An analysis of stereotactic biopsy of brain tumors and nonneoplastic lesions: a prospective clinicopathologic study

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Abstract

**Background:** Appropriate management of progressive, unverified brain lesions should be guided by conclusive pathological diagnosis. Stereotactic biopsy (SB) is established as a less invasive surgical procedure that provides diagnosis. In this prospective study, we analyzed the diagnostic difficulties and risk of SB in the various brain mass lesions, the rate of conclusive pathological diagnosis, and the rate of and the reasons for discrepancy between the intraoperative smear results and conclusive paraffin diagnosis.

**Methods:** Using computed tomography (CT) and/or magnetic resonance imaging (MRI), 130 cases underwent SB procedure to assess intra-axial brain mass lesions. A CT-MRI fusion and a multiplanar image processing stereotactic program were used in cases who had lesions adjacent to the neurovascular and critical areas. The intraoperative evaluations were made with the smear preparations (SPs) of 1 or 2 biopsy specimens. The conclusive diagnosis was achieved by paraffin preparations of the remainder of the biopsies. The discrepancy between the smear results and the conclusive diagnosis was analyzed.

**Results:** Conclusive histopathologic diagnosis was achieved in 99.23% of the cases. A discrepancy between smear results and conclusive diagnosis was detected in 6.98% of the conclusively diagnosed cases. The major reasons for the discrepancy were necrosis and improper quality of the preparations. There was no mortality, and hemorrhage-related morbidity was observed in 1 case (0.7%).

**Conclusions:** Necrosis and the improper quality of the SPs can cause difficulties in establishing a histopathologic diagnosis in SB. Small tissue samples do not decrease the diagnostic yield with the new stereotactic technologies used by an experienced team consisting of a neurosurgeon, pathologist, and radiologist.

**Keywords:** Stereotactic biopsy; Intra-axial brain lesions; Brain tumors; Diagnostic difficulties; Pathology

1. Introduction

SB of brain lesions has been a widely and safely performed procedure since it was first introduced in the late 1970s [6]. SB is indicated in every progressive, unverified intracranial lesion to obtain a histopathologic diagnosis in cases where surgical resection is not preferred treatment. SB ascertains the histological diagnosis of brain lesions with low risk and high accuracy. On the other hand, reported series show various results of diagnostic yield and complications of SB procedures [2,4,7-16]. This study presents a prospective clinicopathologic investigation of a series of patients with intra-axial brain lesions who underwent serial SBs. We aimed to analyze the diagnostic difficulties and the underlying errors and causes, and we attempted to analyze the rate of conclusive pathological diagnosis, the discrepancy between the diagnosis from SP and histological diagnosis, and the risk for complications.

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**Abbreviations:** CT, computed tomography; H&E, hematoxylin-eosin; MRI, magnetic resonance imaging; SB, stereotactic biopsy; SP, smear preparation.

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2. Materials and methods

Between 1995 and 2003, 130 cases with intra-axial brain lesions underwent SB at the Department of Neurosurgery, School of Medicine, Ankara University. Histopathologic evaluation was made at the Department of Pathology, School of Medicine, Ankara University. All biopsy procedures were performed by only 1 neurosurgeon (AS), and all the biopsy materials were evaluated by 2 pathologists (EE and AOH). Thus, standardization of the procedures and a biopsy protocol were established at the beginning of the study for the surgical technique and histopathologic evaluation.

A stereotactic head ring (Riechert-Mundinger; Streicker-Leibinger, Freiburg, Germany) was placed on the patients, usually under local anesthesia. In 16 cases, general anesthesia was used. A CT and/or MRI were obtained under stereotactic condition. In most of the cases, a stereotactic software (Stereoplan 2.0; Streicker-Leibinger), a

