Abstract 682P

Background

Cerebrospinal fluid (CSF)–based liquid biopsy offers a minimally invasive approach to profile central nervous system (CNS) malignancies, such as leptomeningeal metastases (LM) and rare brain tumors. We established comprehensive workflows to isolate CSF-derived tumor cells (csfDTCs) and cell-free tumor DNA (ctDNA), enabling integrated multi-omic analyses to investigate tumor heterogeneity, track clonal evolution, and identify potential personalized therapies.

Methods

CSF from 28 adults with suspected LM and 3 pediatric patients with brain tumors was divided for standard cytopathology and single-cell workflows. Single csfDTCs were isolated, and if possible, ctDNA was extracted in parallel. All cells and ctDNAs underwent whole-genome amplification and copy number variation (CNV) profiling; pediatric csfDTCs were also subjected to mutational and transcriptional profiling. For some patients, matched FFPE tissue from solid metastases was analyzed to assess systemic disease heterogeneity.

Results

In patients with suspected LM, the single cell approach detected csfDTCs in 10/28 (36%) cases while cytopathology identified them in 9/28 (32%) cases. Both methods demonstrated high concordance in 24/28 (86%) patients. Importantly, we were able to detect aberrant CNV profiles in csfDTCs of all 10 patients, including those who tested negative in cytopathology. In contrast, ctDNA analysis from CSF revealed tumor-associated CNVs in only 5/20 (25%) patients. Comparative CNV profiling across metastatic lesions revealed significant heterogeneity and dynamic clonal shifts between CNS-derived and non-CNS-derived metastatic cells. We also performed in-depth analyses on three pediatric patients. Here, transcriptomes aligned with neural lineage and matched histopathologic tumor type. Genomic analyses confirmed clonal origin while uncovering subclonal gains and losses, indicating temporal tumor evolution.

Conclusions

Our proof-of-concept study shows that CSF liquid biopsy enables detection and multi-omic characterization of tumor cells and ctDNA in LM and pediatric brain cancers. By revealing tumor heterogeneity and evolution, this approach holds promise for guiding personalized treatment in the future.

Clinical trial identification

Editorial acknowledgement

Legal entity responsible for the study

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Disclosure

All authors have declared no conflicts of interest.