

Successful Remedy With Osimertinib in a Patient of Thr790Met-positive Non-small Cell Lung Cancer With Leptomeningeal Carcinomatosis and Resistant to Gefitinib

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Research Article

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Abstract

Patients of non-small cell lung cancer (NSCLC) with activated EGFR mutations is more apt to develop leptomeningeal metastasis (LM) than the other types of lung cancers [1]. Examination of circulating tumor DNA (ctDNA) in cell-free cerebrospinal fluid (CSF) has been shown to be useful in detecting the genomic mutations of tumors in central nervous system (CNS) and has also been used to monitor tumor progression and evaluate the response to treatments [2]. Osimertinib, a third-generation EGFR tyrosine kinase inhibitor, is considered to be a recent standardized treatment for EGFR Thr790Met-mutant NSCLC because of its good efficacy in both systemic and CNS metastasis [3].

Main Text

To the Editor:

Patients of non-small cell lung cancer (NSCLC) with activated EGFR mutations is more apt to develop leptomeningeal metastasis (LM) than the other types of lung cancers [1]. Examination of circulating tumor DNA (ctDNA) in cell-free cerebrospinal fluid (CSF) has been shown to be useful in detecting the genomic mutations of tumors in central nervous system (CNS) and has also been used to monitor tumor progression and evaluate the response to treatments [2]. Osimertinib, a third-generation EGFR tyrosine kinase inhibitor, is considered to be a recent standardized treatment for EGFR Thr790Met-mutant NSCLC because of its good efficacy in both systemic and CNS metastasis [3].

A 55-year-old female with a progressive headache and vomiting for one month was admitted to our hospital. She was diagnosed as lung adenocarcinoma with osseous metastasis ten months ago. EGFR mutation was detected in genomic examination, so she was first treated with gefitinib for ten months and finally acquired resistance. A previous enhanced cerebral magnetic resonance imaging (MRI) and PET-CT one month ago showed that there was no obvious abnormality in CNS. Lumbar puncture showed an increased intracranial pressure (>330 mmH₂O) without positive finding of cytology and biochemical examination in CSF. However, a further CSF ctDNA detection by next-generation sequencing technique at the same time showed an EGFR-Thr790Met mutation. After the patient was admitted, a second enhanced MRI was performed and showed comprehensive linear leptomeningeal enhancement in cerebral sulcus (Fig. 1). A second-time cytology and biochemical examination in CSF remained negative. Based on these findings, a diagnosis of leptomeningeal carcinomatosis of EGFR-Thr790Met-positive lung adenocarcinoma (cT3N3M1b: stage IVA) was established. And then, Osimertinib (80 mg/day) was given as a second-line treatment, which showed a good response. The patient's headache and symptom of intracranial hypertension disappeared rapidly after 3 days' Osimertinib. After discharge, Osimertinib (80mg/day) was continue used, and the patient was closely followed-up, there was no obvious toxic and side effects except diarrhea and leukopenia. The lung lesion continued to shrink in the six months' follow-up CT and the intracranial pressure returned to normal without headache anymore.

This report shows a great clinical benefit of Osimertinib in LM patients with positive detection of the EGFR-Thr790Met mutation in CSF. What's interesting was that the examinations of cytology in CSF and neuroimaging were all negative at the beginning, and when the patient's imaging turned positive, the result of CSF cytology examination was still negative one month after the EGFR-Thr790Met mutation detected in CSF. Hence, we propose that the positive findings of CSF ctDNA as liquid biopsy technology based on the detection of cancer-associated gene mutations may be earlier appeared than the imaging findings and the CSF findings. Moreover, this report is characteristic by the lung cancer with headache as the main complaint. The patient's lung lesion was found due to the routine screening of chest CT with novel coronavirus. Just as an old Chinese saying goes, no great loss without some small gain.

Declarations

Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions

Liqing Xu made substantial contributions in drafting the letter. Shengli shen provided the resource. Hongzhou Duan supervised the letter and approved the version to be published.

Data availability

Data are available on demand.

Compliance with Ethical Standards

Funding

The authors did not receive support from any organization for the submitted work.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethical approval

This article does not contain any studies with human participants performed by any of the authors.