Fig. 1. Stereotactic CT-MRI image fusion in a case with pineal region tumors. A: Three-dimensional display of the trajectory of the cannula. B: Preoperative stereotactic surgical planning on multiplanar MRI-fused image program. C: Probe view of the virtual biopsy trajectory in the tumor. D: The probe-view images provide critical surgical information: the trajectory is far away from the internal cerebral veins and other vascular structures. The biopsy tract should stay within the limits of −10 and 10 mm according to the targeted center of the tumor; cisternal and vascular structures at the pineal region may be damaged after +10 mm; no more tumor tissue at 15 mm.
cursor, and digitizer were used to achieve stereotactic target calculation. On the other hand, a CT-MRI fusion and an image processing stereotactic program (Target@; BrainLAB, Munich, Germany) were used in 33 cases who had lesions adjacent to the neurovascular and critical brain areas such as pineal region, brainstem, sylvian fissure, and third ventricle. Using the latest program, multiplanar and 3D reconstructions were obtained for choosing the optimal trajectory. Probe view, that is, 90° planar reconstruction scan to the trajectory, was particularly useful to calculate the precise distance to the vascular structures and the length of the serial biopsy route (Fig. 1). An 8-mm burr hole was used as the entry point; pial surface was observed to avoid blind puncturing. Biopsy forceps (Biopsy forceps, 1.4 mm; Streiker-Leibinger) were used to deliver approximately 1 mm³ of the lesion (Fig. 2). The first biopsy specimen was taken from the surrounding tissue or peripheral part of the lesion, and the following serial biopsies were taken at approximate distances of 1 or 2 mm passing through the volumetric center of the tumor. CT scan was performed in all patients postoperatively.

SPs of 1 or 2 biopsy samples were stained with Diff-Quick (Thermo Shandon, Pittsburgh, PA) and were examined by the pathologists intraoperatively. On the other hand, in cases operated before 2001, SPs were stained with H&E. In addition, the clinical characteristics and CT and MRI scans of each patient were presented to the pathologists. For each case, serial biopsy specimens (ranging from 2 to 24) were obtained for paraffin embedding. The biopsy samples were fixed in 10% buffered neutral formalin, were processed as

<table>
<thead>
<tr>
<th>Location</th>
<th>No. of cases</th>
<th>%</th>
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<tbody>
<tr>
<td>Parietal</td>
<td>40</td>
<td>30.7</td>
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<tr>
<td>Thalamus</td>
<td>23</td>
<td>17.6</td>
</tr>
<tr>
<td>Frontal</td>
<td>16</td>
<td>12.3</td>
</tr>
<tr>
<td>Hypothalamus</td>
<td>8</td>
<td>6.1</td>
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<tr>
<td>Corpus callosum</td>
<td>8</td>
<td>6.1</td>
</tr>
<tr>
<td>Basal ganglia</td>
<td>7</td>
<td>5.3</td>
</tr>
<tr>
<td>Pineal</td>
<td>6</td>
<td>4.6</td>
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<tr>
<td>Occipital</td>
<td>5</td>
<td>3.8</td>
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<tr>
<td>Insular</td>
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<td>3.8</td>
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<tr>
<td>Temporal</td>
<td>4</td>
<td>3.0</td>
</tr>
<tr>
<td>Mesencephalon</td>
<td>2</td>
<td>1.5</td>
</tr>
<tr>
<td>Lateral ventricle</td>
<td>2</td>
<td>1.5</td>
</tr>
<tr>
<td>Third ventricle</td>
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<td>1.5</td>
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<tr>
<td>Pons</td>
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routine histopathologic specimens, and were stained with H&E. Additional immunohistochemical stains were applied for the conclusive diagnosis if necessary. To assess diagnostic pitfalls and difficulties in evaluating SBs, all the SPs of 130 cases were reviewed together by the same pathologists. The reasons for discordance between the SP results and definite diagnosis of the paraffin-embedded materials of the SB procedure were analyzed as well.

3. Results

The age of the 130 cases (85 males, 45 females) ranged from 7 to 82 years (mean, 46 years). Most of the lesions were located in the parietal lobe (30.7%), thalamus (17.6%), and frontal lobe (12.3%) (Table 1). Conclusive histopathologic diagnosis was achieved in 99.23% (129/130) of the cases (Table 2).

