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Case Report
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A Novel MET Exon 14 Skipping Mutation Well Responses to Crizotinib in Lung Adenocarcinoma

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Abstract

MET skipping mutation well responses to crizotinib in lung adenocarcinoma: We report the case of a 68-year-old non-smoker male patient who was diagnosed in February 2019 with a stage IV lung adenocarcinoma. Considering that he was diagnosed with bladder cancer in 2001 and gastric cancer in 2011, the chemotherapy regimen of permetrexil plus oxaliplatin was suspended. In order to probe into the genomic profile of the tumor for targeted therapy, the tissue specimen and the related blood sample were subjected to NGS analysis, and a MET exon 14 skipping mutation (c.3026_3028+11del) was identified. The patient began treatment with crizotinib 250 mg twice a day. After one month of therapy, the tumor volume significantly narrowed (-98%).

Keywords: Crizotinib; Lung adenocarcinoma; Mesenchymal-to-Epithelial Transition (MET); Skipping mutation

Introduction

Mesenchymal-to-Epithelial Transition (MET) exon 14 skipping mutation (loss of exon 14) was a targetable alteration in Non-Small-Cell Lung Cancer (NSCLC) with a frequency up to 5% [1], and the MET inhibitor of crizotinib had the most efficacy among all the targeted drugs. However, crizotinib responded differently to the tumor from - 25% to - 40% in size [2]. Here, we reported a case of a patient with stage IV lung adenocarcinoma harboring a novel MET exon 14 skipping mutation and responded well to small molecule MET inhibitor crizotinib.

Case Presentation

In February 2019, a 68-year-old non-smoker male patient who had been diagnosed with stage IV lung adenocarcinoma 1 month earlier came to our hospital for further treatment. After admission, chest computed tomography shows space-occupying mass measuring 4.0 cm × 3.6 cm × 2.0 cm in the left lower lung with multiple lymph nodes metastases throughout the body (Figure 1A). Considering that he was diagnosed with bladder cancer in 2001 and gastric cancer in 2011, the chemotherapy regimen of permetrexil plus oxaliplatin was suspended.

In order to probe into the genomic profile of the tumor for targeted therapy, the tissue specimen and the related blood sample were subjected to NGS analysis, and a MET exon 14 skipping mutation (c.3026_3028+11del) was identified (Figure 1B and 1C). No other driving gene variants were found. The mutant allele frequency was 33.87%. Likewise, the amplified fragments of tissue sample was smaller than 18S rRNA similarly with MET exon 14 skipping H569 cell lines, further confirming the occurrence of MET exon 14 skipping (Figure 1D). Based on these findings, the patient began treatment with crizotinib 250 mg twice a day. Most notably, imaging after one month of therapy showed significant reduction of tumors. His lung tumor measured 1.0 cm × 0.8 ccm × 0.4 cm in size, meeting RECIST partial response criteria (-98%, Figure 1E). This lasted for only 4 months until he experienced non-disease-related deaths.

Discussion

As far as we know, this is the first report of crizotinib which was a beneficial therapeutic option for a subset of NSCLC with a novel MET exon 14 skipping mutation (c.3026_3028+11del). Although existing dates have shown that NSCLC with MET 14 exon mutation (such as 3077_3082+9del and 3082 G>C) respond well to crizotinib and the response is PR (-40%) [3], in our case, the tumor volume significantly narrowed (-98%). Hence, this report could extend the spectrum and genomic landscape of MET exon 14 skipping mutation, and be favor of the development of personalized therapy.

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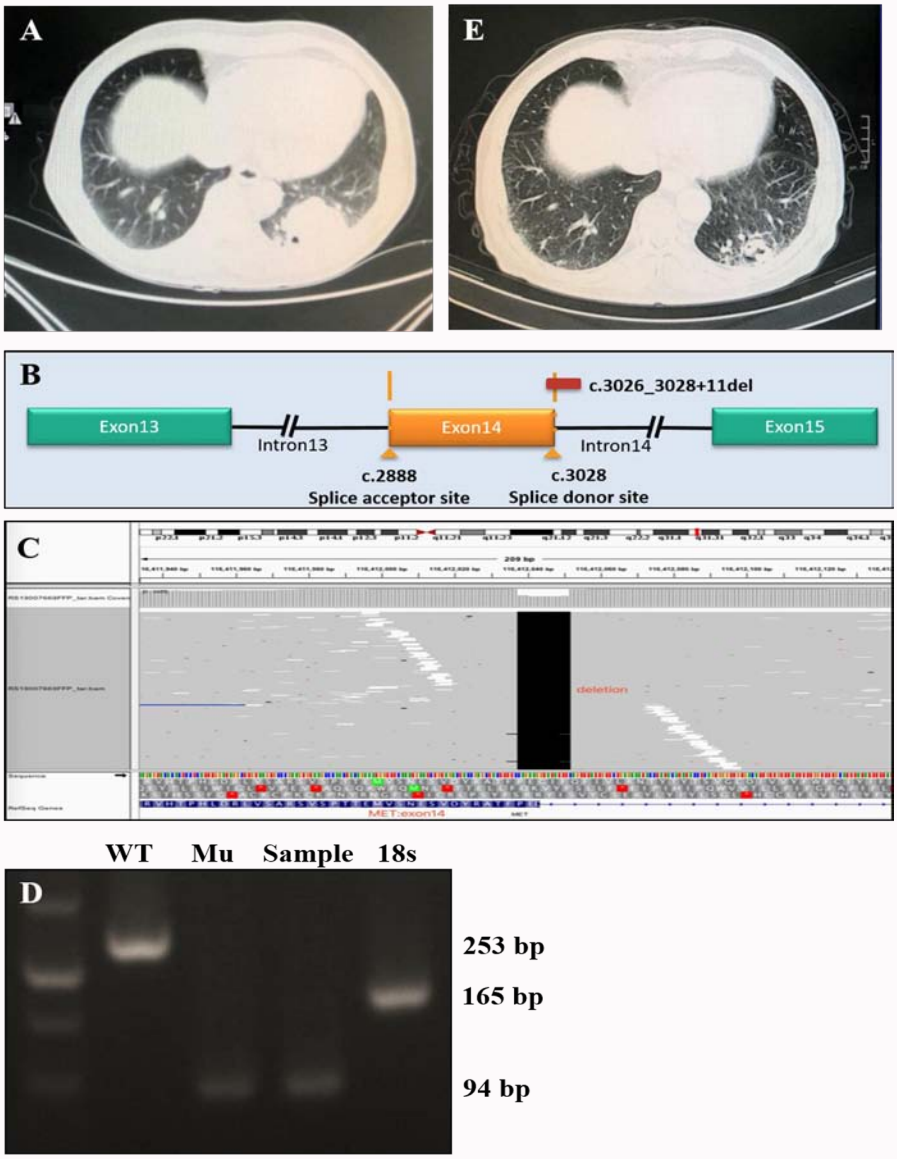

Figure 1: Patient disease diagnosis and treatment. A) chest computed tomography result. B) A MET exon 14 skipping mutation (c.3026_3028+11del) was identified. C) NGS results showing breakpoint of MET exon 14 skipping mutation. D) AMET exon14 skipping H569 cell lines was confirmed by qRT-PCR. E) Tumor response of the patient's left lung after crizotinib treatment.

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