Stereotactic biopsy for intracranial lesions using the Leksell system: usefulness of rapid intraoperative diagnosis

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Objective: Performing stereotactic biopsy using the Leksell system, we discuss its advantages and disadvantages and analyze our intraoperative histopathological and cytological diagnostic success rates.

Methods: We present a series of 47 patients subjected to stereotactic biopsies for a wide variety of brain lesions. The anatomical locations, diagnostic yield, morbidity and mortality rates, and the concordance rates between final histopathological diagnoses, intraoperative histological diagnoses, and intraoperative cytological diagnoses were analyzed.

Results: The final histopathological diagnoses were made in 41 of 47 patients (diagnostic yield, 87.2%). Complications occurred in 2 of 47 patients (4.25%). The mortality rate was 2.1% (1 patient). The concordance rate between final histopathological diagnosis and intraoperative cytological diagnosis was 70.7% (29/41), and the concordance rate between final histopathological diagnosis and intraoperative histological diagnosis was 60.9% (25/41). In 4 of 41 cases, cytology yielded a better quality specimen than did histology for the correct diagnosis.

Conclusions: Stereotactic biopsy using the Leksell system is less invasive and, therefore, useful for deciding adjuvant therapy after the surgical diagnoses of tumors. Using both intraoperative histological diagnosis and intraoperative cytological diagnosis concurrently can compensate for the limitations of each individual method and contributes greatly to the accuracy of the final diagnosis.

Key words: Leksell stereotactic system, brain tumor, intraoperative rapid diagnosis, cytology

Introduction

In the treatment of malignant brain tumors, a pathological diagnosis is important for determining treatment and prognosis. The development of diagnostic imaging has allowed understanding of anatomical position. Stereotactic biopsies for histopathological diagnoses of brain tumors can, therefore, precisely assess the tumor lesions. The diagnostic rates of stereotactic biopsy are generally greater than 90%, and stereotactic biopsy is, therefore, as indispensable to the diagnoses of difficult deep-seated brain tumors as well as to their removal.

Highly accurate preoperative diagnosis is now possible in light of the advancements in diagnostic imaging technologies; however, pathological hallmarks remain crucial to choosing the best therapy. With diagnostic craniotomy and needle biopsy, the goals differ, as well as do the quantities of specimens required. Thus, for intraoperative diagnoses, the degree of difficulty and techniques used also differ. The neuropathologist experiences a great deal of stress and requires skill to perform an accurate intraoperative diagnosis. Therefore, an accurate rapid diagnosis provides the best opportunity to determine the level of neuropathology expertise in the respective medical institutions.

Here we report our experience with a stereotactic biopsy using the Leksell system, discuss its advantages and disadvantages, and analyze our histopathological diagnostic success rates.

Materials and Methods

Patient and lesion characteristics

This study retrospectively investigated 47 patients who underwent stereotactic biopsy using the Leksell system (Elekta Instruments, Atlanta, GA, USA) between August 2004 and April 2012 at the Kitasato University Hospital,
excluding the patients who did not receive an intraoperative diagnosis. Stereotactic biopsies were considered for patients with deep-seated parenchymal lesions that were in eloquent areas of the brain (such as those close in the sensorimotor area, language sensory, motor, language, visual cortex hypothalamus and thalamus, internal capsule, and brainstem), multiple, or lesions with poor general appearance. The patients mean age was 59.0 years (range, 10−83 years; median, 62.0 years); 24 patients were male (51.0%), and 23 patients were female (49.0%).

Lesion location is summarized in Table 1. The lesions were localized to the deep white matter (n = 32), thalamus (n = 5), basal ganglia (n = 4), caudate head (n = 2), corpus callosum (n = 2), trigonum (n = 1), and parietal cortex (n = 1).

