Icotinib, an Effective Treatment Option for Patients With Lung Adenocarcinoma Harboring Compound EGFR L858R and A871G Mutation

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Research Article

Keywords: Icotinib, Lung adenocarcinoma, Compound EGFR L858R and A871G mutation, Partial response

Posted Date: March 24th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-331165/v1

Version of Record: A version of this preprint was published at Investigational New Drugs on April 9th, 2021. See the published version at https://doi.org/10.1007/s10637-021-01108-3.

Abstract

Compound epidermal growth factor receptor (*EGFR*) mutations are defined as double or multiple independent mutations of the *EGFR* tyrosine kinase domain (TKD), in which an *EGFR*-tyrosine kinase inhibitor (TKI)-sensitizing mutation is identified together with a mutation of unclarified clinical significance. Lung adenocarcinoma with compound *EGFR* mutation shows poor clinical response to *EGFR*-TKIs. Kobayashi et al. reported a non-small-cell lung cancer (NSCLC) patient whose tumor had *EGFR* exon21 L858R/A871G mutation presented rapid disease progression to erlotinib. However, in this case, we present an *EGFR* exon21 L858R/A871G mutation patient exerted significant benefit to icotinib, another first-generation *EGFR*-TKI, indicating that different *EGFR*-TKIs have diversiform sensitive sites and therapeutic effects, consistent mutation sites might achieve heterogeneous benefits from different *EGFR*-TKIs. Our case report provides promising *EGFR*-TKI for clinical treatment with *EGFR* exon21 L858R/A871G mutation in NSCLC. More dedicated efforts are needed to clarify their biologic effects on disease course and drug responsiveness.

Short Report

Compound epidermal growth factor receptor (*EGFR*) mutations are defined as double or multiple independent mutations of the *EGFR* tyrosine kinase domain (TKD), in which an *EGFR*-tyrosine kinase inhibitor (TKI)-sensitizing mutation is identified together with a mutation of unclarified clinical significance.[1] In general, lung adenocarcinoma with compound *EGFR* mutation shows poor clinical response to *EGFR*-TKIs.[2] Kobayashi et al. reported a non-small-cell lung cancer (NSCLC) patient whose tumor had *EGFR* exon21 L858R/A871G mutation presented rapid disease progression to erlotinib. [1] Herein, we report icotinib, another first-generation *EGFR*-TKI, is an effective treatment option for patients with lung adenocarcinoma harboring compound EGFR L858R/A871G mutation.

A 59-year-old female was admitted to hospital for intermittent cough in March 2020. Chest computed tomography revealed space-occupying lesion in the right lung. CT-guided percutaneous lung biopsy was conducted. The hematoxylin and eosin staining and immunohistochemical staining results (TTF-1(+), Napsin-A (+), CK7 (+), CK5/6 (-), P40 (-) and Ki67 (15%)) revealed a typical morphology for adenocarcinoma cells. Afterwards, the biopsy specimen was subjected to next-generation sequencing analysis (CAP certificated laboratory), *EGFR* exon21 L858R/ A871G mutation was detected (Fig 1), and no other key driver gene mutation was identified. Subsequently, icotinib (125mg, tid) was immediately administered from Apirl 9th 2020. Clinical and radiological follow-up after 3 months showed no evidence of progression and recurrent and the disease showed partial response (Fig 2 A-B'). On July 6th 2020, radical resection of the right lower lung was performed, postoperative pathologic results revealed invasive lung adenocarcinoma.

Recent advances in tumor genotyping techniques provide not only accurate data, but also a higher probability of identifying atypical and multiple mutations in the *EGFR*-TKD in a single sample. Two major activating mutations in *EGFR* are an in-frame deletion in exon 19 and the L858R substitution in exon 21.

[3] The vast majority of *EGFR* mutations are incisively sensitive to EGFR-TKIs, but other rare mutations including L747S, D761Y, T790M, and T854A confer resistance to EGFR-TKIs.[4]

Previous studies have shown that there are differences in the responses to the *EGFR*-TKIs among compound *EGFR* mutations. Compound mutations that contain sensitizing mutations such as G719X or L858R seem to have good responses to *EGFR*-TKIs.[5] However, those comprised of rare atypical mutations have poor response to *EGFR*-TKIs. In previous reports, a patient whose tumor had *EGFR* exon21 L858R/A871G mutation presented rapid disease progression to erlotinib, indicating that this compound mutation may confer primary resistance to first-generation *EGFR*-TKIs. However, in this case, we present an *EGFR* exon21 L858R/A871G mutation patient exerted significant benefit to icotinib, another first-generation *EGFR*-TKI, indicating that different *EGFR*-TKIs have diversiform sensitive sites and therapeutic effects, consistent mutation sites might achieve heterogeneous benefits from different *EGFR*-TKIs.

