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Successful treatment with alectinib after crizotinib-induced interstitial lung disease

Haruka Chino, Akimasa Sekine, Hideya Kitamura, Terufumi Kato*, Takashi Ogura

Department of Respiratory Medicine, Kanagawa Cardiovascular and Respiratory Center, Japan

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ABSTRACT

We herein report a case of a 46-year-old woman with anaplastic lymphoma kinase (ALK)-rearranged stage IV lung adenocarcinoma who received the ALK inhibitor crizotinib as second-line therapy. On the 47th day following crizotinib initiation, a chest computed tomography scan revealed ground-glass opacities with a clinical manifestation of desaturation, although a partial response to treatment was detected. The diagnosis of crizotinib-induced interstitial lung disease (ILD) was confirmed, and crizotinib was discontinued, followed by the initiation of corticosteroid therapy. After improvement of ILD with corticosteroid therapy, alectinib was administered as salvage therapy, resulting in tumor shrinkage without any recurrence of ILD. To the best of our knowledge, this is the first report of successful alectinib treatment following crizotinib-induced ILD. Our results indicate that alectinib could be a promising alternative treatment option in patients with crizotinib-induced ILD.

1. Introduction

Crizotinib and alectinib are oral selective inhibitors of the echinoderm microtubule-associated protein-like 4 (EML4) anaplastic lymphoma kinase (ALK) rearrangement gene [1]. These drugs are reported to be effective in patients with advanced non-small-cell lung cancer (NSCLC) with EML4-ALK rearrangement and therefore recommended in these patients [2,3]. However, interstitial lung disease (ILD) rarely occurs as a serious, sometimes fatal, adverse event of crizotinib, which requires the cessation of the causative drug. In fact, three of 149 patients have experienced grade 3 or 4 crizotinib-induced ILD requiring the cessation of crizotinib [4,5]. Generally, retreatment with the causative drug could lead to recurrent ILD and therefore should be avoided [6,7]. However, it remains unclear whether the other ALK-tyrosine kinase inhibitor (TKI), alectinib, could also cause ILD in patients with crizotinib-induced ILD. Here, we report a case of a patient with ALK-rearranged NSCLC who developed crizotinib-induced ILD but was safely treated with alectinib.

2. Case report

The patient was a 46-year-old woman with stage IV lung adenocarcinoma cT4N0M1a. Chest computed tomography (CT) revealed multiple nodules in the right upper lobe and malignant pleural effusion. Mutation analysis showed that the tumor was wild-type for epidermal growth factor receptor (EGFR) mutations and revealed the presence of EML4-ALK rearrangement. Fluorescence in situ hybridization analysis revealed an EML4-ALK gene translocation. Four cycles of combination chemotherapy consisting of pemetrexed, calboplatin, and bevacizumab (3 weeks apart) were administered as first-line therapy, followed by maintenance chemotherapy with pemetrexed and bevacizumab; however, disease progression was observed after the fourth course of maintenance therapy. The patient refused to continue chemotherapy because of anxiety about new anti-cancer drugs. Fifteen months after the cessation of therapy, she visited our hospital complaining of dyspnea. Her chest radiograph and CT scan demonstrated an increase in pleural effusion and development of lymphangitis carcinomatosa (Fig. 1). Her Eastern Cooperative Oncology Group performance status score was 2. As second-line therapy, crizotinib was administered at a dose of 200 mg daily, which was increased to 400 mg daily. No additional drug was administered around the time of crizotinib initiation. One week after the initiation of crizotinib, pleural effusion began to decrease, and lymphangitis carcinomatosa improved. On the 47th day following the crizotinib initiation, oxygen saturation by pulse oximetry

* Corresponding author at: 6-16-1, Tomiokahigashi, Kanazawa-ku, Yokohama City, Kanagawa, Japan. Fax: +81 45 786 4770.
E-mail address: t-kato@kanagawa-junko.jp (T. Kato).

