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Review Article

Utilization of frozen sections in the evaluation of chronic epilepsy–related cases

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ABSTRACT

The role of frozen section consultation in the evaluation of chronic epilepsy–associated surgical excisions of brain tissue has not been previously examined. The study retrospectively reviews 335 cases in which a frozen section consultation was obtained in the setting of a resection for chronic epilepsy. In most cases (n = 323), 3 or fewer frozen sections were performed. The most commonly identified pathologies on final diagnosis included tumor or tumorlike lesions (79.1% of cases) and focal cortical dysplasia (20.9% of cases). Frozen section diagnoses discrepant with final diagnoses due to sampling error or misinterpretation were noted in 39 cases and most commonly involved a diagnosis of gliosis or tumor in the setting of a focal cortical dysplasia or diagnosis of gliosis in the setting of a low-grade tumor. In conclusion, frozen section consultation may be particularly useful in the evaluation of neoplasms arising in the setting of chronic epilepsy. Some epilepsy-associated pathology, such as focal cortical dysplasia, may be difficult to diagnose at the time of frozen section and such cases may not be an ideal target for intraoperative frozen section consultation.

1. Introduction

In patients with chronic or medically intractable epilepsy who have failed pharmacologic management, surgery is a well-established therapeutic intervention. The role of frozen section consultation in the evaluation of surgical resections performed in this clinical setting has not been previously studied. Extrapolating from previous studies, which have examined the role of intraoperative consultation in the evaluation of central nervous system lesions, the best results are obtained in cases in whom there is a specific lesion to target for surgical excision. This is well illustrated by neoplasms, which are the most frequent target for frozen section consultation in the overall neuropathology venue. Although tumors clearly make up a significant subset of identifiable pathology in patients with chronic epilepsy [1–7], they are by no means the only pathology encountered; in many locations, nonneoplastic lesions are a more frequent finding [2–4].

The current study explores the role of frozen section consultation in the assessment of chronic epilepsy–associated lesions, based on one institution's retrospective experience with over 2200 epilepsy surgeries over a 20-year period. Particular attention is paid to the diagnostic yield of frozen section consultation as well as pitfalls that may result in discrepant diagnoses at the time of frozen section.

2. Methods and materials

Institutional review board approval was obtained before commencement of this study. The surgical pathology files were searched for all resections by the epilepsy-related neurosurgeons and specifically for cases in which an intraoperative frozen section consultation was performed. Only those cases which involved patients who had medically intractable or chronic epilepsy were included in the study. A total of 2223 epilepsy cases generated over a 20-year period (1990-2010) were screened. Of these cases, frozen sections were performed in 335 patients; these patients formed the study group. For each case, information from the pathology reports including age, sex of the patient, location of the lesion, the number of frozen sections performed, the frozen section diagnoses, and the final pathologic diagnoses were gathered. Information regarding the number of cases in which a diagnosis was able to be made based on the frozen section as well as those cases in which the diagnosis was missed or not made at the time of frozen section was also identified.

3. Results

A total of 335 patients with medically intractable epilepsy, who underwent surgical resection to control seizures and for whom at least 1 frozen section consultation was performed as part of the assessment, form the study group. The patients included 169 males (50.4%) and 165 females (49.6%). At the time of surgery, patients ranged in age from 3 months to 67 years with a mean age of 24.0 years. Of the excised lesions, 166 were known to be situated on the left side (49.5%), 147 lesions on the right side (43.9%), and in 22 cases, the laterality of the lesion was not specified (6.6%). Most of the lesions were situated in the temporal lobe (n = 214, or 63.9%), followed by the frontal lobe (n = 55, or 16.4%), parietal lobe (n = 31, or 9.2%), and occipital lobe (n = 19, or 5.7%). In 12 cases (3.6%), the lesion involved

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multiple lobes, and in 3 cases (0.1%), the precise location of the excised lesion was not known.

In most cases, 3 or fewer frozen sections were performed (n = 323, or 96.4%). In 233 cases, only 1 frozen section was requested. In 63 cases, 2 frozen sections were performed, and in 27 cases, 3 frozen sections were done. Of the remaining 12 cases, 4 frozen sections were evaluated in 7 cases, 5 frozen sections in 2 cases, 6 frozen sections in 1 case, 10 frozen sections in 1 case, and 11 frozen sections in 1 case.

Table 1 summarizes the final diagnoses rendered in all 335 cases in this series. In a subset of cases, more than 1 pathology was observed. Most lesions in which a frozen section was requested involved a neoplasm or a tumorlike lesion (n = 265, or 79.1%). The prevalence of common tumor types observed in the series was in keeping with what others have reported as being common neoplasms encountered in the setting of chronic epilepsy, including most frequently gangliogliomas, low-grade astrocytomas, dysembryoplastic neuroepithelial tumors, low-grade oligodendrogliomas, and low-grade glial/glioneuronal neoplasms. The next most commonly observed pathology included malformations of cortical development or focal cortical dysplasia, which was observed in 70 cases (20.9%). Using the Palmini et al [8] classification, most of these cases represented type I dysplasias (57/70 cases); these lesions were marked by cortical architectural disorganization and dyslamination and were sometimes associated with neuronal cytomegaly. Forty-one cases represented focal cortical dysplasia coexistent with tumor (International League Against Epilepsy type IIIa lesions) [9]. A significant number of vascular malformations (n = 12, or 3.6%), particularly cavernous angiomas (cavernomas), were also observed. Less frequent targets for frozen section intraoperative consultation were cases of hippocampal sclerosis, inflammatory lesions including Rasmussen encephalitis, and remote ischemic damage or infarct.

