Biopsy of diffuse intrinsic pontine gliomas?

JAMES T. RUTKA, M.D., PH.D., F.R.C.S.C.

Division of Neurosurgery, Department of Surgery, The University of Toronto, Ontario, Canada

The authors have performed an important study in which 7 patients with diffuse intrinsic pontine gliomas (DIPGs) underwent biopsy at their institution. These cases were selected from a total of 54 involving patients with pontine tumors who presented to their institution since 2004. The cases in which biopsy was performed were deemed “atypical” in terms of neuroimaging findings. Of these, 2 were shown by neuropathological examination and hierarchical cluster analysis to be cases of pontine primitive neuroectodermal tumors (PNETs), which were treated in a different manner from DIPGs—with aggressive chemotherapy and tandem autologous stem cell transplant in conjunction with radiation therapy.

In 2006, Zagzag et al. 2 reported on 7 cases of brainstem tumors that were proven to be PNETs on the basis of biopsy. In their series, the brainstem PNETs occurred in younger children and were primarily focal lesions in contrast to the DIPGs. However, this report raised the specter that not all intrinsic brainstem lesions in children are DIPGs, and that biopsy in select circumstances would be warranted.

In the current report, Sufit et al. 1 have used the Affymetrix U133 Plus 2.0 GeneChip microarray to examine the 7 brainstem cases in which biopsy specimens were obtained, and have compared these results against those for other pediatric brain tumors, including medulloblastoma, atypical teratoid/rhabdoid tumor, ependymoma, and ganglioglioma to name a few. Their cluster analysis shows that pontine PNETs have a similar genetic profile to supratentorial PNETs, but a different profile, for the most part, from DIPGs. It should be noted that some of the histologically confirmed DIPGs clustered closely to the pontine PNETs.

Why is this study important? It is important because we are approaching an era in which molecular studies of biopsy specimens from brain tumors can be used to help select or validate the use of subsequent therapies, as was shown in the 2 cases of pontine PNETs in which biopsy was performed here. The issue of whether biopsy specimens should be obtained in pontine lesions with atypical DIPG neuroimaging characteristics is becoming less controversial. At our institution, children with pontine tumors undergo biopsy if they have atypical neuroimaging or clinical features. It would be reasonable to perform biopsies of typical DIPGs within the context of a well-defined and structured clinical trial in which molecular analyses are being performed to advance our working knowledge of the genetic origins of these tumors. Biopsy can be performed, as demonstrated in this case series, with acceptable morbidity.

Future studies of brainstem biopsies may take advantage of the latest Affymetrix Gene 1.1 ST array, which “tiles” across the entire transcript, as opposed to the U133 Plus 2.0 GeneChip array, in which the probes were designed to hybridize to the 3′ end of the transcript. These newly designed gene arrays may provide a more robust characterization of the genetic profile of brainstem tumors in children.

Disclosure

The author reports no conflict of interest.

References

Response

MICHAEL H. HANDLER, M.D.,1 ALEXANDRA SUFIT, B.A.,2 AND NICHOLAS K. FOREMAN, M.B.CH.B.2

1Division of Pediatric Neurosurgery, Department of Neurosurgery, and 2Division of Neuro-Oncology, Department of Pediatrics, The Children’s Hospital of Colorado, University of Colorado, Aurora, Colorado

We appreciate the perspective that Dr. Rutka brings to our work. At our institution, we perform biopsies in all cases of atypical DIPGs and have seen our criteria for typicality become more stringent over the years. This has resulted in an increased acquisition of biopsy material, upon which this study was based. We have argued for more aggressive use of biopsy even in cases of typical DIPGs to allow understanding of these tumors in the context of contemporary neurooncology.1 We have begun to perform biopsies in cases of typical DIPGs as part of a national trial to provide better targeted therapy based on molecular analysis.

The question as to which techniques to use to look at the biological characteristics of these tumors, as raised in the editorial, is a difficult one given the rapid advances in high throughput technologies and the small amount of material obtained from biopsy. It is possible that routine probing for “driver” mutations will be as important as analysis of gene expression.

All investigators in this field agree with this editorial observation regarding the importance of advancing “our working knowledge of the genetic origins of these tumors.” There have been striking recent advances in the knowledge about the biology of DIPG. One only needs to look to new descriptions of the mutations specific to DIPGs2 to grasp the importance of these studies to the development of new treatment strategies. Biologically blind Phase I and II studies have failed to advance therapy for this still uniformly fatal tumor of childhood. We look forward to the day when the new advances in biology will result in cures. At that time biopsy of these tumors, which we agree has very acceptable morbidity, should be as routine as for any other brain tumor of childhood.

References


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