In 2 cases, craniotomy and resective surgical procedures were performed after SB; in one of these cases, SB procedure revealed severe lymphocyte-rich inflammatory infiltration in the background of gliosis. In this case, a resective surgery was subsequently performed, and the lesion was diagnosed as an astrocytoma grade III. The other case demonstrated only the features of hematoma both in the SB and in the subsequent resective surgery.
Among the conclusively diagnosed group (129 cases), a discrepancy between SPs and paraffin diagnosis was detected in 9 cases (6.98%) (Table 3). In 3 of the cases, the reason for the discrepancy was the presence of necrosis as a unique finding in the SP (Fig. 3). Improper quality of the SPs in 3 cases and presence of necrosis in addition to the improper quality in 1 case were the primary causes for the discrepancy. In 1 case, the epithelial malignant cells simulated the histiocytes of the granulomatous inflammatory reaction in addition to the improper quality of the SP (Fig. 4). In the other case, morphologic cellular similarities between the pineocytoma and oligodendroglioma caused the discordance between the SP result and the final conclusive paraffin diagnosis. Nine cases had conclusive diagnosis of lymphoma. There was no discrepancy between SPs and conclusive diagnosis in these lymphoma cases. For these patients, when lymphoma was diagnosed during SB procedure, the specific medical treatment was started immediately afterwards, without losing time for the routine paraffin procedure.

There was no operative mortality due to SB procedures. Two silent hemorrhages (<5 mm in diameter) were revealed by postoperative CT scanning. In 1 other case, hemiparesis due to intralesional bleeding (7 mm) was observed. No complication was observed except for these small hematomas, which were close to the internal capsule. Thus, the hematoma-related morbidity was 0.7%, and the silent hematoma rate was 1.5%.

4. Discussion

SB is a safe and efficient procedure, particularly in cases with lesions in which a craniotomy and resective surgery are not indicated primarily. In most such cases, a conclusive diagnosis can be established by SBs alone [1,4,7-16]. Rarely, because of the nature of the lesions, the biopsy specimens can be misdiagnosed or the results of SBs can be insufficient. In reported series, the rate of histopathologic conclusive diagnosis of SBs has shown a great variation, ranging from 60% to 98% [10,11].

Although SB is a safe, efficient, and valuable procedure, it has a morbidity rate ranging from 0.9% to 15% and mortality rate between 0% and 4.2% in reported series [2,10-12,15]. The advances in the SB techniques and imaging modalities have increased the rate of conclusive diagnosis and have decreased the complications. Complex multiplanar imaging modalities show the relationship between the biopsy cannula and biopsy forceps trajectory, and the relationship with the critical neurovascular structures. These new stereotactic technologies provide us excellent and precise stereotactic multiplanar imaging. This is probably a very important factor in obtaining the definitive histopathologic diagnosis and in reducing the rate of complications in SB procedures [10,15]. Kreth et al [10] reported 98% conclusive diagnosis and 0.9% hemorrhage-related morbidity in their SB series. In this series, the complication rate was far below what is commonly reported, as in our series, in which the hematoma-related morbidity was 0.7% and the silent hematoma rate was 1.5%. It is noteworthy that we used nearly the same techniques and instruments as Kreth et al [10]. In our study, a conclusive histopathologic diagnosis was achieved in 129 (99.23%) of 130 patients; thus, a very high diagnostic success rate was achieved. The high rate of conclusive diagnosis and the low rate of morbidity seem to be the results of the advanced surgical planning techniques and instruments.

Although experience of the pathologist is the most important factor in the diagnostic yield, the small size of the samples can be recognized as the major disadvantage of the SB [7,16]. On the other hand, the size and shape of the samples obtained from the SB seem to be correlated inversely with the morbidity and mortality rates. There are several types of biopsy instruments: cup forceps, spiral needles, side cutting instruments, and needle core devices. Spiral needles and Sedan-type side cutting instruments have a higher risk for morbidity; success of the needle core
devices depends on the texture of the tissue [5]. Biopsy forceps seem to be the most useful and less risky. Several types and sizes are commercially available. The forceps we used are one of the smallest sizes available. The size and shape of our forceps may have contributed to the lower rate of complications. Moreover, the conclusive diagnosis rate was high in our study in spite of the small size of the specimens, because the biopsy samples were taken in a serial order, which provided us the possibility of evaluating the different parts of the lesions.

