Gazi Med J 2025;36(4):460-462

DOI: http://dx.doi.org/10.12996/gmj.2024.4074

A Case of Adjuvant Brigatinib in a Patient with ALK-rearranged R0 Resected Oligometastatic Lung Cancer

ALK-Rearranjmanı Olan Oligometastatik Akciğer Kanser Tanılı R0 Rezeke Edilmiş Hastada Adjuvan Brigatinib Tedavisi

Oktay Ünsal[1], Nalan Akyürek[2], Osman Yüksel[3], Abdullah İrfan Taştepe[4], Ahmet Özet[1]

[1]Department of Medical Oncology, Gazi University Faculty of Medicine, Ankara, Türkiye
[2]Department of Pathology, Gazi University Faculty of Medicine, Ankara, Türkiye
[3]Deparment of General Surgery, Gazi University Faculty of Medicine, Ankara, Türkiye
[4]Deparment of Thoracic Surgery, Gazi University Faculty of Medicine, Ankara, Türkiye

ABSTRACT

Anaplastic lymphoma kinase (ALK) rearrangement is detected at a low rate in non-small cell lung cancer (NSCLC). Patients with ALK rearrangements have poor responses to conventional cytotoxic chemotherapy. Brigatinib is one of the ALK-tyrosine kinase inhibitors recommended for first-line treatment in metastatic NSCLC. Local ablative therapies are applied in the treatment of oligometastatic disease in NSCLC. In this case, a patient with lung adenocarcinoma with ALK-rearranged isolated adrenal metastasis was treated with adjuvant brigatinib after sequential surgery. A 23-month disease-free survival was obtained. The case reported here represents the use of adjuvant therapy with ALK inhibitors in ALK-positive oligometastatic NSCLC in eligible patients.

Keywords: ALK rearrangement, brigatinib, lung cancer, oligometastasis, targeted therapy

ÖZ

Anaplastik lenfoma kinaz (ALK) rearranjmanı, küçük hücreli dışı akciğer kanserinde (KHDAK) düşük oranda tespit edilir. ALK rearranjmanı olan hastalar konvansiyonel sitotoksik kemoterapiye zayıf yanıt verir. Brigatinib, metastatik KHDAK'de birinci basamak tedavi için önerilen ALK-tirozin kinaz inhibitörlerinden (ALK-TKI'ler) biridir. KHDAK'de oligometastatik hastalığın tedavisinde lokal ablatif tedaviler uygulanır. Bu olgu, ALK-rearranjmanı olan izole adrenal metastazlı akciğer adenokarsinomlu bir hastadır, ardışık cerrahi sonrası adjuvan brigatinib ile tedavi edilmiştir. Yirmi üç aylık hastalıksız sağkalım elde edilmiştir. Burada bildirilen vaka, ALK pozitif oligometastatik KHDAK'li uygun hastalarda ALK inhibitörlerinin adjuvan tedavisinin kullanımını temsil etmektedir.

Anahtar Sözcükler: ALK rearranjmanı, brigatinib, akciğer kanseri, oligometastaz, hedefli tedavi

INTRODUCTION

Non-small cell lung cancer (NSCLC), which accounts for most lung cancer cases, is the main cause of cancer-related mortality (1). Although there are many developments in immunotherapy and chemotherapy, the prognosis of patients with advanced disease is still poor. The advent of anaplastic lymphoma kinase-tyrosine kinase inhibitors recommended (ALK-TKI) has completely altered the management strategy and prognosis of patients with advanced NSCLC with ALK fusion.