With the clinical application of more sensitive and precise tumor genotyping systems, rare *EGFR* mutations of unknown biological and clinical significance are frequently encountered in routine clinical practice. Our case report provides promising *EGFR*-TKI for clinical treatment with *EGFR* exon21 L858R/A871G mutation in NSCLC. More dedicated efforts are needed to clarify their biologic effects on disease course and drug responsiveness.

Declarations

Author declarations section:

Ethics approval and consent to participate: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from the patient for participating this case.

Consent to publication: Informed consent was obtained from the patient for publication of this case.

Availability of data and material: Not applicable.

Competing interests: The authors declare that they have no conflict of interest.

Funding: This work was supported by National Natural Science Foundation of China under Grant No.81800090.

Authors' contributions:

Conception/Design: Lin-ling Jin, Zhen-zhen Wu

Provision of study material or patients: Yan-li Wang, Dong-sheng Chen

Collection of data: Si Li, Mingzhe Xiao

Data analysis and interpretation: Lin-ling Jin, Zhen-zhen Wu

Manuscript writing: Lin-ling Jin, Dong-sheng Chen

Final approval of manuscript: All authors

Acknowledgment: We thank Chuang Qi from Jiangsu Simcere Diagnostics for his kindly assistance.

Compliance with Ethical Standards section:

Disclosure of potential conflicts of interest: The authors declare that they have no conflict of interest.

Research involving Human Participants and/or Animals: YES, Research involving Human Participants. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from the patient for participating and publication of this case.

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Figures

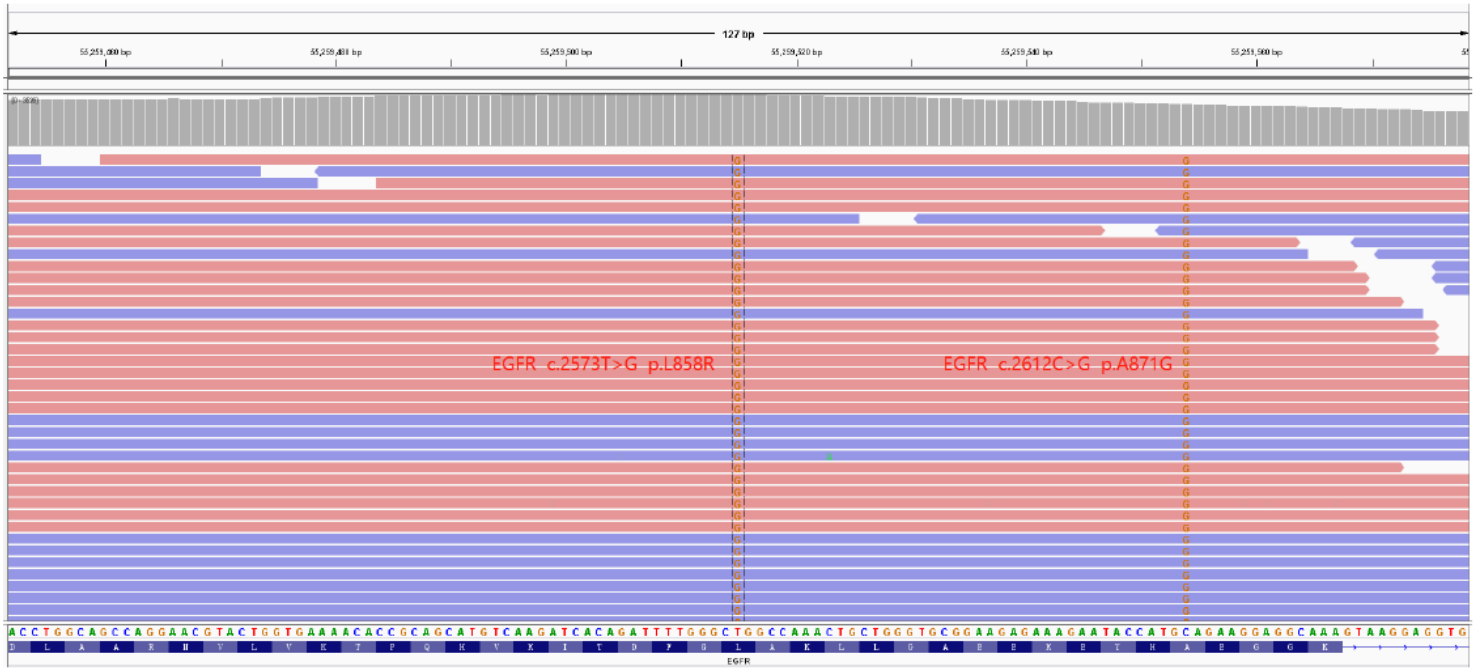

Figure 1

Next-generation sequencing result of compound EGFR L858R and A871G mutation.

