Neurosurgical forum
Letters to the editor

Pontine Tumors

Abstract

Object. Empirical radiotherapy is the current treatment for children with diffuse pontine lesions that have imaging characteristics of an infiltrative malignant astrocytoma. The use of chemotherapeutic agents is, however, currently under investigation in the treatment of these tumors. To be included into a trial, patients need a definitive histological diagnosis. The authors present their prospective study of the stereotactic biopsy of these lesions during a 4-year period.

Methods. A suboccipital, transeferrubellar approach was used to obtain biopsy samples in 24 children.

Results. Two patients suffered deficits. Both had a transient (<2 months) new cranial nerve palsy; one of these patients also experienced an exacerbation of a preoperative hemiparesis. No patient died during the perioperative period. A histological diagnosis was made in all 24 patients as follows: 22 had a malignant infiltrative astrocytoma, one had a low-grade astrocytoma, and one had a pilocytic astrocytoma. The diagnosis of the latter two patients affected the initial treatment after the biopsy.

Conclusions. The findings of this study imply that stereotactic biopsy sampling of a diffuse pontine tumor is a safe procedure, is associated with minimal morbidity, and has a high diagnostic yield. A nonmalignant tumor was identified in two of the 24 patients in whom the imaging findings were characteristic of a malignant infiltrative astrocytoma. With the advent of new treatment protocols, stereotactic biopsy sampling, which would allow specific tumor characterization of diffuse pontine lesions, may become standard.

To THE EDITOR: I read with great interest the recent article written by Roujeau et al. (Roujeau T, Machado G, Garner MR, et al: Stereotactic biopsy of pontine lesions in children. J Neurosurg [1 Suppl Pediatrics] 107:1–4, July, 2007). The purpose of the authors’ study was to demonstrate that stereotactic biopsy sampling of a diffuse pontine tumor is a safe procedure associated with minimum morbidity. I wish, however, that their article had given us more information about the prognostic utility of the biopsy samples. The specific information that readers of the journal would like to know is whether the patients with benign disease had a benign course and whether knowing the pathology in the biopsy sample made a difference in patient treatment and outcome. The authors mentioned that 10 of their patients were still alive after a follow-up period ranging from 0.2 to 2.1 years, but in fact the paper does not mention survival related to biopsy diagnosis, and the relatively long survival rate for these 10 patients, most of whom must have had malignant tumors, is unexplained. In other words, this paper demonstrates that biopsy of diffuse pontine tumors is safe but does not demonstrate that the biopsy has clinical utility. The authors mentioned the possibility of sampling errors, and I would be very interested in learning whether the two patients with benign tumors fared better than the rest of the patients in the series—or if in fact the pathology was irrelevant to their clinical course.

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To THE EDITOR: In a recent article (Roujeau T, Machado G, Garnett MR, et al: Stereotactic biopsy of pontine lesions in children. J Neurosurg [1 Suppl Pediatrics] 107:1–4, July, 2007), Roujeau et al. reported their experience with stereotactic biopsy sampling of diffuse pontine lesions in children. We read this paper with great interest and we offer some commentary that may be helpful for the authors.

The authors have to be congratulated for their prospective study of 24 children who underwent stereotactic biopsy of a diffuse brainstem lesion. It has been traditionally believed that diffuse brainstem lesions (especially diffuse pontine lesions) should be treated empirically by radiotherapy, leaving almost only dorsally exophytic tumors suitable for surgery. These lesions are supposed to be astrocytomas, most of them being high-grade gliomas with an average overall survival of <1 year. In fact, this situation led to a very poor understanding of these malignant tumors and especially of their biological behavior. A better understanding of this biology could certainly be useful for defining more effective treatment strategies than the current ones. In that sense, diffuse pontine lesions deserve special interest.

There are a few points of concern, however, that we would like to offer for discussion. Little is mentioned about the possibility of these children benefiting from non- (or less) invasive methods of diagnosis. For example, magnetic resonance spectroscopy is able to distinguish different degrees of malignancy (from low to high grade) in childhood brainstem tumors by determining choline/creatine, choline/N-acetylaspartate ratios, lipid and lactate levels, and even if the neurosurgeon is faced with atypical diffuse pontine lesions. In these latter series, although small or retrospective, the benefit of this noninvasive method is of no doubt. Even FDG–positron emission tomography studies may help in differentiating anaplastic/high-grade gliomas in pediatric brainstem gliomas. Some single photon computed tomography studies, although probably less interesting, may be useful tools for evaluation of these children. One may argue that all these methods can be associated with one another to better and much more safely assess the grading of a brainstem tumor.

