Combined magnetic resonance imaging– and positron emission tomography–guided stereotactic biopsy in brainstem mass lesions: diagnostic yield in a series of 30 patients

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In the management of brainstem lesions, the place of stereotactic biopsy sampling remains debatable. The authors compared the results of magnetic resonance (MR) imaging, positron emission tomography (PET), and histological findings obtained in 30 patients who underwent an MR image– and PET-guided stereotactic biopsy procedure for a brainstem mass lesion.

Between July 1991 and December 1998, 30 patients harboring a brainstem mass lesion underwent a stereotactic procedure in which combined MR imaging and PET guidance was used. Positron emission tomography scanning was performed using [18F]-fluorodeoxyglucose in 16 patients, methionine in two patients, and with both tracers in 12 patients. Definite diagnosis was established on histological examination of the biopsy samples. Interpretation of MR imaging findings only or PET findings only were in agreement with the histological diagnosis in 63% and 73% of cases, respectively. Magnetic resonance imaging and PET findings were concordant in 19 of the 30 cases; in those cases, imaging data correlated with histological findings in 79%. In seven patients who underwent one PET-defined and one MR imaging–defined trajectory, at histological examination the PET-guided samples were more representative of the tumor’s nature and grade than the MR imaging–guided samples in four cases (57%). In 18 patients PET scanning was used to define a biopsy target and provided a diagnostic yield in 100% of the cases.

Although the use of combined PET and MR imaging improves radiological interpretation of a mass lesion in the brainstem, it does not accurately replace histological diagnosis that is provided by a stereotactically obtained biopsy sample. Combined information provided by MR imaging and PET in stereotactic conditions improves the accuracy of targeting and the diagnostic yield of the stereotactically biopsy sample; an MR imaging– and PET-guided stereotactic biopsy procedure is a safe and efficient modality for the management of mass lesions of the brainstem.

KEY WORDS  •  positron emission tomography  •  brainstem  •  stereotaxy  •  biopsy  •  neoplasm

The management of brainstem mass lesions remains controversial; particularly when the lesion cannot be removed and is of an infiltrating nature, the benefit of a stereotactic procedure is still debatable.16,17,23 One objection to performing a brainstem stereotactic biopsy procedure is that it may not be reliable because the tumor may be heterogeneous.13,26 Moreover, this heterogeneity often necessitates multiple sampling, which may be dangerous in the brainstem. Some authors also contend that obtaining histological diagnosis of brainstem tumors by a biopsy procedure is not necessary in most cases because of the effectiveness of modern cerebral imaging modalities, especially MR imaging.23 In that respect, PET scanning may also be of interest, as this imaging technique provides independent metabolic information that may be helpful in determining the nature and aggressiveness of brain tumors.11,12 However, for some authors, obtaining a stereotactic biopsy sample of brainstem mass lesions remains the best diagnostic procedure because a presumptive diagnosis based on MR imaging findings alone may lead to inaccurate diagnosis and, more importantly, erroneous treatment.4

In several recent studies the authors have encouraged the use of PET scanning during stereotactic brain biopsy procedures to increase reliability of sampling by optimiz-
ing target selection. Since 1991, we have routinely incorporated PET in our planning of stereotactic biopsy sampling of cerebral tumors. To determine the additional value of PET we evaluated the use of combined PET/MR imaging in 30 patients in whom stereotactic biopsy samples of a brainstem lesions were obtained.

Clinical Material and Methods

Between July 1991 and December 1998, 30 patients with a brainstem mass lesion underwent a stereotactic procedure in which combined PET/MR imaging guidance was used. Patient age varied between 4 and 78 years (median 43 years); four patients were younger than 18 years of age (Table 1). The male/female ratio was 14:16. Symptoms consisted of walking disturbances in 22, visual impairment in 13, signs of intracranial hypertension (headache, nausea, and drowsiness) in 11, dysphagia or dysarthria in eight, and hemiparesis in six. The lesion was centered on the midbrain in 12 patients, the pons in 14, and the medulla in four patients; associated obstructive hydrocephalus was present in five patients (two children and three adults) and was treated by ventriculostomy or placement of a ventriculoperitoneal shunt in three and two cases, respectively. The PET-guided biopsy procedure was in accordance with the ethical guidelines of our institution.

