Stereotaxic biopsy of intrinsic lesions of the brain stem

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Despite improved brain-stem imaging by magnetic resonance and high-resolution x-ray computerized tomography, definitive diagnosis and therapy of intrinsic lesions of the brain stem require histological verification. A stereotaxic approach to brain-stem lesions provides a high yield of positive histological diagnosis with a low incidence of morbidity. A series of 14 stereotaxic procedures performed on 12 patients with intrinsic lesions of the mesencephalon, pons, and medulla is reviewed. A detailed description of the transfrontal approach used by the authors is presented. Definitive pathological diagnosis was obtained in all patients. There was no operative mortality and only one case of permanent neurological deficit. The significance of accurate histological diagnosis in the therapy of brain-stem lesions is discussed.

KEY WORDS • brain stem • stereotaxic biopsy • glioma

MANAGEMENT of intrinsic brain-stem lesions is controversial. Empirical therapy continues to have advocates who warn of the hazards of biopsy as well as the assumed poor prognosis of the patient.3,11,19 Although high-resolution x-ray computerized tomography (CT) and magnetic resonance imaging (MRI) can precisely locate small brain-stem masses, definitive diagnosis and therapy require study of tissue.4,9 Very few brain-stem lesions can be resected successfully, and biopsy is necessary to prevent the possibility of inappropriate treatment.7

Open surgical approaches to the brain stem frequently provide negative or inadequate sampling of the lesion, although gross cystic lesions can be successfully decompressed by these techniques.10,13 However, open biopsy, whether by posterior fossa craniectomy or by subtemporal craniotomy, represents a major surgical procedure with attendant morbidity. The optimal surgical technique should provide a high diagnostic yield with low incidence of morbidity and mortality, and allow for decompression of cystic lesions. Computerized tomography-guided stereotaxic surgery has been a reliable and safe approach to diverse deep lesions of the brain.1,13 Since 1979, many descriptions of stereotaxic biopsy of mesencephalic and pontine lesions have been published.1,4,6,13,15,18 In this report, we present our experience with management of patients with mass lesions of the mesencephalon, pons, or medulla using a transfrontal stereotaxic approach. To our knowledge, a transfrontal approach to lesions of the medulla oblongata has not been previously reported. We discuss our surgical techniques and their advantages and potential complications.

Clinical Material and Methods

Twelve consecutive patients with mass lesions of the brain stem underwent 14 CT-guided stereotaxic procedures at the University of Michigan (Table 1). These cases were derived from a series of 64 patients who had a CT-guided stereotaxic biopsy or aspiration performed from January, 1984, through November, 1985. Six patients were female and six were male, with an age range from 3 to 67 years. All patients underwent preoperative cerebral angiography and high-resolution CT. Four patients had preoperative MRI. Eight lesions were located in the mesencephalon, three in the pons, and one in the medulla. These lesions were stereotaxically biopsied, and any cysts present were decompressed. A progressively enlarging cyst developed in two patients following radiation therapy for their brain-stem glioma. In one case (Case 3), a cannula for decompression was placed stereotaxically and was subsequently used for radioisotope instillation. Radioisotope was placed into the cyst at the time of stereotaxic surgical aspiration in a second patient (Case 12).

A Leksell stereotaxic frame was used with either a
Stereotaxic biopsy of brain-stem lesions

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Location of Lesion</th>
<th>Pathology</th>
<th>Postoperative Therapy</th>
<th>Survival or Follow-Up Period (mos)</th>
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<td>9</td>
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<td>2</td>
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GE 8800 or a 9800 CT/T scanning unit.* The CT scans consisted of 1.5-mm contiguous slices including the immediate region of the lesion with 5-mm sections to complete the scanning to the vertex. The more rostral scanning was needed for surgical planning. Reformatted coronal and sagittal images, including the center and lateral extents of the lesion, were obtained with the scanner software (Fig. 1). Patients were studied after bolus intravenous contrast infusion of 60% meglumine iothalamate (Conray 60). The CT scans were obtained in the radiology department and the patient was then moved to the operating room for the remainder of the procedure.

