Crizotinib Induced Rapid Remissions of Lung Adenocarcinoma

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Case Report

We present an imaging case of rapid pulmonary remission in a 50-year-old smoking woman. Our patient was a strong smoker (30 pack years), she has a pulmonary adenocarcinoma in right middle lobe with multiple pulmonary metastases.

At first, she developed symptoms of strong coughing, for which she was referred in our center for further diagnosis and treatment. Histopathology from bronchoscopic tumor filled middle lobe showed pulmonary adenocarcinoma (radiologic stage T4 N3 M1).

The mutation of epidermal growth factor receptor (EGFR) could not be detected; however she does have major expression of anaplastic lymphoma kinase (ALK) mutation. 81% of tumor cells were detected with rearrangement of ALK-gene.

She was treated with crizotinib, with success. We treated the patient with standardized regular dosage of 250 mg 1-0-1 at daily basis. The patient tolerated the treatment altogether really well; a dose reduction was never required.

We could observe a rapid pulmonary tumor remission shortly after two months of antineoplastic therapy. The CT-Scans (Figures 1 and 2) revealed significant tumor remission of the primary pulmonary tumor (Figure 1) and pulmonary metastases (Figures 1 and 2).

The CT-scan showed a tumor mass of right middle lobe with multiple bilateral metastases before the therapy with crizotinib (Figures 1a and 2a). CT-scans (Figures 1b and 2b) revealed significant tumor remission after 8 weeks therapy with crizotinib.

Our patient tolerated the therapy with crizotinib well. She takes her medication on a regular and constant basis with only couple of minor side effects. She never suffered strong coughing, pneumonitis and cardiovascular arrhythmia. We will keep on clinical monitoring of our patient, in which the patient will be clinically evaluated every four weeks.

Discussion

This is a short report about a patient with non-small cell lung cancer (NSCLC) Adenocarcinoma. Our patient did not have mutation of epidermal growth factor receptor (EGFR). However, a very strong cell mutation of anaplastic lymphoma kinase (ALK) was demonstrated. Our patient was a strong smoker with around 30 pack years.

ALK rearrangements were identified in NSCLC in 2007 by two independent groups. Soda et al. developed retroviral-based cDNA expression libraries to screen for novel oncogenes [1,2]. They identified an echinoderm microtubule associated protein-like 4 (EML4)-anaplastic lymphoma kinase (EML4-ALK) fusion transcript that possessed transforming activity in 3T3 cells [2]. Treatment with the same ALK inhibitor resulted in the absence of EML4-ALK/3T3 cells in the lung and prolonged survival [2]. In summary, Soda et al. convincingly demonstrated that EML4-ALK is a unique driver mutation in NSCLC and that inhibition of EML4-ALK activity in vivo led to the reduction of lung cancer burden.

Cancer cells harboring EML4-ALK rearrangement become dependent on or “addicted” to ALK and hence are highly sensitive to ALK kinase inhibition [3].

Patients with advanced ALK-positive NSCLC are sensitive to ALK-targeted therapies. It is important to diagnose patients with ALK-rearranged NSCLC early as possible in the treatment course to initiate effective antitumor treatment.

The prognostic significance of ALK rearrangement in NSCLC has not been settled. In two separate reports [4,5] Shaw et al. did not demonstrate any significant differences in Overall Survival (OS) for patients with NSCLC by EML4-ALK status in the era before crizotinib. Lee et al. showed that patients with ALK-rearranged NSCLC had the shortest overall survival compared to wild-type patients, but the difference was not significant [6].

Many patients with ALK-positive NSCLC derive initial substantial

Figure 1: Contrast-enhanced tomography revealed a pulmonary mass within the right middle lobe, before (1a) and 8 weeks after the therapy (1b) with crizotinib.

Figure 2: Contrast-enhanced tomography revealed bilateral pulmonary metastases before (2a) and 8 weeks after the therapy (2b) with crizotinib.
clinical benefit from crizotinib, the benefit with tumor remission is however relatively short-lived because of the development of acquired resistance. Acquired tumor cell resistance has emerged as the major hurdle preventing ALK inhibitors, and targeted therapies in general, from having a truly durable therapeutically impact on patients. In Conclusion, our patient tolerate the medication overall well. She did not have diarrhea, coughing, cardiovascular arrythmia or pneumonitis. More reports are required to further evaluate the clinical effect and potential side effects of crizotinib.

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