RESEARCH ON GLIOBLASTOMA MULTIFORME GENETIC BIOMARKERS IN LIQUID BIOPSY

SUMMARY

Although solid tumor is the most widely used basic tool for cancer diagnosis, staging and prognosis today, this method is an invasive surgical biopsy method. However, as a tumor grows, it can change over time, spread and be exposed to anti-cancer drugs. Tumor biopsies taken when the disease is first diagnosed may not reflect the later status of the cancer. Repeated biopsies to get up-to-date information about cancer can cause possible complications such as pain, infection, and bleeding. Cancer cells that spread to different parts of the body may be different from the cancer in the area where they started. And for this reason, it is not possible for a tumor biopsy taken from a part of the body to adequately represent cancer in the body.

Liquid biopsy is a non-invasive method performed to detect circulating tumor cells or DNA fragments of tumor cells. Blood; Circulating cells contain many biological materials such as platelets, extracellular vesicles, mRNA, miRNA, protein and cell-free DNA (cfDNA). Some of the cfDNA in the blood of cancer patients also includes circulating tumor DNA (ctDNA) released by tumor cells through apoptosis, necrosis or active release. As tumors grow in volume and increase in number, ctDNA and CTC (circulating tumor cells) are released into the bloodstream. In this case, using circulating blood and tumor-specific mutations in the clinically important ctDNA sequence may act as a new type of cancer biomarker.

Glioblastoma multiforme (GBM) is the most common brain tumor in adults. It is one of the most rapidly progressing and deadly tumors. The high heterogeneity of GBM hinders diagnosis and therapeutic intervention and needs the identification of biomarkers for early diagnosis that allows accurate patient classification and personalized treatment. Repeat surgery may not always be possible to define the molecular profile of tumor progression. Therefore, liquid biopsy is a promising approach to detect and molecularly characterize GBMs in particular. It is also thought to have a potential clinical benefit, which can facilitate early detection of cancer and improve patient follow-up by managing tumor progression and monitoring response to treatment.

In our study, patients (n=10) and control group (n=3) were examined with a Next generation sequencing panel (NGS), which includes 63 gene regions that were previously associated with GBM and may also be associated, hotspot exon and exon-intron junction regions. The panel was performed with Illumina NextSeq 500/550Dx in the solid tumors and plasmas of ten volunteer patients and the plasmas of the healthy control group. QIAGEN Clinical Insight (QCI) software was used for bioinformatics workflow and analysis.

In the study, known pathogenic and/or novel variants were detected in the tissues of seven patients. Mutations were detected in TP53 gene in six patients, PTEN in four patients, MET in one patient, and EGFR gene in one patient. In the analysis of the copy number variation (CNV), the number of readings above normal in the EGFR genes in five patients, MET in two patients, PDGFRA in one patient, KIT in one patient, and RPN2 genes in one patient were obtained. Mutations and amplifications detected in the tissues of the patients could not be detected in the liquid biopsy samples.

Keywords: Biotechnology, panel sequencing, biomarker, oncology, glioblastoma