In fact, one of the rationales for the use of stereotactic biopsy of brainstem lesions is the “fear” of overdiagnosing benign lesions, leading to potentially dangerous overtreatment of indolent lesions. Here again, two comments have to be made. On the one hand, it is true that the diagnosis of a brainstem pilocytic astrocytoma is sometimes very difficult to establish with only neuroimaging data. Nevertheless, pilocytic astrocytomas almost always exhibit a massive contrast enhancement on computed tomography and magnetic resonance (MR) scans (which is the case in Fig. 3). This massive contrast enhancement is very different from that sometimes seen with malignant lesions, and it is surprising that this diagnosis was not discussed before biopsy.

On the other hand, in terms of prognosis, the fact that a pontine lesion could be a low-grade astrocytoma (Grade II astrocytoma) does not seem to make the prognosis less devastating. This was not pointed out as such in the article.
Moreover, we are very interested in the follow-up course of the patient whose MR image is shown in Fig. 2 as—even if the pathological diagnosis is one of a low-grade glioma—there are sufficient arguments to suspect this lesion was a higher-grade lesion (pons location, diffuse lesion, hypointense signal on T1-weighted images, presence of an area of Gd enhancement). One must always bear in mind that biopsy sampling may lead one to underdiagnose the severity of a tumor. This can not be excluded because only small biopsy samples can be obtained and samples are not always representative of the whole tumor.

The authors concluded that the procedure was associated with “minimal morbidity.” In this series, the immediate postoperative morbidity (described here as a new neurological deficit) was as high as 8.3%, which is still much higher than the morbidity rate of stereotactic biopsy performed for supratentorial tumors. Do we have the right to increase the risk of morbidity for these patients with incurable disease? Nevertheless, if one thinks that biopsy is mandatory in selected cases, diffusion tensor imaging seems to be a promising tool in allowing a better recognition of motor, sensory, and transverse pontine tracts, which could yield a better characterization of the target.

The article seems to us sometimes very directive, up to the conclusion and the assessment that this method “may become standard.” This seems to us not really acceptable in these terms. Obviously, stereotactic biopsy of diffuse pontine lesions in children may be considered again if patients benefit from very targeted treatments ( radiosensitizers, anti-epidermal growth factor receptor [EGFR], and anti–vascular endothelial growth factor [VEGF]) and for whom there may be a need for histological evidence and a study of EGFR expression, VEGF expression, and loss of PTEN before treatment.

One of the key points is that, because molecular characterization of these tumors is still lacking and may be useful, one should always propose autopsy to the family at the time of a patient’s death. In conclusion, stereotactic biopsy of diffuse pontine lesions in children appears to be neither safe nor to be recommended as a gold standard. In our opinion, biopsy should be discouraged in this situation. It is of paramount importance that research on these tumors be safely managed.

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References

To the Editor: I read with interest the article by Roujeau et al. (Roujeau T, Machado G, Garnett MR, et al: Stereotactic biopsy of pontine lesions in children. J Neurosurg [1 Suppl Pediatrics] 107:1–4, July, 2007). While I appreciate the therapeutic utility for tissue sampling with respect to novel biological treatment modalities, one needs to be careful in the interpretation of the study results. This article further supports the notion that histological sampling for diagnostic purposes is not required and, in fact, should be discouraged in children with typical clinical and imaging presentations of diffuse pontine glioma. Although 2 (8.3%) of 24 patients had a diagnosis other than a diffuse malignant brainstem tumor, these 2 cases are in need of further discussion.

First, the MR image in Fig. 3 has neuroimaging characteristics that are not in keeping with diffuse pontine glioma, and hence the diagnosis of juvenile pilocytic astrocytoma may have been predicted. Second, no details were provided regarding time to progression or ultimate outcome in the patient whose MR image is shown in Fig. 2. The eventual disease progression and requirement for radiotherapy probably indicate some element of diagnostic sampling error. Thus, I would conclude that although the paper again supports the safety of diagnostic sampling in patients with suspected diffuse pontine gliomas, it also underscores the accuracy of the clinical and neuroimaging diagnosis and further supports the notion that these children should not be subjected to diagnostic sampling on a routine basis. Last, the expertise of these authors in no doubt contributed to the low rate of morbidity and should highlight that this procedure should not be considered to be routine or requisite in the management of diffuse pontine gliomas in children.

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Response: We would like to thank Drs. Souweidane, Scott, and Klein and their colleagues for taking an interest in our work.

At our institution, all children presenting with diffuse