40 Brain and Spinal Cord

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General Comments

In some respects, pathologic evaluation of specimens from the central nervous system (CNS) is less complicated than evaluation of other organs, because requests for margins and the need for extensive specimen dissections are unusual. On the other hand, CNS specimens are usually small, and care must be taken to preserve the tissue. Do not use all of the tissue by freezing the entire specimen. This is especially true for specimens of the spinal cord. These can be minute, yet major therapeutic decisions often depend on the results of the pathology studies. In all cases, it is essential to keep the clinical and radiologic findings in mind when processing specimens from the CNS.

Ultrasonic aspirations are widely used for tumor resections. As a consequence, much of the specimen may be lost unless it is recovered from the instrument's bag receptacle. The fragments may be difficult to interpret histologically but can be invaluable. They are entirely suitable for molecular or cytogenetic studies.

Cytologic Preparations

Cytologic preparations are essential in the frozen section and permanent section evaluation of all surgically excised brain lesions. These should be prepared in every case for which a frozen section is requested. As illustrated, the preferred procedure is as follows: A minute portion of the fresh specimen is placed on a glass slide and, with considerable pressure, smeared between an opposing slide. The slides are separated and immersed *immediately* in 95% alcohol. Following fixation for 45 to 60 seconds, the preparation is stained and coverslipped. I prefer routine staining with hematoxylin and eosin.

