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Liquid biopsy for the detection of H3K27m in patients with brainstem tumors

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Abstract

The treatment of diffuse brainstem tumors is prescribed in most cases without morphological or molecular genetic verification. "Liquid biopsy" is a minimally invasive technique that provides information about the biology of tumors without a standard biopsy. We set out to determine the informativeness of this diagnostic method for detecting H3K27 and BRAF V600E mutations in patients with diffuse brainstem tumors. Thirty patients (10 children, 20 adults) with radiologically verified brainstem tumors underwent CSF collection via lumbar puncture. Cell-free DNA (cfDNA) isolated from the CSF was used for detection of H3F3A K28M and BRAF V600E mutations via digital droplet PCR. In 23 patients, the study of these mutations was performed in parallel in the pool of cfDNA and DNA isolated from tumor tissue obtained during a standard tumor biopsy. A mutation in the BRAF gene was not detected in any patient. The H3F3A K28M mutation was detected in 7 samples of cfDNA and 8 samples of DNA isolated from tumor tissue obtained from 23 patients for whom the study was performed in parallel. The sensitivity and specificity of H3F3A K28M mutation detection in CSF and tumor tissue were 87.5% and 100%, respectively ($P < 0.001$, relative risk = 0.063, 95% CI: 0.009-0.417). Minimally invasive diagnosis of diffuse brainstem tumors via the "liquid biopsy" method is informative for the detection of specific H3F3A K28M mutations and allows the verification of the diagnosis of diffuse midline glioma with H3K27 (H3K28M) alterations without a standard biopsy. Despite the promising results, an important limitation of the work is the small sample size, which affects the statistical results and conclusions. Large multicenter studies are needed to further investigate the value of liquid biopsy in brainstem gliomas.

Keywords: Brainstem gliomas; Diffuse midline glioma; Glial brainstem tumor; H3K27m mutation; Liquid biopsy; Sensitivity of liquid biopsy.