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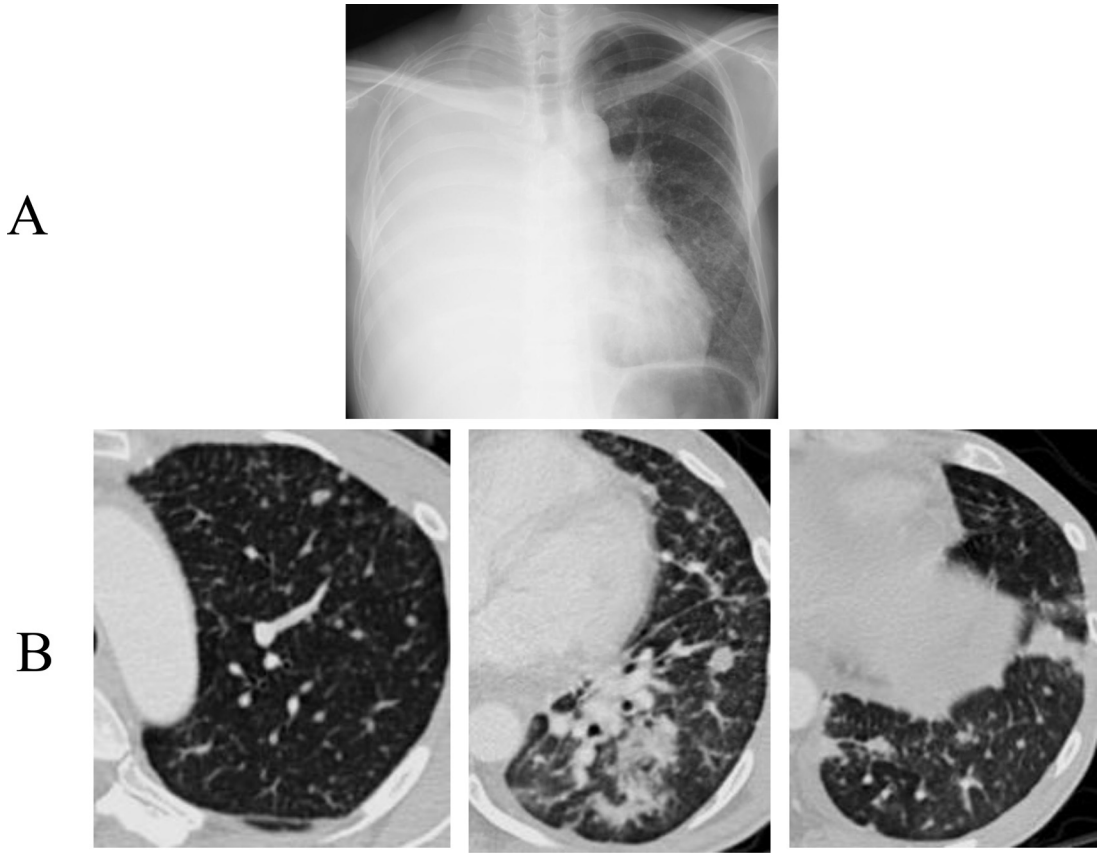

Fig. 1. Chest radiograph and CT on admission. (A) Chest radiograph revealed right pleural effusion and multiple nodules in the left lung field. (B) Chest CT demonstrated multiple small nodules and interstitial thickening in perihilar and peribronchovascular distribution.

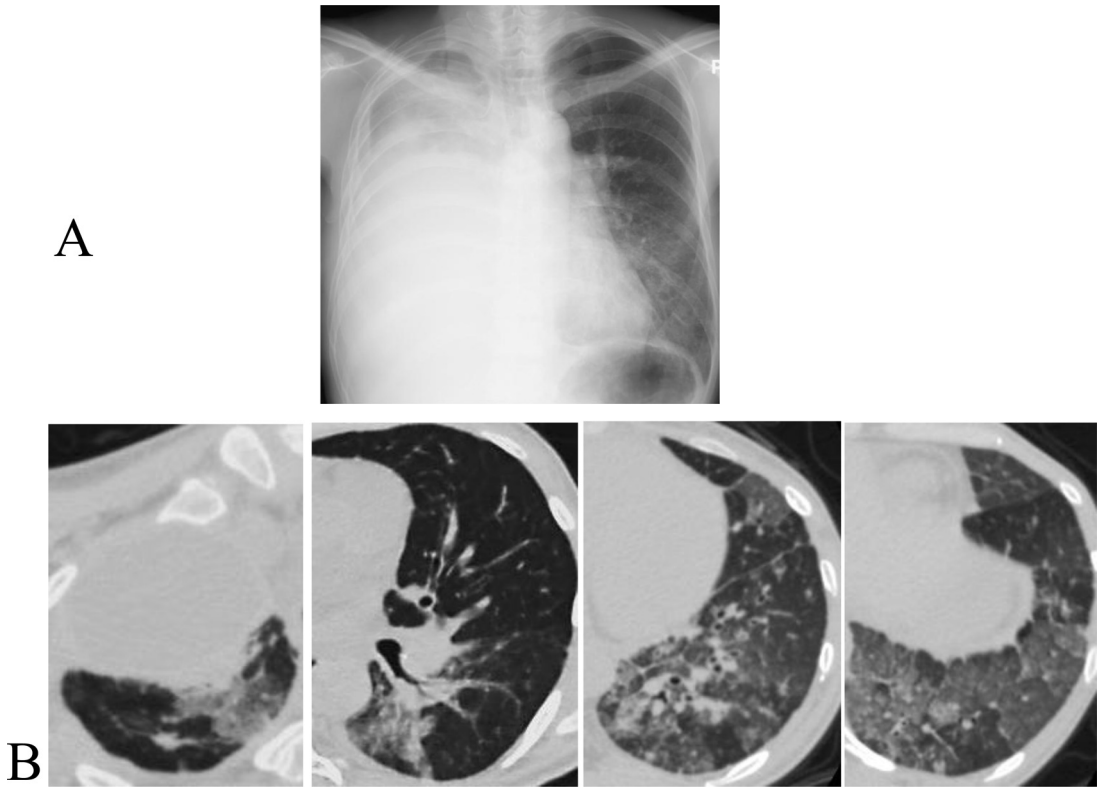

Fig. 2. Crizotinib-induced interstitial lung disease (ILD), fourty-seven days after initiating crizotinib. (A) Chest radiograph revealed ground-glass opacity in the left lung, although right pleural effusion decreased. (B) Her CT scan showed diffuse ground-glass opacities in both lungs despite the improvement of lymphangitis carcinomatosa.