In the cases that required multiple frozen sections, a diagnosis was made by the fourth frozen in all cases. When the frozen section diagnosis was compared with the final diagnosis, a discrepancy was noted in 39 cases. Table 2 summarizes the type of discrepancies that were observed in this subset of cases. The most common misinterpretations involved making a diagnosis of gliosis in the setting of a focal cortical dysplasia or neoplasm (Fig. 1A and B). Of the 39 cases, 21 cases were felt to probably represent sampling errors, that is, the diagnostic lesion was not sampled at the time of frozen section or the sampling was insufficient to render a diagnosis (Fig. 2A and B). In this category, the most commonly observed examples of this were cases in which diagnosis of gliosis was made in the setting of a focal cortical dysplasia. In the remaining 17 cases, the discrepancy between the frozen section diagnosis and permanent section was interpreted as representing an error of interpretation (Fig. 3A and B, 4A and B); the most common examples of this included cases in which tumors were misinterpreted as representing gliosis or focal cortical dysplasia at the time of intraoperative consultation. Of the 9 cases in which a final diagnosis of meningioangiomatosis was rendered, 4 of them were misinterpreted at the time of frozen section as representing either glioma, gliosis, or a meningioma.

In 47 cases (14.0%), 2 significant diagnoses that could have potentially accounted for the patient's chronic epilepsy were diagnosed. In only 1 of these cases, a glioneuronal neoplasm, accompanied by focal cortical dysplasia, were both diagnoses made at the time of frozen section. In 38 of these instances, only 1 of the 2 diagnoses was made at the time of frozen section consultation; in most of these cases, a diagnosis of tumor was made in the presence of a coexistent focal cortical dysplasia. In 8 cases, neither diagnosis was made at the time of frozen section consultation. In this latter category, 7 cases represented a low-grade glioneuronal neoplasm or hamartoma with accompanying focal cortical dysplasia, and 1 case represented a ganglioglioma with accompanying hippocampal sclerosis.

Table 1
Summary of final diagnoses (n = 335)

Lesion	No. of cases
Tumor/tumorlike lesions	265 (79.1%)
Ganglioglioma	73
Low-grade astrocytoma	38
Low-grade glial/glioneuronal neoplasm	32
Dysembryoplastic neuroepithelial tumor	29
Low-grade oligodendroglioma	23
Low-grade glioma, not otherwise specified	16
Low-grade mixed glioma	13
Meningioangiomatosis	9
Glioneuronal hamartoma	9
Pleomorphic xanthoastrocytoma	4
Composite ganglioglioma/dysembryoplastic neuroepithelial tumor	4
Hypercellular tissue, rule out low-grade glioma	3
Astroblastoma (angiocentric glioma)	2
Protoplasmic astrocytoma	2
Epidermoid cyst	2
Pilocytic astrocytoma	2
Pilomyxoid astrocytoma, subependymal giant cell astrocytoma, anaplastic pleomorphic xanthoastrocytoma, anaplastic ganglioglioma	1 each
Malformation of cortical development/focal cortical dysplasia	70 (20.9%)
Palmini et al type I A	54
Palmini et al type I B	3
Palmini et al type II A	1
Palmini et al type II B	7
Not otherwise specified	5
Vascular malformation	12 (3.6%)
Cavernous angioma	10
Not otherwise specified	2
Gliosis	18 (5.4%)
Hippocampal sclerosis	5 (1.5%)
Inflammatory	5 (1.5%)
Rasmussen encephalitis	2
Chronic encephalitis/vasculitis	2
Meningitis	1
Remote ischemic damage/infarct	4 (1.2%)
Others (heterotopic neurons, focal hippocampal neuronal loss, and gliosis; no pathologic changes)	1 each

4. Discussion

Intraoperative consultation is a well-established means of evaluating tissue sampled from the patient at the time of surgery to assess adequacy of the specimen and at times to guide intraoperative management. The diagnostic accuracy of the procedure is well documented and is usually greater than 90% in most studies [10–19]. In many series, most lesions reported represent neoplasms. The diagnostic yield in nonneoplastic lesions of the central nervous system is significantly lower, usually less than 90% [11,20–23].

In 2 previously published series, Plesec and Prayson [18,19] reviewed 1 institution's experience with frozen section discrepancies

Table 2
Summary of cases where the frozen section diagnosis was discrepant with the final diagnosis

Final diagnosis	Frozen section diagnosis	No. of cases (n = 39)
Focal cortical dysplasia	Gliosis	10
Focal cortical dysplasia	Tumor	3
Tumor	Gliosis	9
Gliosis	Low grade glioma	4
Inflammatory lesion	Gliosis	3
Remote infarct/ischemic damage	Gliosis	2
Meningioangiomatosis	Glioma	2
Meningioangiomatosis	Gliosis	1
Meningioangiomatosis	Meningioma	1
Cavernous angioma	Gliosis	1
Gliosis	Vascular malformation	1
Low-grade astrocytoma	Ganglion cell proliferation	1
Hamartoma	Gliosis	1