A craniotomy and resective surgery can sometimes be required in the cases with insufficient or nonconclusive SB results. In our series, 2 cases underwent a resective surgery after SB. In one of these cases, the diagnosis of hematoma was confirmed by both SB and the removal of the mass by craniotomy. In the other case, only gliosis with severe inflammatory infiltration was seen during pathological examination after SB. Afterwards, the patient underwent a resective surgery and was diagnosed as astrocytoma grade III. Because gliosis with an inflammation can be the neighboring part of a tumor or a gliosis can mimic a low-grade glial tumor, such cases with a mass lesion should be referred for resective surgery or repeated SB procedures.

Because SB is a 2-step procedure that includes interpretation of SPs intraoperatively and paraffin preparations postoperatively, there could be some discrepancies between the results of smear and paraffin preparations. In the literature, discordance between smear and paraffin preparations has been reported as ranging from 5% to 38.46%. The presence of massive necrosis and the absence of diagnostic histological component in the small biopsies were the reported causes of the discordance in those studies [3,4,7,13]. Ostertag et al. [13] reported 5% discrepancy between the diagnosis from the SP and the subsequent histological diagnosis. In our series, we found a discrepancy between SPs and conclusive diagnosis in 6.97% (9/129) of the cases in whom a conclusive diagnosis was achieved. Our study revealed presence of necrosis and improper quality of the preparation as the major causes of the discordance. Necrotic tumors could cause problems in SB interpretations in both smear and paraffin preparations. In cases in whom only necrosis is detected in SP, the pathologist should acquire additional samples. If the presence of only necrosis persists, the case must be deferred for the paraffin preparations to evaluate the other samples taken for paraffin. If the only finding is necrosis in the final paraffin sections, rebiopsy or resective surgery must be offered. In our cases whose SP results showed necrosis, all of the cases were later diagnosed as high-grade malignant tumors (Table 3). Moreover, necrosis also decreases the quality of the SP. Epithelial histiocytes could be confused with atypical cells in the smears, as in the cases where we confused the atypical cells with epithelioid histiocytes. The quality of the SPs is one of the most important factors in evaluating the cytological details. Improper quality caused the difficulties in diagnosis of the glial tumor vs metastasis and gliosis and in the diagnosis between tumors having cytological similarities, such as pineocytoma and oligodendroglioma. In addition, intraoperative SPs seem to be useful in the early management of the cases with brain lesions, such as lymphoma, until the conclusive diagnosis is achieved if the clinical course and radiological nature of the case support the diagnosis.

5. Conclusions

The SB procedure should be performed by an experienced and specialized team consisting of a neurosurgeon, pathologist, and radiologist. The lesions should be evaluated with the multiple serial biopsies, especially to improve the diagnostic accuracy of the SBs. The same pathologist should do interpretation of the smear and paraffin preparations. The presence of gliosis, necrosis, and hematoma, and the improper quality of the SPs can cause difficulties in establishing a conclusive histopathologic diagnosis. Small tissue samples do not decrease the diagnostic yield; however, the size of the biopsy material seems to be directly related to the hemorrhage-related complications. New stereotactic multiplanar imaging technologies support the orientation of the surgeon to the biopsy trajectory and localization of the critical neurovascular structures. The new stereotactic planning technology provides a chance for maximal histological verification while reducing the rate of hematoma-related complications. Experience and specialization of the neurosurgeon are very important factors in SB procedures, as much as in vascular, spinal, and other fields of neurosurgery.

Acknowledgment

This study was supported by a research grant from the Scientific Research Project Department, Ankara University, Ankara, Turkey.

References


