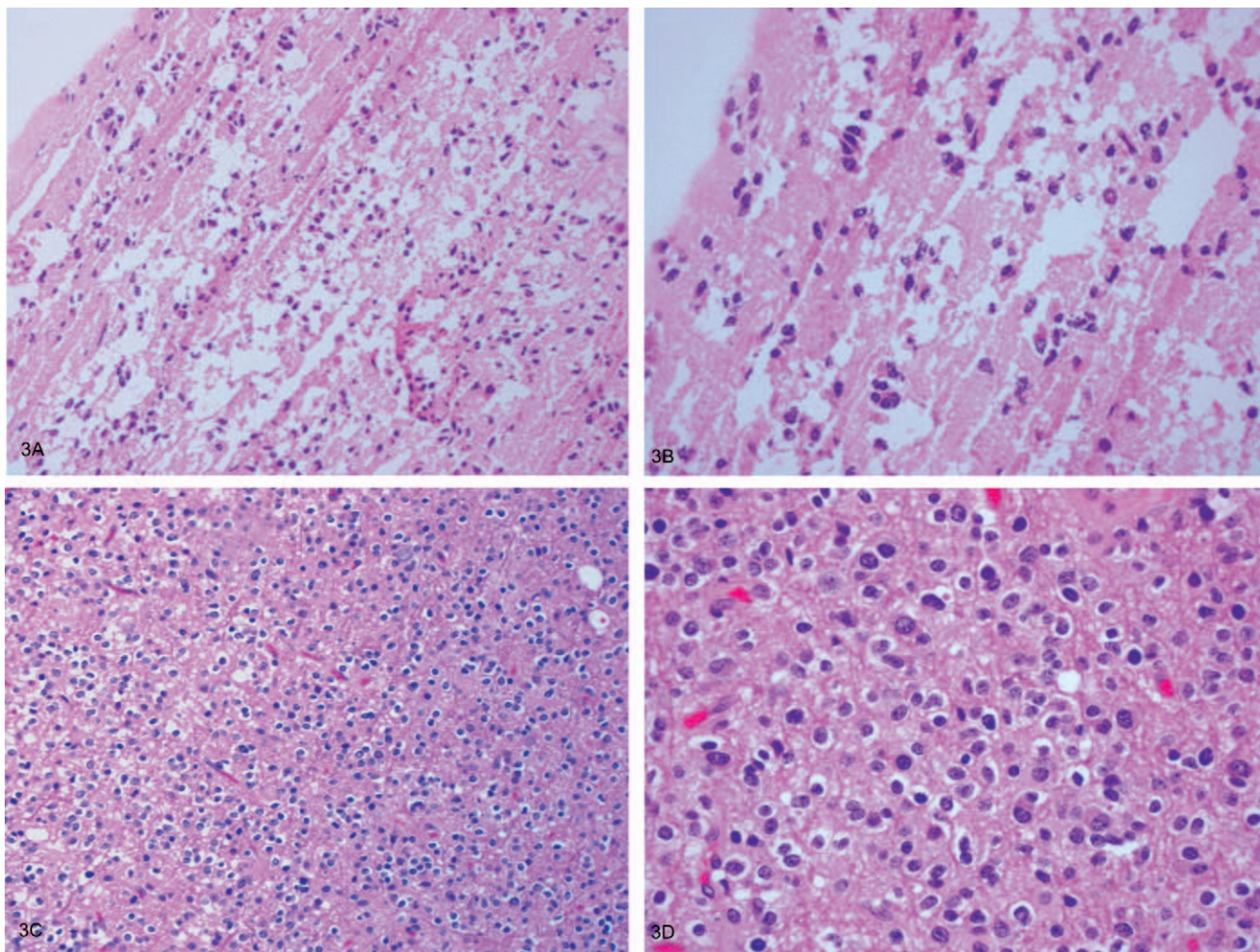
eventual distinction with permanent sections is more critical. As long as treatment will not be predicated on the FS assessment, the distinction between the 2 tumor types is not critical at FS. A diagnosis of "glioma" along with indication of the differential diagnosis and some indication of grade is usually adequate at FS. There are some differences regarding grading thresholds between the 2 glioma types that might present a challenge if one is not sure of the tumor lineage. In most instances, stratification into "low grade" (World Health Organization grade II) versus "high grade" (World Health Organization grade III or IV) is sufficient at FS.