A transfrontal approach was used in all cases. The angle of trajectory was determined by analysis of the sagittal and coronal reformatted images (Figs. 1 and 2). Sagittal reconstruction was used to determine the lateral angle of the trajectory. A trajectory was planned lying parallel to and through the brain-stem axis. This approach traversed the lateral ventricle in most cases, with a risk of hemorrhage from damaged choroid plexus or subependymal veins; however, significant bleeding from these structures rarely occurs. Additionally, the basilar, posterior cerebral, and vertebral arteries, and the internal cerebral veins were visualized and thus avoided. The trajectory was planned to avoid the brain-stem surface and its pial vessels. The interpeduncular cistern must not be traversed for risk of damage to vessels supplying the midline brain stem. Coronal reformatting permitted visualization of the tentorial edge so that adjacent vascular and neural structures would not be damaged; it also facilitated calculation of the arc angle. Biopsy coordinates were determined by the Leksell CT coordinate scale and the CT scan software. The trajectory angles were measured directly from the reformatted CT images.

Surgery was performed under local anesthesia in eight patients; general anesthesia was necessary only in the four youngest children. Older cooperative children tolerated local anesthesia without difficulty. All stereotaxic procedures were performed in the Fowler position. A 7-mm diameter burr hole was utilized which permitted cauterization of the underlying dura and pia. Neurostimulation of the target was utilized which permitted avoidance of the underlying dura and pia. Unipolar stimulation at 5 and 50 Hz with a 1-msec pulse width to 10 V was performed through the entire trajectory of the lesion. A biopsy site was chosen where stimulation at 6 V resulted in no motor or sensory phenomenon.

A specimen of the lesion and cyst drainage were obtained through a 1.5-mm diameter cannula fitted with a stopcock. If this instrument failed to produce sufficient tissue, a 2.1-mm diameter cannula with a slotted aperture, 1 cm in length, was used. The results of frozen section examination determined if an additional specimen was required. If the center of the lesion was necrotic, the periphery was sampled to obtain viable tumor.

Results

Positive pathological diagnosis was obtained in all cases. High-grade astrocytoma was found in six patients, benign astrocytoma in four, and grade II to III astrocytoma in one. A vascular malformation was seen in one patient.

Radiation therapy prior to biopsy considerably increased the difficulty of obtaining diagnostic material

* Leksell stereotaxic frame manufactured by AB Elekta Instruments, Decatur, Georgia; CT/T scanning units manufactured by General Electric Medical Systems, Milwaukee, Wisconsin.
and grading astrocytomas in Cases 1, 2, 7, and 12. The average number of frozen sections required to assure diagnostic material in the previously irradiated group was $2.8 \pm 2.2$ (standard deviation) per case, while an average of $1.6 \pm 1.1$ frozen sections per case were necessary in nonirradiated patients. The nondiagnostic sections usually consisted of wholly necrotic material and less often of gliosis.

Previous irradiation and/or chemotherapy lessened our ability to reliably grade astrocytomas according to Kernohan’s classification. In the cases treated prior to biopsy, it was not always possible to differentiate spontaneous necrosis from radiation or drug-induced necrosis. Previous therapy also increased nuclear hyperchromasia and caused thickening of the vascular walls, adversely affecting assessment of other criteria of Kernohan, including nuclear pleomorphism and endothelial proliferation. When evaluating previously treated specimens of neoplasm, the most useful of Kernohan’s criteria were total cellularity and mitotic index. Hypercellularity of the vascular wall, as distinguished from thickening or necrosis of the wall, was sometimes helpful.

Permanent neurological deficit as a result of surgery occurred in one patient (Case 8). This 29-year-old woman presented with a 3-month history of progressive ataxia, dysphagia, dysarthria, lethargy, and quadriparesis, greater on the left than the right. Three days before surgery, following a generalized motor seizure, she became bilaterally decerebrate and required intubation. Twelve hours post-ictally she began to follow simple commands, but her neurological deficits progressed. A CT scan demonstrated a diffuse brain-stem mass. Stereotaxic biopsy for diagnosis was considered indicated because of the patient’s atypically rapid course. During surgery under local anesthesia, she developed increased spasticity of the left arm and leg. No hemorrhage was present on a postoperative CT scan, and the deficit was attributed to excessive manipulation. Progressive neurological deterioration continued in the postoperative period despite radiation therapy, and the patient died 1 month later.