Stereotactic biopsy procedure
After placement of the Leksell stereotactic head-frame, all patients underwent magnetic resonance (MRI) imaging or computed tomography (CT). The target site, entry point, and trajectory were preoperatively planned on the workstation, always avoiding vascular or eloquent structures. The trepanation was performed under local or general anesthesia. A side-cutting (10 × 1.4 mm) needle 2.5 mm in diameter was used for the biopsy. Tissue specimens were obtained from 4 different directions and sent to the pathology laboratory for frozen sectioning and cytological preparations. If there was no pathological diagnosis, additional samples were taken from another enhancing region of the lesion along a single trajectory. CT was performed for all patients immediately after the biopsy and 24 hours after biopsy. The cause of complications such as intracranial bleeding and cerebral edema was confirmed.

Results
The final histopathological diagnosis was made in 41 of 47 patients (diagnostic yield, 87.2%; Table 2). The final histopathological diagnoses in these 41 patients were malignant lymphoma (n = 24), diffuse astrocytoma (n = 3), anaplastic astrocytoma (n = 3), glioblastoma (n = 9), germinoma (n = 1), and intravascular malignant lymphomatosis (n = 1). There were six undiagnosed patients.

Complications occurred in 2 patients (4.25%).

Table 2. Summary of final histological diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant lymphoma</td>
<td>24 (51.1)</td>
</tr>
<tr>
<td>Diffuse astrocytoma</td>
<td>3 (6.4)</td>
</tr>
<tr>
<td>Anaplastic astrocytoma</td>
<td>3 (6.4)</td>
</tr>
<tr>
<td>Glioblastoma</td>
<td>9 (19.15)</td>
</tr>
<tr>
<td>Germinoma</td>
<td>1 (2.1)</td>
</tr>
<tr>
<td>Intravascular malignant lymphomatosis</td>
<td>1 (2.1)</td>
</tr>
<tr>
<td>Not diagnostic</td>
<td></td>
</tr>
<tr>
<td>Multiple sclerosis, suspected</td>
<td>2 (4.3)</td>
</tr>
<tr>
<td>Neuro behcet, suspected</td>
<td>1 (2.1)</td>
</tr>
<tr>
<td>Diffuse astrocytoma, suspected</td>
<td>1 (2.1)</td>
</tr>
<tr>
<td>Negative</td>
<td>2 (4.3)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>47 (100)</strong></td>
</tr>
</tbody>
</table>

Table 3. Concordance rates between final histological diagnosis, intraoperative histological diagnosis, and intraoperative cytological diagnosis

<table>
<thead>
<tr>
<th>Final histological diagnosis (N = 47)</th>
<th>Intraoperative histological diagnosis</th>
<th>Intraoperative cytological diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant lymphoma (24)</td>
<td>19/24 (79.2%)</td>
<td>19/24 (79.2%)</td>
</tr>
<tr>
<td>Diffuse astrocytoma (3)</td>
<td>1/3 (33.3%)</td>
<td>1/3 (33.3%)</td>
</tr>
<tr>
<td>Anaplastic astrocytoma (3)</td>
<td>0/3 (0%)</td>
<td>2/3 (66.6%)</td>
</tr>
<tr>
<td>Glioblastoma (9)</td>
<td>4/9 (44.4%)</td>
<td>6/9 (66.6%)</td>
</tr>
<tr>
<td>Germinoma (1)</td>
<td>1/1 (100%)</td>
<td>1/1 (100%)</td>
</tr>
<tr>
<td>Intravascular malignant lymphomatosis (1)</td>
<td>0/1 (0%)</td>
<td>0/1 (0%)</td>
</tr>
</tbody>
</table>
only complication observed was hemorrhage at the puncture. Glioblastoma was the histological diagnosis for the 2 patients with hemorrhage. The mortality rate was 2.1% (1 patient)—a 46-year-old woman diagnosed with a glioblastoma of the thalamus. The death occurred as a consequence of intracranial hemorrhage.

The concordance rate between final histopathological diagnosis, intraoperative histological diagnosis, and intraoperative cytological diagnosis is presented in Table 3.