Histologically, oligodendrogliomas tend to be more cellular and less pleomorphic than astrocytomas. Oligodendroglial tumor nuclei appear round and uniformly hyperchromatic; however, freezing tissue often produces irregularities in the nuclear contours of an oligodendroglioma, making it look similar to an astrocytoma.<sup>14</sup> Cytologic preparations can be helpful in circumventing these processing-related changes, providing a rapid method of demonstrating the relative uniformity of oligodendroglial tumor cells. Although not at all specific, other helpful features more commonly observed in oligodendroglioma in-

clude calcifications; frequent presence of perivascular, perineuronal, and subpial aggregates of tumor cells; and "germinal-like" nodules of hypercellularity. As is widely known, the characteristic perinuclear halos are an artifact of formalin fixation and will not be evident at FS.<sup>6,14</sup>

### CNS Lymphoma

The difficulty in the differential diagnosis of CNS lymphoma often arises in cases in which the tissue sample is limited, in pretreated lesions, and in cases with an atypical radiologic imaging study. Histologically, diagnostic challenges often arise when an infiltrative pattern is seen with the presence of reactive astrocytes in the background, suggesting a glial tumor. Cytologic preparations are often superior to FS in demonstrating the predominance of large, discohesive cells with relatively abundant cytoplasm and prominent nucleoli, typical of diffuse large B-cell lymphoma, which accounts for most cases.<sup>6</sup> Classic lymphoma nuclei are round or notched and vesicular with prominent nucleoli. A histologic hallmark is angiocentricity with angioinvasion; however, this feature may resemble "secondary structures of Scherer," seen in cortical involvement by a glioma. Perineuronal satellitosis is not observed in CNS



**Figure 3.** A 52-year-old man with recent-onset grand mal seizures and left frontal lobe mass. A and B, Frozen sections reveal hypercellular white matter with irregular, hyperchromatic glial cells, diagnosed as low-grade astrocytoma (hematoxylin-eosin, original magnifications  $\times 200$  [A] and  $\times 400$  [B]). C and D, Paraffin-embedded sections show hypercellular white matter with relatively uniform, hyperchromatic cells and characteristic artifactual perinuclear halos. The final diagnosis was low-grade oligodendroglioma (hematoxylin-eosin, original magnifications  $\times 200$  [C] and  $\times 400$  [D]).