Transient neurological deficit occurred in one patient (Case 10). This 34-year-old man presented with a 2-month history of paresthesias of the left arm and both legs, dysarthria, left arm paresis, and ataxia. Immediately after the biopsy, the patient’s neurological examination was unchanged. Approximately 10 minutes later, the patient reported increased left hemiparesis. Postoperative CT scanning revealed a small hemorrhage into the tumor. The patient was treated with increased corticosteroids and progressive improvement was ob-
served. His neurological status returned to the preoperative level in 3 weeks.

Aspiration of liquefied necrosis in a cystic tumor resulted in neurological improvement in two patients (Cases 3 and 12). In Case 3, the patient presented with a cystic mass which was decompressed at the time of biopsy with reduction of neurological symptoms occurring 2 days after surgery. Since the patient had been treated with dexamethasone for 1 week preoperatively, the improvement was not considered secondary to steroids. Following radiation therapy the cyst recurred. A Holter ventricular cannula was placed stereotactically via a transfrontal approach and the cyst was decompressed. A Rickham reservoir was attached to the cannula. The patient improved and was discharged. Frequent percutaneous aspirations were necessary and it was elected to instill a radioactive chromic phosphate-32 ($^{32}$P) suspension to obliterate the cyst. After this interstitial therapy, the cyst size remained stable on CT scanning until her death 4 months later from tumor progression. In the second case (Case 12), the patient developed an enlarging pontomesencephalic cyst with hemiparesis following empiric radiation therapy for a brain-stem lesion. At the time of biopsy 2 cc of proteinaceous fluid was aspirated, and neurological improvement was seen 1 day postoperatively. Two weeks later, neurological deterioration recurred and a follow-up CT scan demonstrated that the cyst had increased 1.5 times in volume from its preoperative size. At that time, radioactive $^{32}$P suspension was placed into the cyst after repeat stereotaxic aspiration. The patient's hemiparesis again improved, and repeat CT scans have shown a stable cyst size for 2 months.

Four patients had preoperative ventriculoperitoneal shunting. One patient (Case 9) required intraoperative ventriculostomy. The ventriculostomy tube was removed 3 days postoperatively and the patient did not require subsequent shunting.

Outcome has correlated well within the histological grade of the tumor. Patients with benign astrocytoma have remained stable or improved. Four patients with high-grade astrocytomas died between 1 and 9 months following surgery. The two surviving patients with high-grade astrocytomas have had clinical and radiographic evidence of tumor progression. The single patient with a nontumor diagnosis (Case 2) had a lesion pathologically consistent with a vascular malformation in the mesencephalon. His preoperative course consisted of acute deficits followed by stabilization or improvement lasting 13 months. Although his preoperative angiography failed to demonstrate a vascular lesion, the surgical specimen revealed large numbers of arterioles and venules with surrounding hemosiderin indicative of old hemorrhage. He developed acute right arm and face hypesthesia and increased hemiparesis 3 months after operation. This late deterioration is not believed to be related to the surgical procedure. Aside from the slight focal loss of substance from biopsy, the postoperative CT scan was identical to the preoperative CT appearance which had been stable for 3 years.

**Discussion**

Even though high-resolution CT and MRI provide excellent sensitivity and topographic relationships of small brain-stem lesions, definitive diagnosis and therapy require accurate pathology. No imaging technique to date provides this information. Diagnostic errors and complications of inappropriate empirical therapy are well documented. Neurosurgical approaches to brain-stem masses have included the transcaldosal, subtemporal retromastoid, supracerebellar subtentorial, and suboccipital techniques. $^{2,7,10,17,18}$ Although recent series of patients subjected to open biopsy demonstrate low incidences of morbidity and mortality, a high rate of nondiagnostic tissue was obtained. $^{10,13}$ Since many lesions do not present at the surface, surgeons are often reluctant to dissect deeply into the brain stem and therefore fail to obtain an accurate specimen.