Magnetic resonance imaging and PET studies were performed in stereotactic conditions to obtain data for the planning of the stereotactic procedure; details of the methods used for such data acquisition and planning have been previously described. Positron emission tomography scanning was performed with FDG in 16 patients, with MET in two patients, and with both tracers in 12 patients. Briefly, a carbon fiber head ring unit was attached to the patient’s head in a normal or inverted position after induction of a local anesthesic; MR imaging followed by PET scanning was performed using a four-plate localizing system, with either MR-enhancing or [18F]-fluoride solution fiducials, fixed on the base ring and generating a 12-mark referential on MR and PET slices. Surgical planning was then performed. The target was selected as the center of the zone at which abnormal metabolism was demonstrated on PET after the image was projected onto the corresponding stereotactic MR slice. In some cases two trajectories were performed to account for the discordance between MR imaging and PET. The surgical aspect of stereotactic biopsy procedure was performed in the operating room after induction of a general anestheis. Based on the location of the lesion within the brainstem, we performed a transfrontal or transcerebral approach, as described by Coffey and Lunsford.

For the purposes of data analysis, we retrospectively reviewed the PET and MR imaging protocols made before

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<th>Case No.</th>
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HM = high malignancy; LM = low malignancy; — = not performed.
obtaining the biopsy sample (and therefore independently of histological determinations), and the results of histological analysis of the biopsy specimen. For MR imaging, when more than one diagnosis was suggested, only the most likely was considered (Table 1), which should be the case for the management of this lesion when biopsy samples are not obtained. We used PET scanning to indicate the degree (high or low) of tumor malignancy, as shown in Table 1. We first examined the results of each imaging modality separately and compared them with histological diagnoses to define the percentage of accurate data provided by PET alone or by MR imaging alone. We then compared the results of PET with MR imaging analysis and separated patients in two groups according to the agreement or disagreement between MR and PET findings. In the group in which there was discordance between PET and MR imaging interpretations, we determined which of those two imaging modalities provided correct information about the lesion’s histological type. In cases in which there were concordant PET and MR imaging interpretations, we compared those data with histological findings to calculate the diagnostic yield of the combination of those two imaging modalities. The diagnostic yield of PET-only and/or MR imaging-only findings was evaluated to determine the superiority or complementary role of PET (Table 2).

Results

Based on the location of the tumor within the brainstem, the stereotactic biopsy sample was obtained via a transfrontal approach in 12 and a transpontine approach in 18 patients. A total of 40 trajectories were performed in the 30 patients: three trajectories aimed at cyst aspiration and 37 biopsy trajectories (1.23 ± 0.43 [mean ± standard deviation] biopsy trajectories per patient). Until 1995, two trajectories were performed when there was a discrepancy between PET- and MR imaging–based targeting data as part of the prospective study previously published. More recently, because PET data have been shown to improve the diagnostic yield of biopsy, we have endeavored to perform only one trajectory to lower the risks of the procedure. A precise histological diagnosis was established in all patients, and diagnosis was confirmed by the patient’s clinical course. There were 18 gliomas, including nine glioblastomas, five anaplastic astrocytomas, and four low-grade gliomas; other lesions included three metastases, two lymphomas, one leukemic infiltration, one ependymoma, one gangliocytoma, one pineoblastoma, and three inflammatory lesions (one isolated central nervous system vasculitis and two cerebral infections).

Information provided by PET, MR imaging and histological examination in all patients is shown in Table 1. If we consider only one factor—detection of malignancy—MR imaging findings correlated with histological results in 19 patients, and PET results correlated with histological findings in 22 patients (Table 2). In the comparison between MR imaging and PET data obtained in each patient we found discordant results between the two modalities in 11 patients (37%). In cases in which there was discordance between MR and PET data, MR imaging findings were in agreement with histological findings in four and PET in seven cases. In only 19 patients (63%) were MR imaging and PET data concordant; in this group, there was correlation between imaging and histological results in 15 cases (79%).