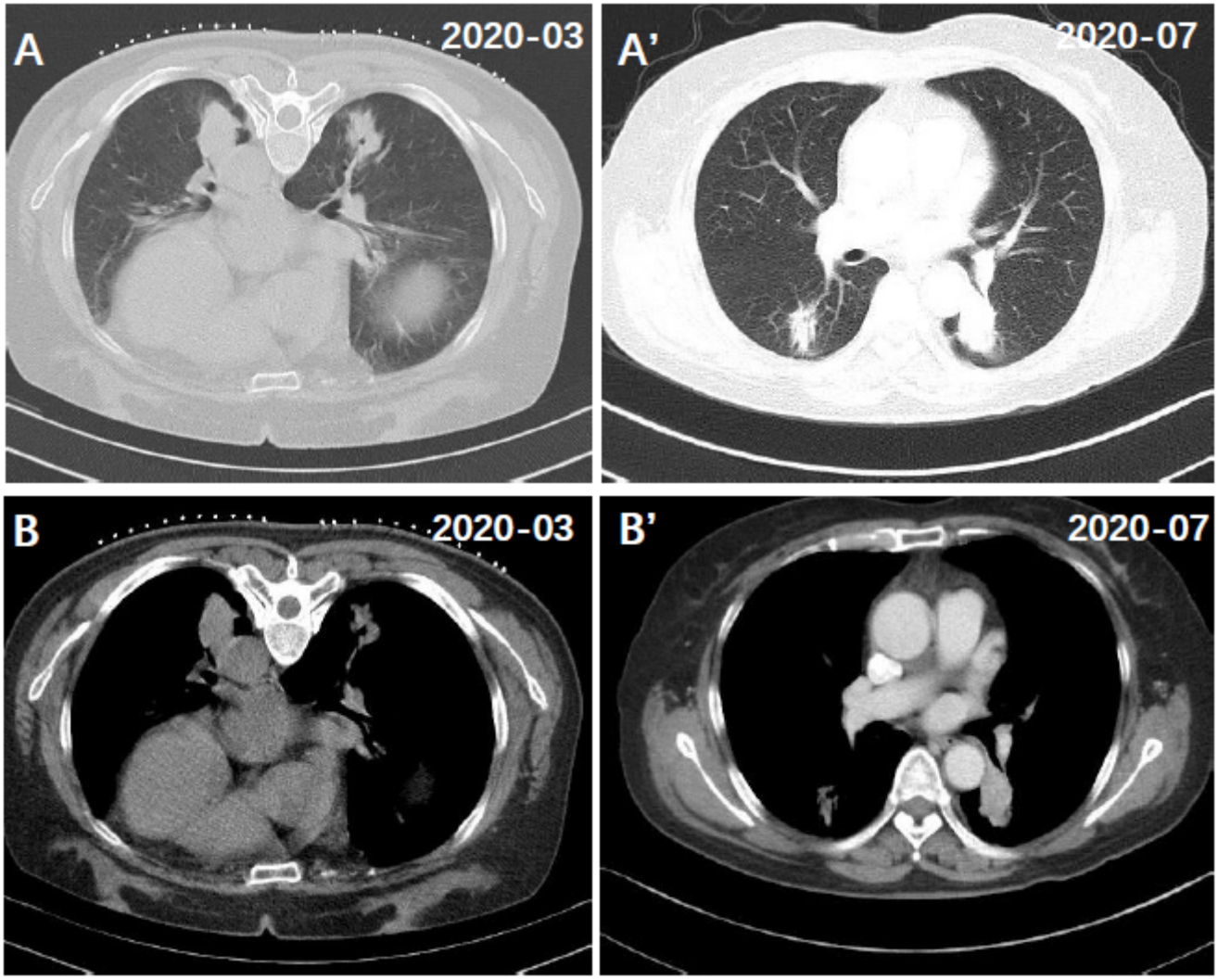

Figure 2

Tumor response during icotinib treatment. (A, B) Baseline before icotinib treatment. (A', B') 3 months after icotinib treatment.