Diffuse intrinsic pontine glioma biopsy indications

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Stereotactic biopsy of Diffuse intrinsic pontine glioma is essential to obtain a pathologic diagnosis and is associated with low morbidity. This technique is important to elucidate biological characteristics of these tumors in order to direct multidisciplinary treatment plans possibly involving chemotherapy, radiation therapy, or other future clinical trial interventions for children with DIPGs [1)]

A multidisciplinary consensus conference on pediatric neurosurgery was held in February 2011, where 92 invited participants reviewed evidence for clinical management of hypothalamic chiasmatic glioma (HCLGG), diffuse intrinsic pontine glioma (DIPG), and high-grade glioma (HGG). Twenty-seven statements were drafted and subjected to online Delphi consensus voting by participants, seeking >70% agreement from >60% of respondents; where <70% consensus occurred, the statement was modified and resubmitted for voting. Twenty-seven statements meeting consensus criteria are reported. For HCLGG, statements describing overall therapeutic purpose and indications for biopsy, observation, or treatment aimed at limiting the risk of visual damage and the need for on-going clinical trials were made. Primary surgical resection was not recommended. For DIPG, biopsy was recommended to ascertain biological characteristics to enhance understanding and targeting of treatments, especially in clinical trials. For HGG, biopsy is essential, the World Health Organization classification was recommended; selection of surgical strategy to achieve gross total resection in a single or multistep process should be discussed with the PNMDT and integrated with trials based drug strategies for adjuvant therapies [2)] , but routine DIPG biopsy continues to be debated. Most neurosurgeons agreed that DIPG biopsy within a clinical trial should be supported, with the aims of defining the procedure risks, improving understanding of tumor biology, and evaluating new treatment targets. Careful family counseling and consent remain important [3)].

In 2015 Puget et al.,performed a prospective analysis of children with typical appearance of DIPG who had a stereotactic biopsy in our unit since 2002. Technical approach, complications, histopathological results, and samples processing are exposed. The literature on this subject is discussed.

Results: Reviewing our own 130 cases of DIPG biopsies and previous published data, these procedures appear to have a diagnostic yield and morbidity rates similar to those reported for other brain locations (3.9 % of transient morbidity in our series). In addition, the quality and the quantity of the material obtained allow to (1) confirm the diagnosis, (2) reveal that WHO grading was useless to predict outcome, and (3) perform an extended molecular screen, including biomarkers study and the development of preclinical models. Recent studies reveal that DIPG may comprise more than one biological entity and a unique oncogenesis involving mutations never described in other types of cancers, i.e., histones H3 K27M and activin receptor ACVR1.

Stereotactic biopsies of DIPG can be considered as a safe procedure in well-trained neurosurgical teams and could be incorporated in protocols. It is a unique opportunity to integrate DIPG biopsies in clinical practice and use the biology at diagnosis to drive the introduction of innovative targeted therapies, in combination with radiotherapy [4)]

In 2017 Carai et al. performed 7 pontine needle biopsies. Specimens were diagnostic and useful for molecular analysis in all cases. No surgical complications were observed. One child showed a transient neurologic worsening related to the biopsy that resolved within 2 weeks. The combination of the precoronary approach and use of the stereotactic ROSA system allowed single-session surgeries in all cases.

Pontine biopsy for DIPG is a safe procedure in selected centers. The advantages of the single-session procedure we described might be of particular interest in the pediatric setting [5)].

In the absence of frozen tumor specimens, body fluids–such as cerebrospinal fluid (CSF), serum, and urine–can serve as more readily accessible vehicles for detecting tumor-secreted proteins. We analyzed a total of 76 specimens, including CSF, serum, urine, and normal and tumor brainstem tissue. Protein profiling of CSF from patients with DIPG was generated by mass spectrometry using an LTQ-Orbitrap-XL and database search using the Sequest algorithm. Quantitative and statistical analyses were performed with ProteoIQ and Partek Genomics Suite. A total of 528 unique proteins were identified, 71% of which are known secreted proteins. CSF proteomic analysis revealed selective upregulation of Cyclophillin A (CypA) and dimethylarginase 1 (DDAH1) in DIPG (n = 10), compared with controls (n = 4). Protein expression was further validated with Western blot analysis and immunohistochemical assays using CSF, brain tissue, serum, and urine from DIPG and control specimens. Immunohistochemical staining showed selective upregulation of secreted but not cytosolic CypA and DDAH1 in patients with DIPG. In this study, we present the first comprehensive protein profile of CSF specimens from patients with DIPG to demonstrate selective expression of tumor proteins potentially involved in brainstem gliomagenesis. Detection of secreted CypA and DDAH1 in serum and urine has potential clinical application, with implications for assessing treatment response and detecting tumor recurrence in patients with DIPG [6)].

The decision to perform a biopsy for a diffuse intrinsic pontine glioma (DIPG) is not a straightforward one due to the location and characteristics of these tumors. DIPGs are highly aggressive and primarily affect children. In most cases, a biopsy may not be recommended due to the risks associated with the procedure and the typical behavior of DIPG. However, there are certain indications that may prompt a medical team to consider a biopsy in the context of a DIPG diagnosis:

Diagnostic Uncertainty: If the initial imaging studies (such as MRI or CT scans) do not provide a clear diagnosis or if there is doubt about the nature of the tumor, a biopsy may be considered to confirm the presence of a glioma and determine its specific characteristics.

Clinical Trials: Some clinical trials and research studies may require a confirmed diagnosis through a biopsy as an inclusion criterion. These trials often involve experimental treatments or therapies, and participation may be an option for some patients.

Personalized Treatment: In rare cases, a biopsy may be performed to obtain tissue for molecular analysis. This analysis can help identify specific genetic mutations or alterations within the tumor. This information may guide treatment decisions, such as identifying potential targeted therapies.

Future Research: Biopsy samples can be valuable for research purposes. They contribute to a better understanding of DIPG biology and may lead to advancements in the development of new treatments and therapies.

It's important to emphasize that the decision to perform a biopsy for DIPG is made on a case-by-case basis and involves careful consideration of the potential risks and benefits. The medical team, including neurosurgeons, oncologists, and other specialists, will assess the individual patient's situation, weigh the pros and cons, and discuss the implications with the patient and their family. The overall prognosis for DIPG is typically very poor, and treatment options are limited, so the focus is often on palliative care and symptom management. Biopsy, when performed, is typically done with the aim of obtaining diagnostic or research information rather than curative treatment.

Recomended Literature

Kieran MW. Time to rethink the unthinkable: upfront biopsy of children with newly diagnosed diffuse intrinsic pontine glioma (DIPG). Pediatr Blood Cancer. 2015 Jan;62(1):3-4. doi: 10.1002/pbc.25266. Epub 2014 Oct 4. PMID: 25284709 [7)].

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