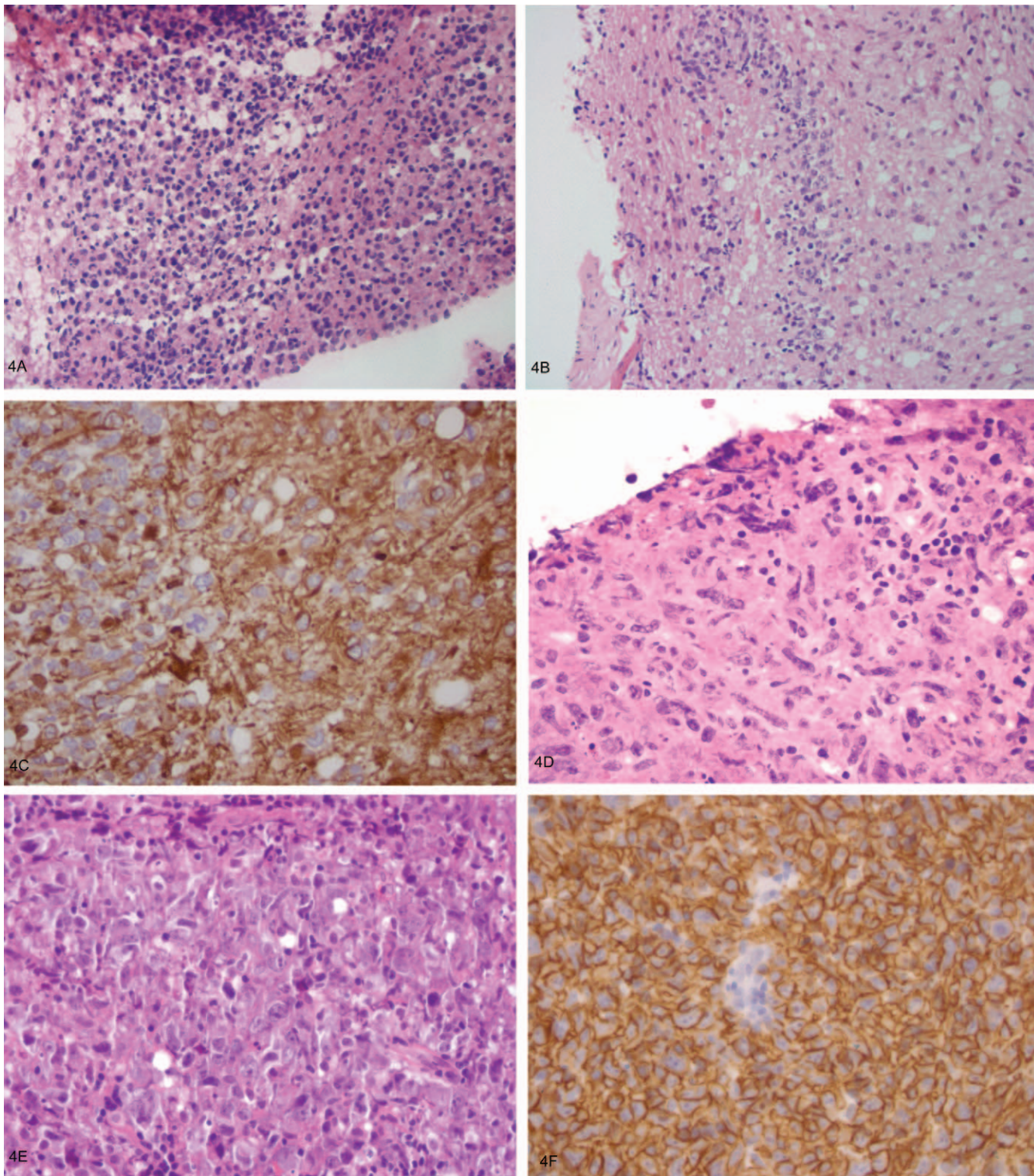
lymphoma. The angiocentric pattern may not be appreciable on a limited biopsy or in cases in which the tumor growth is confluent. Lymphomas are particularly sensitive to steroids and will undergo marked necrosis with treatment, making diagnosis potentially challenging. Tumors with large numbers of benign tumor-infiltrating lymphocytes may resemble a benign inflammatory process such as vasculitis, infection, or demyelinating disease. In the absence of these characteristic features, it may be quite difficult to distinguish a malignant lymphocytic infiltrate from a high-grade glioma (anaplastic oligodendroglioma or small cell glioblastoma) at FS.

The glioma versus lymphoma differential at FS can have significant treatment implications. Central nervous system lymphoma is not usually resected; a biopsy diagnosis will abort the surgery. High-grade gliomas may be the target of a gross total resection or intracavity radiation.<sup>11</sup>

