

Case Report

# Anaplastic Lymphoma Kinase-Positive Lung Cancer with Mucoepidermoid Carcinoma Differentiation: A Case Report

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## Keywords

Lung cancer · Mucoepidermoid carcinoma · Anaplastic lymphoma kinase fusion · Alectinib · Rare cancer

## Abstract

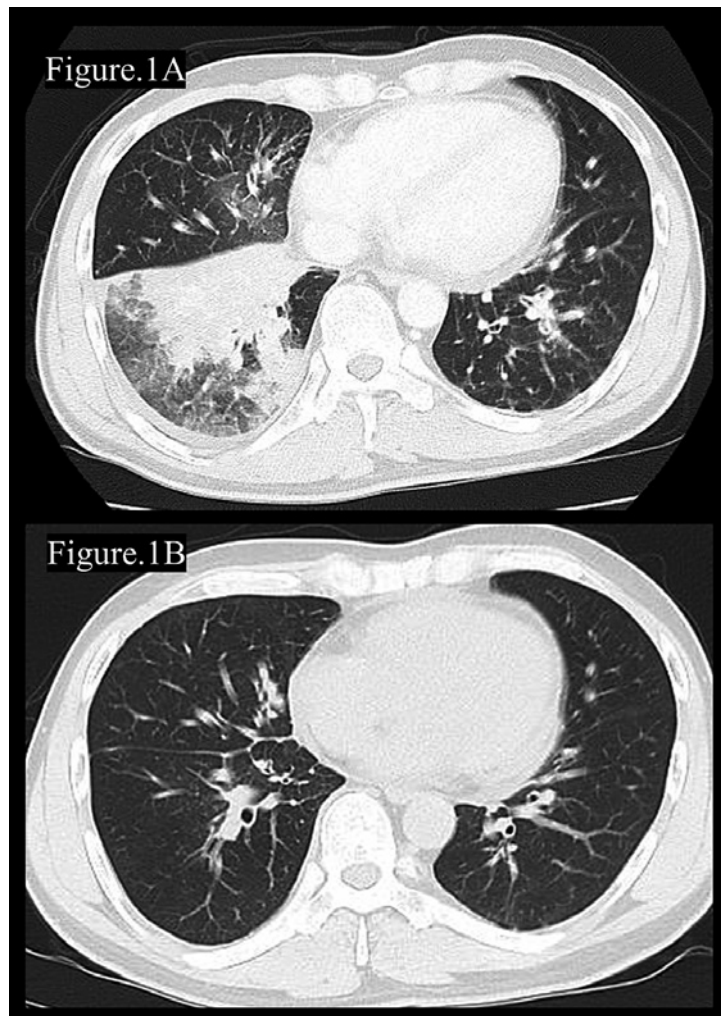
Mucoepidermoid carcinoma (MEC) of the lung is an extremely rare tumor, and a standard chemotherapy has not been established. Furthermore, little work has been conducted on the genetic characteristics of MEC. We herein report the case of a 42-year-old nonsmoking male patient who was referred to our hospital due to cough. Chest computed tomography demonstrated infiltration and atelectasis in the right lower lobe. He was eventually diagnosed with non-small cell lung cancer (NSCLC) with MEC differentiation corresponding to clinical stage IVA (cT4N2M1a[PLE]). Genetic testing for EGFR mutations was negative, but positive for anaplastic lymphoma kinase (ALK) fusion gene. After 2 weeks of first-line treatment with alectinib, the tumor decreased in size and his symptoms improved. Advanced MEC is a rare tumor, and reports on the treatment of ALK-positive NSCLC with MEC differentiation are rare.

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## Introduction

The development of anaplastic lymphoma kinase (ALK)-tyrosine kinase inhibitors (TKIs) has significantly improved the prognosis of non-small cell lung cancer (NSCLC) with the ALK fusion gene. The genetic analysis of cancer cells is the standard of care to select the effective treatment for patients with advanced NSCLC; however, the genetic characteristics of several rare subtypes of NSCLC, such as pulmonary mucoepidermoid carcinoma (MEC) are not fully understood. We herein report a rare case of a 42-year-old man with ALK-positive NSCLC with MEC differentiation who was treated with alectinib, an ALK-TKI.