Informed consent

Informed consent was obtained from the individual included in the letter.

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Figures

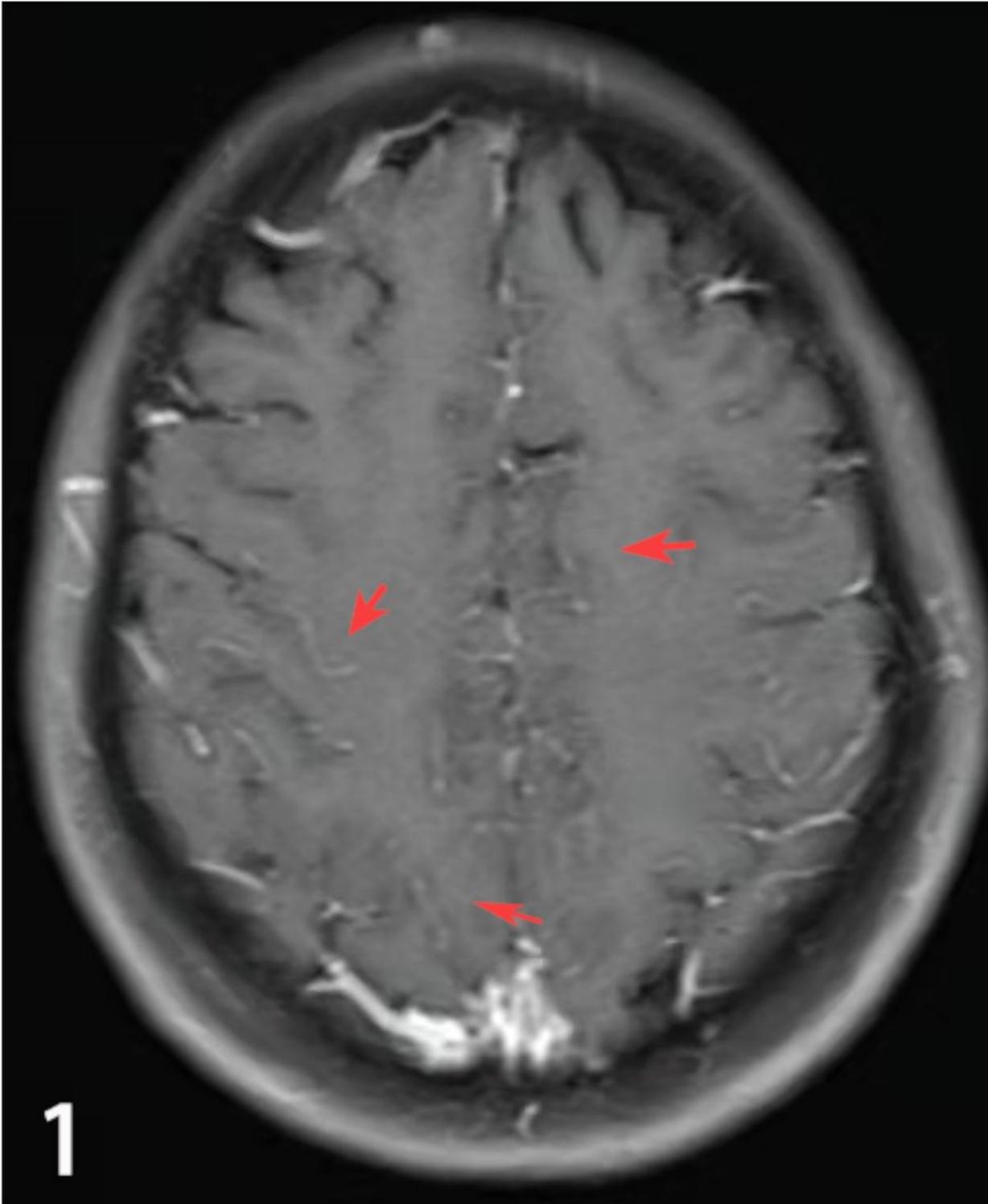


Figure 1

A second-time cerebral contrast-enhanced MRI shows diffuse, and linear enhancement along the surface of the cerebrum (arrows).