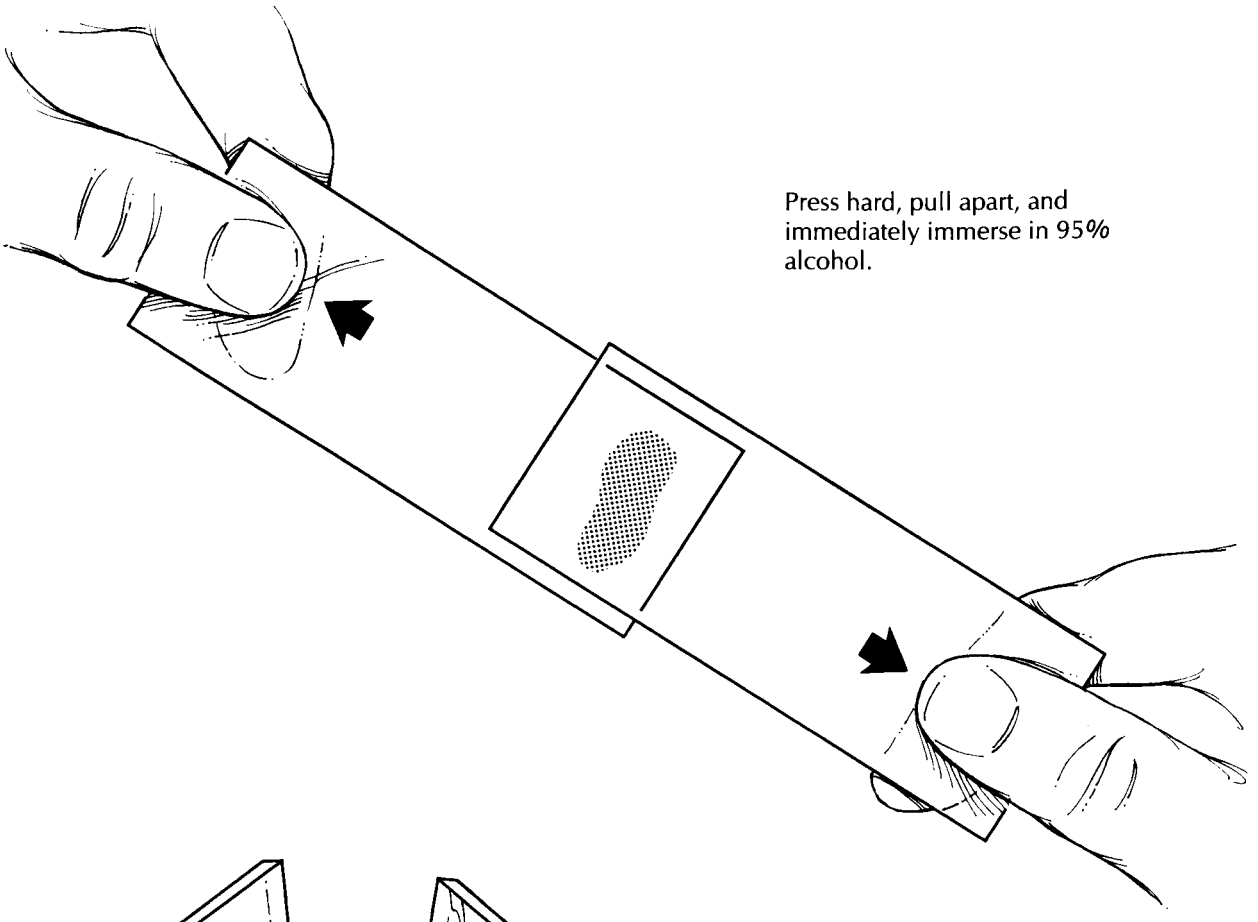
Needle Biopsy Specimens

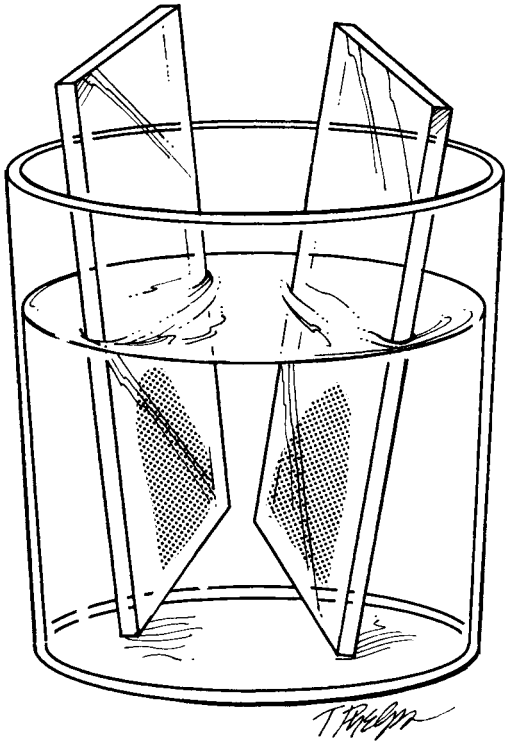
Needle biopsy specimens need to be interpreted and handled with special care. The evaluation should begin with cognizance of the clinical and radiographic findings. The chance of making an error is vastly increased when these specimens are studied in a vacuum devoid of clinical or radiographic information.

Begin your examination with the cytologic preparation as described above. One of the remaining fragments of tissue can then be used for a frozen section if desired. If an abnormality is established by the smear, a frozen section may not be necessary. Unless you are assured of additional tissue, it is generally wise to freeze only one or two cores at the time of initial examination, holding others in reserve. Throughout the process, review these slides in reference to the radiographic images to ensure that abnormal tissue is obtained and that the findings are consistent with the images. Close contact with the surgeon is extremely important. As is true for biopsies from other body sites, small specimens can be colored with eosin to facilitate identification at the time of embedding and sectioning.

Frozen Sections/Permanent Sections

Freezing must be accomplished as rapidly as possible to minimize the formation of ice crystals.





Small Brain Biopsies for Glial Neoplasms

1. Take a 1 mm core of the specimen and smear it between two glass slides. Immediately fix the slides in 95% alcohol, and then stain them for cytologic evaluation.
2. Avoid freezing all of the tissue when a frozen section evaluation is requested. Set a portion of the tissue aside for routine processing, or find out from the surgeon if more tissue will be provided later.
3. When performing a frozen section, freeze the tissue rapidly. Rapid freezing will minimize tissue distortion caused by the formation of ice crystals.

Ice crystals are generally avoidable in certain neoplasms, such as meningiomas, but frequently not in infiltrating gliomas from edema-rich white matter. The recommended procedure is to establish a base of semifrozen mounting medium on a cold chuck. The medium should not be completely frozen, because solidly frozen medium will slowly freeze the tissue and encourage the formation of ice crystals by gradually drawing heat from the small specimen. Therefore, place the specimen on the partially frozen base, and immediately immerse it in liquid nitrogen. After freezing, the specimen can then be covered with additional mounting medium and refrozen. Cut and stain sections by standard methods.

In the case of gliomas, especially the well-differentiated variety (e.g., astrocytoma and oligodendroglioma), it is extremely important that blocks be available from tissue that is *not* subject to prior frozen section. Prior freezing produces nuclear angulation and hyperchromatism, which can make it difficult to distinguish between gliomas and to distinguish reactive or normal brain from an infiltrating glioma. Unless you are assured of more tissue by the surgeon, use only a portion of the specimen for a frozen section.