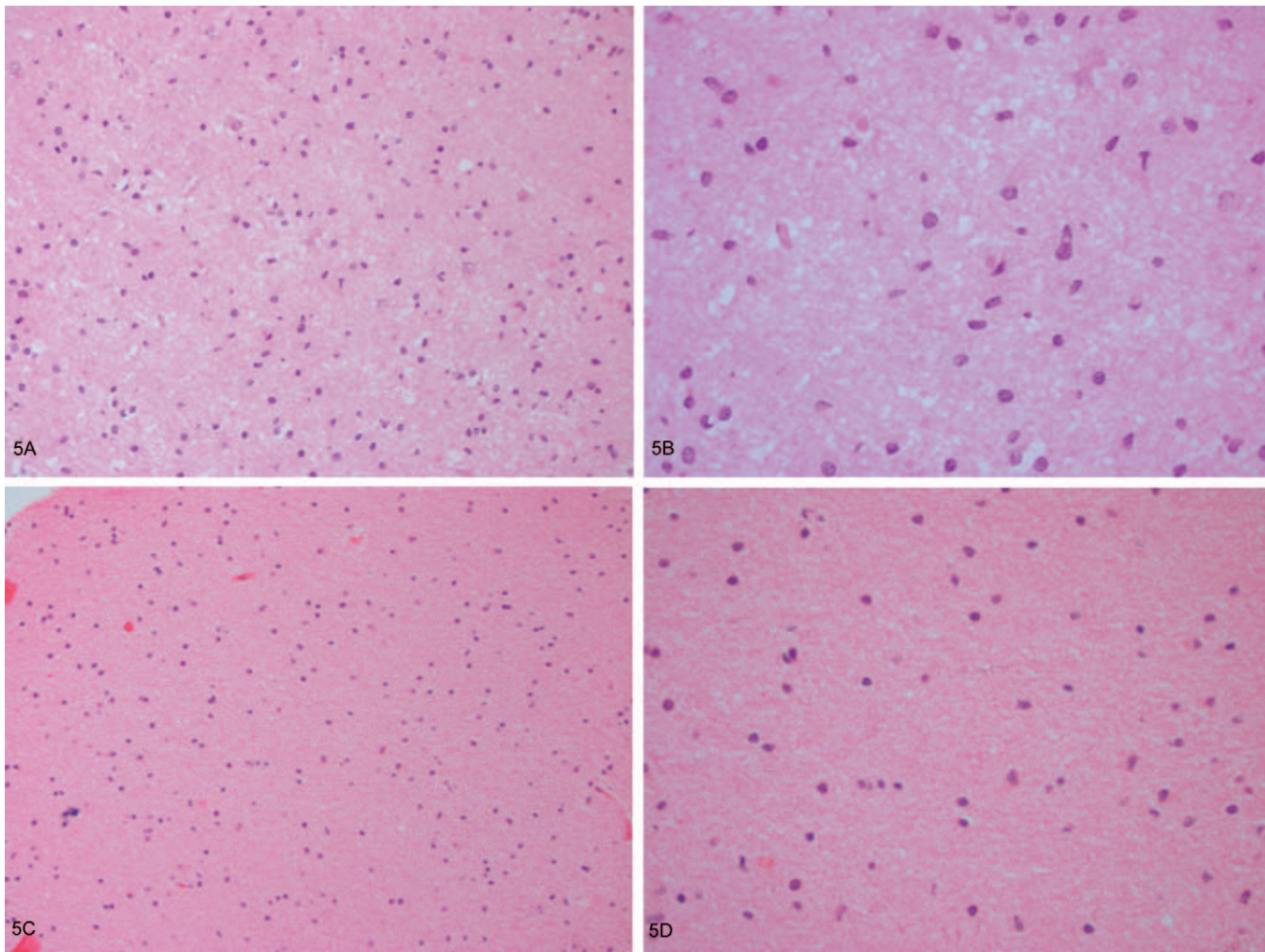
#### Reactive From Neoplastic

Distinguishing between reactive astrocytosis (gliosis) and a low-grade glial neoplasm is one of the most difficult differential diagnostic challenges in surgical neuropathol-