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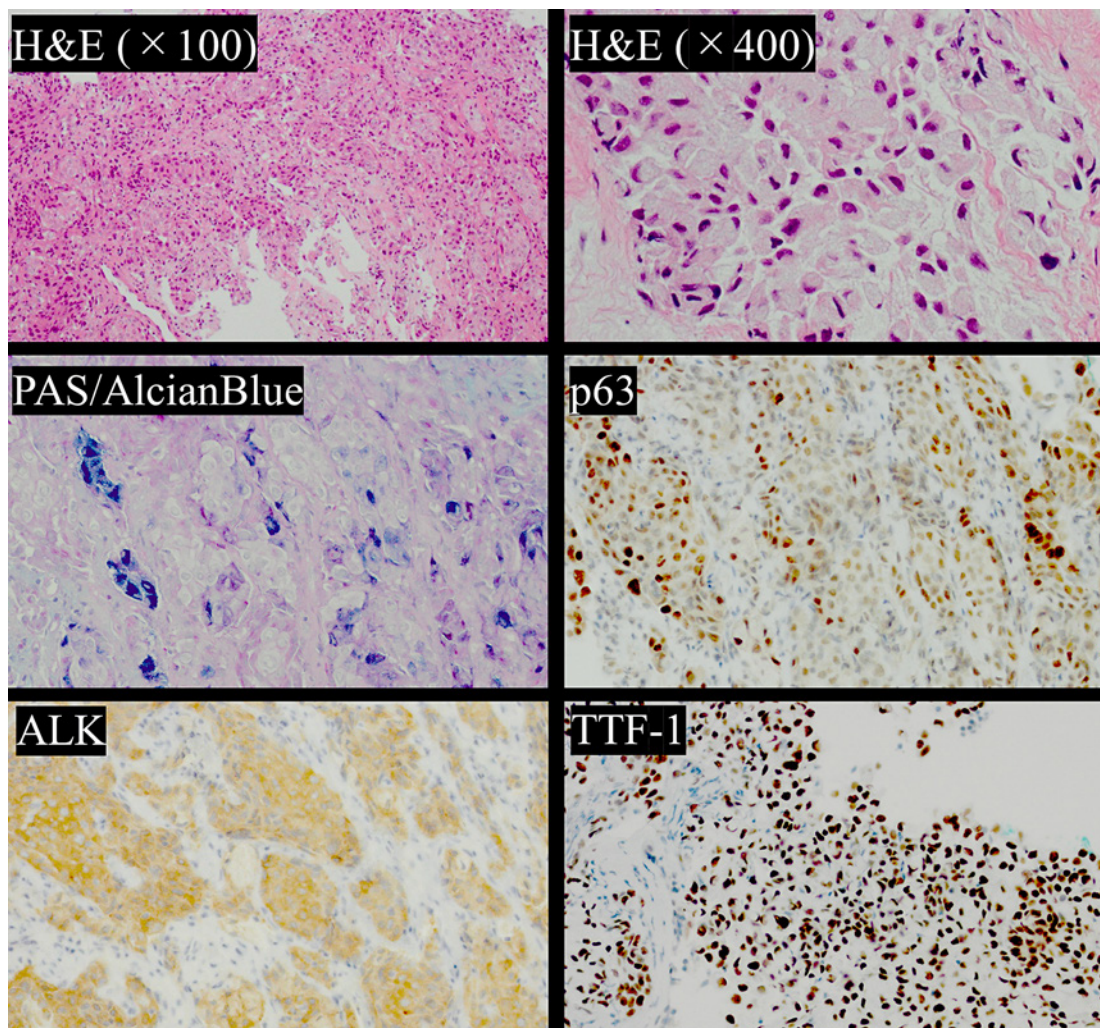


**Fig. 1.** A computed tomography scan on admission showed infiltration and atelectasis in the right lower lobe (A). After the administration of alectinib for 2 months, the infiltration and atelectasis were observed to have shrunk (B).

### Case Report

A 42-year-old nonsmoking man with no significant medical history was referred to our hospital due to a 2-month history of cough. Chest X-ray and chest computed tomography (CT) showed infiltration and atelectasis in the right lower lobe (Fig. 1A). He was treated with ampicillin/sulbactam for 10 days; however, his chest X-ray showed no improvement. He received transbronchial lung biopsy for the diagnosis of the infiltration in the right lower lobe.