Our series also included four pediatric patients who ranged in age from 4 to 14 years (average 10.75 years). In our department, we do not often obtain biopsy samples of brainstem lesions in children because MR imaging can provide adequate data to define a specific therapeutic course in most cases. In the four children included in our series biopsy samples were obtained because the tumor grade could not be definitely established on MR imaging. In these four children, the most likely diagnosis based on MR imaging findings was erroneous in all cases. The tumor grade as determined on PET scanning, was in agreement with histological results in two cases (50%).

In 18 patients we preferred to use PET for defining the biopsy target because PET outlined a high metabolic area either inside the tumor area, as defined on MR imaging, or near the area of gadolinium enhancement. In these 18 patients, the diagnostic yield of the image-guided biopsy procedure was 100%. In seven patients MR imaging and PET studies revealed two different target areas for biopsy; in those cases we performed one PET- and one MR imaging–defined trajectory. Histologically, in seven patients, the PET-guided biopsy samples were more representative of the tumor’s nature and grade than the MR imaging–guided samples in four cases (57%).

The benefit of obtaining biopsy samples is illustrated by the results in one patient (Case 29), whose neuroimaging studies are shown in Fig. 1. This patient was shown to harbor a nonenhancing lesion of the midbrain on MR imaging: FDG-PET revealed hypometabolism within the tumor area. This information led us to a presumptive diagnosis of low-grade glioma. However, because anaplastic foci were found at histological examination, the definite diagnosis was anaplastic astrocytoma. We initiated appropriate radio- and chemotherapy. Another example is illustrated in the patient in Case 15 (Fig. 2); because this patient harbored a large brainstem lesion that was highly enhanced on MR imaging after administration of gadolinium, the lesion was therefore suspected to be a high-grade glioma. The absence of uptake of FDG and MET demonstrated on PET indicated a diagnosis of low-grade tumor. Histological examination of the MR imaging– and PET-guided stereotactic biopsy sample confirmed the diagnosis of Grade II fibrillary astrocytoma.

To estimate the safety of performing such a biopsy procedure in the brainstem, we reviewed the mortality and
morbidity rates associated with this procedure. In our series, no patient died as a result of the procedure. Two patients experienced a transient worsening of their preoperative neurological deficits, but no patient suffered permanent postoperative deficit.

Discussion

Management of Mass Lesions of the Brainstem

The management of mass lesions of the brainstem remains controversial. Although the use of image-guided stereotactic brain biopsy is regarded as a safe and reliable procedure for the management of supratentorial lesions, its application in lesions involving the brainstem remains limited. Recent progress in modern neuroimaging techniques, especially high-resolution MR imaging, allows us to determine more precisely the location and extension of brainstem tumors, and it may provide some specific characteristics of their nature. Hence, the challenge is to know whether the use of MR imaging alone is precise enough to provide an accurate diagnosis, or at least to allow for classification of patients into specific treatment groups, and, consequently, if a pathological diagnosis is still mandatory before initiating any therapy. In this context, PET may play an additional role that will help in such decision making.

PET as a Diagnostic Tool for Mass Lesions of the Brainstem

Many authors have illustrated the good correlation between tumor grade and tumor metabolism as measured by PET, both with FDG or methionine as markers. In many studies good correlation between the tumor grade and the PET-determined metabolism of cerebral gliomas has been demonstrated. Hypermetabolic areas observed on PET scans correspond to malignant components of these heterogeneous tumors. In other series the authors have also found a direct relation between PET-defined metabolism and prognosis. The use of PET may provide similar information concerning brainstem mass lesions that it does for supratentorial tumors. Actually, there is sparse information reported on PET-defined metabolism of brainstem tumors in the literature. In a study of brainstem metabolism in normal and pathological cases, Di Chiro, et al. have found the same relation between tumor grade and glucose metabolism on PET studies in brainstem tumors as in those of the hemisphere. Analysis of their results emphasizes the presence of regional metabolic differences in most brainstem tumors, reflecting the malignant heterogeneity of glioma in the brainstem. In some case reports the results underscore the superiority of PET over MR imaging for brainstem tumors in demonstrating discrete tumor progression into the brainstem, as well as PET’s superior ability to differentiate tumor progression from postirradiation edema or necrosis.