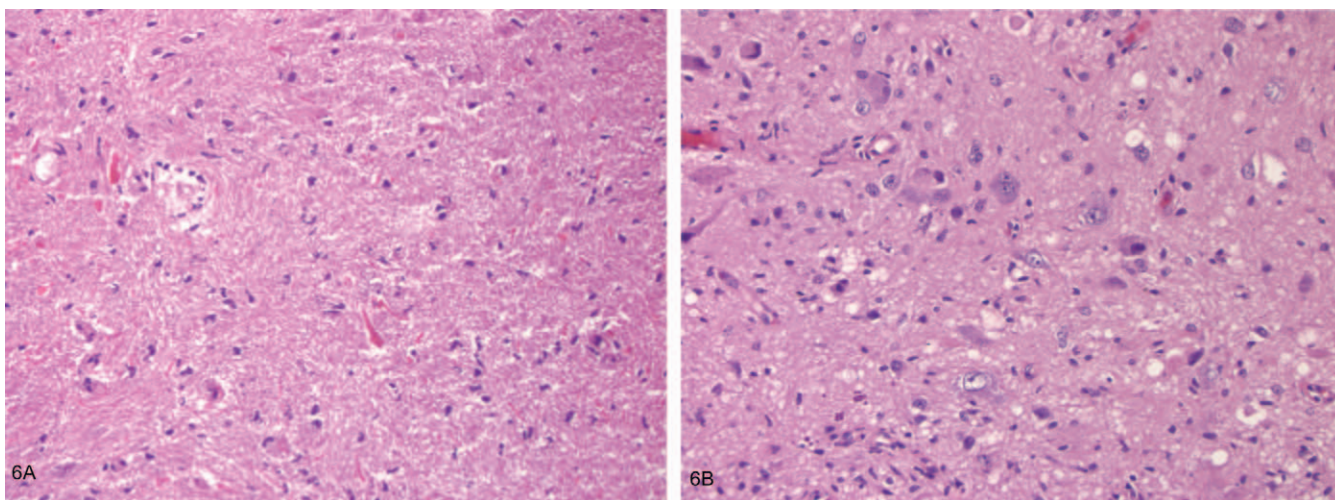
ogy. It is common to find at least some degree of gliosis adjacent to and associated with a tumor. Microscopically, the hypercellularity observed in gliosis, because of reactive astrocytes, tends to be evenly distributed, whereas the distribution of neoplastic cells is uneven in tumors. The nuclei of reactive astrocytes are slightly enlarged and eccentrically positioned within abundant, eosinophilic cytoplasm with stellate processes. A low nuclear-cytoplasmic ratio is maintained. Occasional binucleate cells can be encountered. In contrast, many tumor cells found in low-grade fibrillary astrocytomas have increased nuclear-cytoplasmic ratios with little discernible cytoplasm. Astrocytoma nuclei have markedly irregular contours with hyperchromasia and unevenly distributed chromatin. Differentiating the shorter and thinner cytoplasmic processes of gemistocytic astrocytoma cells from the longer, tapering processes of reactive astrocytes often requires immunostaining, making these differentiating features of little utility at FS. Additional "soft" or infrequently encountered clues suggesting glioma rather than gliosis include the presence of mitotic figures, especially atypical ones, microcystic change (difficult to assess at FS because of arti-



**Figure 4.** A through C, An 83-year-old woman with multifocal ring-enhancing lesions in temporal-parietal lobes. A, Frozen section shows relatively small, round cells with scant cytoplasm, diagnosed as lymphoma (hematoxylin-eosin, original magnification  $\times 200$ ). B, Paraffin-embedded section reveals necrosis rimmed by a pseudopalisade of tumor cells with pleomorphic, hyperchromatic nuclei (hematoxylin-eosin, original magnification  $\times 200$ ). C, Glial fibrillary acidic protein immunostain is positive in the tumor cells. The final diagnosis was glioblastoma multiforme (immunoperoxidase, original magnification  $\times 100$ ). D through F, A 74-year-old man with 2 ring-enhancing hemispheric masses. D, Frozen section demonstrates haphazardly arranged atypical cells with pleomorphic nuclei with prominent nucleoli, diagnosed as malignant astrocytoma (hematoxylin-eosin, original magnification  $\times 400$ ). E, Paraffin-embedded section shows densely packed large, atypical cells with vesicular chromatin and prominent nucleoli (hematoxylin-eosin, original magnification  $\times 400$ ). F, CD20 immunostain is diffusely positive. The final diagnosis was diffuse large B-cell lymphoma (immunoperoxidase, original magnification  $\times 100$ ).



**Figure 5.** A 48-year-old woman with bilateral frontal lobe masses. A and B, Frozen sections show irregularly distributed, mildly atypical cells in the white matter; a low-grade glioma was favored (hematoxylin-eosin, original magnifications  $\times 200$  [A] and  $\times 400$  [B]). C and D, Paraffin-embedded sections reveal more evenly spaced, less atypical-appearing cells. The final diagnosis was gliosis (hematoxylin-eosin, original magnifications  $\times 200$  [C] and  $\times 400$  [D]).