The concordance rate between final histopathological diagnosis and intraoperative cytological diagnosis was 70.7% (29/41). The concordance rates by cytology type were: malignant lymphoma, 79.2% (19/24); diffuse astrocytoma, 33.3% (1/3); anaplastic astrocytoma, 66.6% (2/3); glioblastoma, 66.6% (6/9); and germinoma, 100% (1/1). A concordance rate could not be calculated for intravascular malignant lymphomatosis (0/1).

The concordance rate between final histopathological diagnosis and intraoperative histopathological diagnosis was 60.9% (25/41). The concordance rates by histological type were: malignant lymphoma, 79.2% (19/24); diffuse astrocytoma, 33.3% (1/3); glioblastoma, 44.4% (4/9); and germinoma, 100% (1/1). Concordance rates could not be calculated for anaplastic astrocytoma (0/3) or intravascular malignant lymphomatosis (0/1).

In 4 of 41 cases, cytology yielded better quality specimens for correct diagnosis than did histology (Figure 1). There were no cases for which intraoperative cytological diagnosis was inferior to intraoperative histopathological diagnosis in cases of anaplastic astrocytoma and glioblastoma.

Discussion

A histological analysis is important when the treatment of brain tumor is planned. Stereotactic brain tumor biopsy is appropriate even when lesions are located deep in the brain or within eloquent areas in the brain, where they are inaccessible by open surgery.

Conway et al. reported that stereotactic brain tumor biopsy is indicated for 1. lesions relatively inaccessible, 2. lesions accurately localized, or 3. "mass effect" minimal and reversible lesions.1 Patient factors indicating stereotactic biopsy include advanced age or patients who are prone to risks with general anesthesia.2 We enforced the use of stereotactic biopsy for patients with deep-seated brain tumors such as those in the basal ganglia, multiple lesions, or lesions with poor general appearance.

On the basis of the recent literature, stereotactic biopsy may provide the diagnoses in 91.7% to 99.3% of cases.3,6

Figure 1 A. Present the representative case which intraoperative cytological diagnosis was superior to intraoperative histopathological diagnosis.

Intraoperative histological diagnosis (gliosis H&E × 20)

There is no tumor cell in the specimen without gliosis.

Figure 1B. Intraoperative cytological diagnosis: Tumor cells with round nuclei existing surrounding vessels (Anaplastic astrocytoma)

Figure 1C. Final histopathological diagnosis: Tumor cells with round nuclei existing surrounding vessels (Anaplastic astrocytoma)
Our diagnostic rate was 87.2%. Our rate of tumor diagnoses was higher (97.8% [41/42]). Correct diagnoses of inflammatory and demyelinating diseases are difficult; this has lead to a decrease in our diagnostic rate. Our cases were not all easily distinguishable. The case of primary germinoma arising from the midbrain was diagnosed as multiple sclerosis for a long period of time, and the case of malignant lymphoma for which a differential diagnosis was Neuro-Behçet’s disease was also difficult to confirm.

Stereotactic biopsy has diagnostic value for the differential diagnosis of tumors. Although a histopathologic diagnosis could not be performed, there was a case in which it was diagnosed as an internal disease by both clinical symptoms and imaging. Therefore, even if a definite diagnosis is not made, it is important to be able to confirm the exclusion of brain tumor.

Yamada et al. reported that 91 biopsies using the Leksell stereotactic system were performed, in which the diagnosis was histologically confirmed in 84 cases (92.3%). The improved diagnostic rate gives rise to the view that the progress in image guidance systems has had a major influence on the improvement of the diagnostic rate. This technique enabled a more accurate approach to assess lesions; we, therefore, confirm that the rate of diagnosis improved. Jacobsen et al. reported that technical errors, incorrect choice of targets, heterogeneity of the tumor, tumor consistency, migration of masses away from the probe, and the tiny fragments of tissue in the biopsy itself can lead to a negative biopsy, either singly or in combination. The limitations of this technique include low quantities of specimen and frequent crushing of the specimens, making rapid intraoperative diagnostic yield difficult, consequently decreasing the rate of final diagnoses. Jain et al. investigated the correlation of stereotactic brain biopsy diagnostic yield with the number of biopsy bits and the site within the brain. The present study reported that stereotactic procedures involving multiple bits are associated with a high diagnostic yield.