A histopathological examination revealed non-small cell carcinoma entirely composed of mucoepidermoid carcinoma features (Fig. 2). Numerous mucus-rich atypical cells were identified, and the nuclei of the atypical cells were enlarged. Neither tubular formation nor squamous differentiation were observed. Mitosis was detected in some of the tumor cells, but no cellular pleomorphism was observed. PAS/Alcian Blue staining revealed Alcian Blue-positive mucus in the tumor cells. An immunohistochemical analysis demonstrated that the tumor cells without mucus were positive for p63 (Fig. 2). The Ki-67 index was 5–10%. The number of mitotic nuclei was less than 1/10 HPF. Based on these results, we initially diagnosed the patient with low-grade MEC. A genetic analysis of the tumor cells revealed ALK fusion gene. An additional immunohistological examination with TTF-1 was positive. Finally, the patient was diagnosed with NSCLC with MEC differentiation (as opposed to MEC).



**Fig. 2.** Pathological analyses: hematoxylin and eosin (H&E) staining and immunohistochemical analyses (PAS/Alcian Blue, p63, ALK, TTF-1).

Contrast-enhanced CT and positron emission tomography/CT identified metastases in the mediastinal and supraclavicular lymph nodes and pleural effusion, indicating that the clinical stage was cT2aN3M1a(PLE), cStage IVA. The patient received alectinib (250 mg/day), and a significant effect was observed (Fig. 1B). At 16 months after the start of treatment, there were no obvious exacerbations of the disease.

### Discussion

We reported a rare case of ALK-positive NSCLC with MEC differentiation that was treated with alectinib.

MEC is a rare malignant tumor, accounting for 0.1–0.2% of all lung cancers [1]. The utility of chemotherapy and radiotherapy in these cases remains controversial [2]. The efficacy of molecular targeted treatment in patients with MEC is controversial. Although several published articles suggest that MECT1/3 fusion gene is common in MEC [3, 4], no medications



targeting the MECT1/3 fusion gene have been developed. Han et al. [5] reported that a patient with MEC responded well to gefitinib, an EGFR-TKI.

The frequency of ALK gene alteration is rare in MEC. Zhen et al. [6] reported that 26 of the 34 cases initially diagnosed with MEC were actual MEC, while the remaining 8 cases were MEC-like tumors. Twenty-six cases of MEC were immunohistochemically positive for CK7, Muc5Ac, p40, and p63. EGFR was positive in 11 of 26 patients, but negative for TTF-1, Calponin, HER2, and ALK in all patients. Eighteen cases of MEC had clearly positive FISH signals. MECT rearrangement was identified in 12 of 18 cases. In contrast, all of 8 MEC-like tumors were positive for p63 and 5 of the 8 were positive for TTF-1 and ALK [6]. Six cases of MEC-like carcinoma had clearly positive FISH signals; none had MECT rearrangement. Although histological findings showed mucoepidermoid carcinoma features in our case, immunohistological findings showed p63 and TTF-1 positivity and a genetic analysis showed ALK fusion gene alteration. We finally diagnosed the patient with NSCLC with MEC differentiation as “MEC-like carcinoma” (as opposed to MEC), as reported by Zhen et al. Our case showed a durable response to alectinib treatment.

We reported the case of a young man with ALK-positive NSCLC with MEC differentiation who responded well to alectinib treatment. Even in rare lung cancers, such as those with MEC features, treatable genetic mutations might be detected, as we reported in the present study. It is important to analyze the genetic alterations to avoid missing therapeutic opportunities even when the tumor shows rare features.

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## Statement of Ethics

This research adhered to the guidelines for research involving human subjects and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Written informed consent was given by the patient to publish his case information and details.

## Conflict of Interest Statement

The authors declare no conflicts of interest in association with the present study.

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## Author Contributions

T.S. made a substantial contribution toward the concept and design of the study and in data acquisition and interpretation. Y.M., T.M., and K.U. were involved in drafting the manuscript and critical revision of the intellectual content. T.S. approved the final version of the manuscript submitted for publication. All authors read and approved the manuscript.

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