The prognosis for patients with brain-stem tumors appears to depend on the tumor grade. $^{13,16}$ In the case of gliomas, four patients in our series with high-grade astrocytoma died between 1 and 9 months following surgery. Although many reports have documented the relationship of survival to grade of glioma, most treatment protocols of these lesions do not require histological diagnosis and frequently cannot reach a statistically valid conclusion. $^{5,10,12,13}$ Since stereotaxic biopsy can provide histological specimens with a low complication rate, this procedure should be considered for all patients entering therapy studies.

The transfrontal approach permits a route to all divisions of the brain stem, and minimizes the risk of pial surface hemorrhage. Sagittal and coronal CT reformatted images of the brain stem permit rapid determination of a trajectory that avoids midline, tentorial, and brain-stem vascular structures. Most lesions are not confined to one division and infiltrate along the brain-stem axis, and the transfrontal approach allows tissue sampling at various depths along this axis. The ability to biopsy the center of a brain-stem lesion as well as the periphery should reduce sampling error. $^{14}$ Other stereotaxic trajectories to the brain stem are the transtentorial and transcerebellar routes. $^{1,4,6}$ We have not used the transventricular route so as to avoid the risk of hemorrhage at the pial surfaces of the cerebellum or mesencephalon. The transcerebellar route has been advocated for the lateral pons or cerebellar peduncle; however, general anesthesia is required, and deeper sampling along the brain-stem axis is not possible with this approach. With local anesthesia in a cooperative patient, the transfrontal approach can safely be used to reach the mesencephalon, pons, and medulla.

Neurostimulation of the biopsy site was an integral aspect of the surgical technique. Responses to stimulation included contralateral tonic or clonic movement,

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Neurostimulation of the biopsy site was an integral aspect of the surgical technique. Responses to stimulation included contralateral tonic or clonic movement,
paresthesias, tonic gaze deviation, spontaneous laughter, and fear accompanied by nausea. In three cases, the biopsy site was changed when stimulation at low voltage resulted in motor or sensory phenomena. Negative stimulation to 6 V was used to define the range of the trajectory considered safe for biopsy. In order that the maximum information might be obtained from neurostimulation techniques, use of general anesthesia was restricted to young children who would not cooperate under local anesthesia.

Two patients had craniofacial radiation therapy 18 and 19 years prior to stereotaxic biopsy for unrelated lesions. The therapy ports included the brain stem. The preoperative CT scans in both patients demonstrated diffuse infiltrative intra-axial brain-stem lesions. Since additional irradiation was potentially hazardous because of the risk of radiation necrosis, histological verification was considered essential. Both patients experienced rapid progression of their tumor despite aggressive postoperative radiation therapy. It is interesting to note that our only incidence of morbidity occurred in these patients. Radiation therapy may cause dystrophia and easily traumatized friable tissue and thus predispose to complications.

Case 2 demonstrates one of the hazards of empirical treatment in an unbiopsied patient. This 31-year-old man had been diagnosed as having brain-stem glioma based on CT scans and clinical presentation 3 years before his admission for stereotaxic biopsy. Completion of radiation therapy and chemotherapy was followed by marked deterioration, necessitating nursing care for 1 year. The patient and family were warned of a poor prognosis; however, the patient improved and stabilized. The appearance of a resting tremor 3 years later led to reevaluation. Stereotaxic biopsy revealed tissue consistent with a vascular malformation without evidence of neoplasm. This case reinforces the need for histological examination before initiating therapy. Definitive diagnosis by stereotaxic biopsy at presentation would have significantly altered his therapy, prognosis, and perhaps the resultant morbidity.

Since resectable tumors of the brain stem are uncommon, the surgical goal for most lesions is biopsy and/or cyst decompression. A CT-guided stereotaxic brain-stem biopsy provides better diagnostic yield, comparable and perhaps even improved morbidity, and equivalent cyst decompression capabilities when compared to open surgical approaches. Definitive pathological diagnosis avoids the complications of inappropriate therapy, provides valuable prognostic information, and can direct statistically meaningful research into innovative therapy techniques. A CT-guided stereotaxic biopsy should be considered in the treatment of all intrinsic brain-stem lesions.

References


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