Electron Microscopy

To a large extent, immunohistochemistry has replaced electron microscopy as a diagnostic tool; however, in certain instances the latter technique is invaluable. Accordingly, it is appropriate to hold some tissue in reserve in glutaraldehyde (embedding later if necessary) for neoplasms for which classification may be difficult after review of the frozen section. Tissue may also be embedded from encephalitic lesions if viruses are suspected, because no immunohistochemical agents are commercially available for many classes of potential viral pathogens.

Processing of Tissues From Specific Entities

Meningiomas are frequently submitted with a dural attachment and arrive as either a complete en bloc excision or, more often, as a series of small fragments. Prognostically significant information relates to histologic features of the lesion as well as the interface of the tumor with surrounding tissues, that is, the brain and the skull. The surface of the mass adjacent to the brain should be sectioned, if identified, particularly if portions of the brain adhere to the surface. At least one section through the base of the tumor on the dura should also be taken. Decalcified sections of bone are appropriate to evaluate skull invasion.

Gliomas are an exceedingly heterogeneous group in terms of their macroscopic and microscopic characteristics. Generally, margins are not an issue and do not, unless specifically stated by the surgeon, affect the treatment of the patient. Fragments of ependymomas, oligodendrogliomas, and astrocytomas, in which little normal brain is recognized, do not need to be sampled in regard to the extent of the disease, although it is prudent to attempt such a localization. In larger en bloc specimens of gliomas, however, a series of marked and recorded sections passing from the tumor into the macroscopically normal brain is appropriate. In the case of malignant gliomas with central necrosis, the most diagnostic tissue is usually found in the cellular rim immediately surrounding the necrotic area. Sections from this area are therefore appropriate. In the case of well-differentiated gliomas (e.g., astrocytoma and oligodendroglioma), the tissue may not appear markedly abnormal, and multiple sections are necessary, particularly from areas in which the white matter is discolored.

Malignant gliomas after radiotherapy may have extensive therapy-related changes, such as coagulation necrosis. In this setting, multiple tissue sections should be submitted so as not to miss potential foci of active recurrent tumor.

Oligodendrogliomas are increasingly diagnosed by molecular techniques. The molecular laboratory can be consulted in regard to specific tissue preparation (e.g., fresh frozen, etc...).

Lymphomas are generally recognized during the frozen section process and, in the sporadic form in the nonimmunocompromised patient, they are often suspected on the basis of the neuroimaging features. In this setting, tissue can be reserved frozen for special marker studies (see Chapter 41), although most of the relevant markers for the simple purpose of establishing a clinical diagnosis can be performed on paraffin-embedded sections. A clinical history of prebiopsy steroid treatment is significant, as CNS lymphomas in this setting may be little more than

a mass of macrophages and few if any residual neoplastic cells.

Pituitary adenomas are often approached via the transsphenoidal route, and the specimens are often small. Care must be taken not to freeze all of the specimens, as the resultant artifact complicates interpretation of permanent sections. Close communication with the surgeon is essential.

Creutzfeldt-Jakob disease is a rare disorder that is occasionally diagnosed in a cortical biopsy specimen. Although there appears to be only a very small likelihood that pathology personnel will contract Creutzfeldt-Jakob disease from these specimens, caution is appropriate considering the devastating consequences of this disease. Details of this issue are discussed by Brown.[20] Basically, the tissues are fixed in a standard formalin solution for at least 48 hours. The tissues are then placed in a cassette and decontaminated by immersion with periodic agitation in a 95% formic acid solution. The tissue will turn clear. After this, the tissue is placed in formalin again for 1 to 2 days. The tissues can then be treated as any other routine specimen, although some laboratories prefer to hand process them separately. Generally, frozen sections are not recommended on tissues from demented patients.

Specimens taken to control seizures are usually from the temporal lobe. Often they consist of "lateral" and "medial" temporal lobe specimens. The latter contains the hippocampus, which must be examined carefully for the presence or absence of "mesial" or "hippocampal" sclerosis (i.e., neuronal loss and gliosis).

Important Issues to Address in Your Surgical Pathology Report on Brain and Spinal Cord Biopsies

- What procedure was performed?
- What are the type and grade of the neoplasm? (For glial neoplasms, be sure to document the grading system employed.)
- What is the size of the neoplasm?