Yamaguchi et al. reported that intraoperative photodynamic diagnosis using stereotactic fluorescence biopsy is useful for brain tumors. The existence of the tumor is likely confirmed by stereotactic fluorescence biopsy of a crushed specimen. Thereby, a better specimen can be submitted for histopathological diagnosis; and, thus, the diagnostic rate is most likely increased. Moreover, the frequency of repeated biopsies decreases, and the operating time will most likely be shortened.

The concordance rates between the final histopathological diagnosis and a rapid intraoperative diagnosis were high for malignant lymphoma. Because malignant lymphoma may primarily require radiotherapy and chemotherapy without extensive surgical intervention, this result is very important. However, the concordance rate was low for glioma. Because cytological details of glioma vary in a collected lesion, small specimens make diagnosis difficult.

When preservation of cellular form is insufficient, diagnosis of malignant lymphoma is difficult. Cytological preparations are, therefore, more suitable than frozen sections. There was no difference between frozen sections and cytological preparations in the present study with respect to the diagnosis of malignant lymphoma. This result is indeed evidence that the pathologists in our hospital are highly skilled in making frozen sections equivalent to permanent preparations. However, even expert pathologists cannot make correct diagnoses without proper sampling. Cytological preparations were superior to frozen sections in glioma; cytological preparations without freezing artifacts can preserve cytological detail. Katrina et al. reported that the advantages of using cytological preparations are that they are faster, simpler, and less expensive to prepare and require less equipment than frozen sections. Thus, using both intraoperative histological diagnosis and intraoperative cytological diagnosis concurrently can compensate for each technique’s limitations and contributes greatly to the accuracy of the final histological diagnosis.

In a review of a large series of stereotactic brain biopsies, the morbidity rate was reported to range from 2.9% to 5%. Yamada et al. reported that the Leksell system, as well as other stereotactic apparatus, was useful for diagnostic tissue sampling; we experienced no operative deaths and our morbidity rate was very low (1.1%). The main complication of hemorrhage occurs in approximately 2% to 8% of cases. Reported morbidities related to stereotactic brain biopsy include seizure, stroke, and infection. There have been few reports of metastasis along the stereotactic trajectory. Morbidity risks increase for deep-seated biopsies, malignant gliomas, and lymphomas. Other factors, such as a history of hypertension or diabetes mellitus, preoperative corticosteroid or antiplatelet agents, and a low (<150,000/mm³) platelet count have been shown to increase the bleeding risk. Shooman et al. reported that multiple sampling along a single trajectory captures appropriate histological specimens without aggravating the risk of intracranial hemorrhage. Our postoperative intracranial hemorrhage cases were subject to factors such as deep-seated biopsies and malignant glioma.

Most sites of intraoperative bleeding are capillary or
venous. Intraoperative bleeding can usually be easily controlled by the implementation of conventional methods, including cannula irrigation, head elevation, and induced hypotension. Kutlay et al. reported that the balloon compression technique that was useful in the management of persistent intraoperative bleeding could not be stopped by conventional methods of hemostasis. For cases in which hemorrhage cannot be controlled, the origin of hemorrhage cannot be confirmed in stereotactic brain biopsy under direct visualization. This is the disadvantage of this technique. If intraoperative bleeding cannot be stanched, craniotomy becomes necessary to staunch the bleeding. Craniotomy is, however, risky for seriously ill or elderly patients. When the lesions are deep-seated, there is a risk of normal brain injury. The prevention of bleeding is necessary before hand. Investigation into a simulation of the surgeon's view using an image processor would be indispensable. By performing simulation, we avoid injury to important structures, such as cerebral arteries or ventricles, and likely reduce complications.

References