**Figure 6.** A 15-year-old boy with large frontal lobe mass and seizures. A, Frozen section demonstrates mildly atypical astrocytes in a fibrillary background and prominent Rosenthal fibers, diagnosed as pilocytic astrocytoma (hematoxylin-eosin, original magnification  $\times 200$ ). B, Dysmorphic neurons in addition to the previously described glial component. The final diagnosis was ganglioglioma (hematoxylin-eosin, original magnification  $\times 200$ ).

factual changes that can be created at FS), microcalcifications, and satellitosis of tumor cells around neurons or vessels (secondary structures of Scherer).

Radiation changes may present a particular challenge at FS. The atypia and necrosis associated with radiation may mimic a glioblastoma multiforme; a history of radiation is typically available at FS, which should alert the pathologist. Vascular sclerosis with perivascular lymphocytes and necrosis associated with numerous macrophages are clues to prior radiation therapy.

### Tumor Overgrading

Frozen section can introduce changes that are not typically seen in paraffin-embedded, permanent sections, making it difficult to accurately assess cellularity and pleomorphism. The most important differentiating features at FS in distinguishing a high-grade glioma from a low-grade glioma are the presence of mitotic figures (especially atypical), tumor cell necrosis, and vascular proliferation. These features are much more reliable at the time of FS than the subjective assessments of cellularity and pleomorphism. An error in overgrading at FS may impact on the accuracy of the final diagnosis. An erroneous high-grade glioma diagnosis may prompt the surgeon to prematurely terminate the surgery, believing that diagnostic tissue in agreement with the imaging impression of a high-grade glioma has been successfully obtained. One also has to be careful of not confusing a low-grade childhood glioma such as pilocytic astrocytoma with a higher grade astrocytoma. Clinical history (especially age and location) and imaging findings are useful in alerting one to the possibility of one of these low-grade tumors. Further complicating the FS interpretation is the fact that many of these low-grade astrocytoma variants display certain morphologic features (prominent cellularity, nuclear pleomorphism, vascular proliferation, and rarely mitoses) that are typically associated with higher grade fibrillary astrocytomas. Being alert to morphologic clues such as Rosenthal fibers, granular bodies, or prominent numbers of perivascular lymphocytes may assist at arriving at the proper intraoperative assessment.

### Miscellaneous Discrepancies

Much of the spectrum of gliomas and their variants were considered as FS diagnoses in the miscellaneous category (Table 3). This is not an unexpected finding given the scope of the study. The corresponding final permanent section diagnoses revealed a somewhat wider array of diagnoses. Of special note, gangliogliomas were misclassified on 3 occasions. Two cases were considered to be pilocytic astrocytomas, and the third was thought to represent a dysembryoplastic neuroepithelial tumor at FS. Gangliogliomas, pilocytic astrocytomas, and dysembryoplastic neuroepithelial tumors overlap clinically and morphologically, and sampling may have played a role in the discrepancies encountered. Gangliogliomas are characterized microscopically by dysmorphic, haphazardly arranged

ganglion cells with an intermixed glioma of pilocytic or diffuse astrocytoma type. The ganglion cell component may be only focally present in a given tumor. Therefore, if the ganglionic component is poorly represented at FS, the lesion is morphologically similar to a low-grade glioma. Dysembryoplastic neuroepithelial tumors are usually characterized by multiple mucin-rich cortical-based nodules resembling a microcystic oligodendroglioma; the neuronal component is devoid of appreciable cytologic atypia (in contrast to ganglioglioma). Again, poor sampling of the characteristic dysembryoplastic neuroepithelial tumor features leaves a lesion quite suggestive of a microcystic glioma.

The role of FS in the intraoperative consultation is important. Being aware of potential pitfalls and what lesions typically cause the most problems are important in bettering one's ability to provide a quality consultation. Communication with the neurosurgeon remains important in minimizing the potential for error.

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