The data derived from our series of 30 image-guided stereotactic procedures in which biopsy samples were obtained of brainstem mass lesions indicate that the degree of malignancy of the tumor is more accurately estimated using PET than MR imaging (73% and 63%, respectively). However, information provided by PET is mainly limited to what it indicates regarding the degree of malignancy and does not demonstrate the nature of tumor.

Fig. 1. Case 29. A nonenhancing lesion of the midbrain was revealed on MR imaging; FDG-PET demonstrated hypometabolism within the tumor area. Upper Left: T1-weighted MRI image. Upper Right: Fast fluid attenuated inversion–recovery MR image. Lower Left: T2-weighted MR image. Lower Right: An FDG-PET scan. The stereotactic biopsy target is shown on the T1-weighted MR image and FDG-PET scan.

Fig. 2. Case 15. This patient harbored a large brainstem lesion that became highly enhanced on MR imaging after injection of gadolinium; it was therefore suspected to be a high-grade glioma. Due to the lack of FDG and MET uptake on PET, a diagnosis of low-grade tumor was suspected. Upper Left: Nongadolinium-enhanced MR image. Upper Right: Gadolinium-enhanced MR image. Lower Left: An MET-PET scan. Lower Right: An FDG-PET scan.
or its precise location, as does MR imaging. Therefore, we find that PET- and MR imaging–defined data are complementary in the management of brainstem tumors. In this series, when these two complementary modalities provided concordant data, the diagnostic yield of cerebral imaging was increased up to 79%. However, in 43% of the patients MR imaging and PET provided discordant findings, and in four patients unexpected histological results were demonstrated despite the correlation of MR and PET data; therefore, the need for obtaining a histological diagnosis by performing a stereotactic biopsy procedure before initiating therapy remains, in our opinion, essential.

Use of PET as a Localizing Tool for Stereotactic Biopsy

In most series found in recent literature, conventional computerized tomography– or MR imaging–guided stereotactic biopsy sampling of brainstem lesions yielded appropriate results in 90 to 95% of cases. In this series, the MR imaging– and PET-based stereotactic biopsy allowed us to make precise histological diagnoses in all patients. The incorporation of PET in the stereotactic planning allows us to better define the appropriate target at which to obtain the biopsy sample and, therefore, to increase the diagnostic yield. Moreover, because better targeting will decrease the number of biopsy trajectories and samples, the risk of injuring the brainstem will be reduced.

We have demonstrated in our series that in some cases the biopsy target was more accurately defined on PET than MR imaging and that it increased the diagnostic yield of the biopsy procedure. These results are in accordance with those reported in our previous prospective study in which we demonstrated that, for stereotactic biopsy of cerebral tumors, the inclusion of PET in the biopsy planning procedure will provide better targeting. In this study, most PET scanning has been performed using both FDG and MET tracers in a prospective manner so as to allow for analysis of information provided by each tracer; the results of our study have been published recently and demonstrate the close correlation and complementary role of FDG and MET for target selection in stereotactic brain biopsy procedures.

Conclusions

In this study, we have demonstrated that although the use of MR imaging and PET improves the diagnostic yield of brainstem mass lesions, cerebral neuroimaging alone is unable to provide in all cases sufficient information on brainstem tumors to specify adequately the required treatment without histological examination. A PET- and MR imaging–stereotactic procedure in the brainstem is a low-risk and accurate procedure that permits pathological diagnosis before initiating the appropriate treatment.

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