ALK gene rearrangements encode driver fusion oncoproteins and account for approximately 5% of NSCLC cases (2). After crizotinib, multiple second-generation (e.g., ceritinib, brigatinib, alectinib) and

Cite this article as: Ünsal O, Akyürek N, Yüksel O, Taştepe Aİ, Özet A. A case of adjuvant brigatinib in a patient with alk-rearranged R0 resected oligometastatic lung cancer. Gazi Med J. 2025;36(4):460-462

Address for Correspondence/Yazışma Adresi: Oktay Ünsal, Department of Medical Oncology, Gazi University Faculty of Medicine, Ankara, Türkiye
E-mail / E-posta: oktayunsal@gazi.edu.tr
ORCID ID: orcid.org/0000-0002-3215-8457

Received/Geliş Tarihi: 13.12.2023
Accepted/Kabul Tarihi: 26.02.2024
Publication Date/Yayınlanma Tarihi: 13.10.2025

third-generation (e.g., lorlatinib) ALK-TKIs have been developed for patients with ALK-positive NSCLC, all with higher potency and greater central nervous system penetration than crizotinib (3).

Adjuvant-targeted therapy suggests a viable management option, and patients can also improve survival outcomes (4-6). However, no randomized controlled trials have been reported for patients with ALK-positive locally advanced NSCLC. Here, we present a patient with lung adenocarcinoma with isolated adrenal metastasis at the time of diagnosis, who underwent sequential surgery followed by brigatinib therapy.

CASE REPORT

A 56-year-old, never-smoker male patient applied to the Medical Oncology Clinic in February 2021 with complaints of cough and dyspnea, for a month. Computed tomography (CT) revealed a 29 mm mass in the upper lobe of the left lung (Figure 1a). A transthoracic biopsy was performed on the patient. The pathology result was reported as lung adenocarcinoma. Systemic positron emission tomography (PET)/CT imaging revealed a 26x24 mm mass, regional lymph node metastasis at the ipsilateral hilar and ipsilateral mediastinum lymph nodes, and isolated right adrenal (110x80x50 mm) (Figure 1b) metastasis (cT1cN2M1b, stage IVA, 8th AJCC). Molecular tests have been sent. There was no metastasis on cranial imaging. Gemcitabine (1000 mg/m^2, day 1 and day 8) plus cisplatin (75 mg/m^2, day 1) chemotherapy was started in the patient whose laboratory values were normal, and ECOG performance score was 1. It was reported from the pathology department that molecular tests could not be performed due to insufficient material. After four cycles of chemotherapy, partial response according to RECIST 1.1 criteria was obtained in control imaging (cT1bN1M1) (Figures 2a and 2b). At this stage, as a result of multidisciplinary discussion, sequential surgery was planned for the patient with lung cancer with isolated adrenal metastasis. The preoperative endocrinological evaluation was performed. First, right adrenalectomy surgery was performed. Afterwards, left upper lobectomy and mediastinal lymph node dissection were performed with video-assisted thoracic surgery. Molecular tests were planned again from the lung surgical material. No pathology was detected in postoperative cranial magnetic resonance imaging, thoracic, and abdominal CT. The pathological tumor size was 0.4 cm, and one metastasis was detected in lymph node number 10 (pT1aN1M1). ALK expression was detected using immunohistochemistry (ALK D5F3, Ventana) and fluorescence *in situ* hybridization. An additional two cycles of platinum-based chemotherapy was planned for the patient. However, brigatinib 180 mg/day was started because ALK was positive. The patient's disease-free survival (DFS) with brigatinib was 23 months at the last follow-up. No grade 3/4 adverse events or disease progression occurred at the last follow-up in November 2023. The patient's treatment with brigatinib 180 mg/day and close follow-up continues.

DISCUSSION

Here, we present a 56-year-old male patient with lung adenocarcinoma with isolated adrenal metastasis at the time of diagnosis, who was treated with sequential surgery and adjuvant brigatinib after chemotherapy. Chemotherapy was started, and partial response was obtained in the patient who had isolated adrenal metastasis at the time of diagnosis and whose biopsy material was insufficient for molecular tests. We planned sequential surgery for our patient, who was evaluated as multidisciplinary. The postoperative treatment plan was changed after ALK rearrangement was detected in the surgical material.

Although the frequency of ALK rearrangements is very low, it is clinically important. The advent of oncogenic driver mutations, such as ALK mutations, means that a subset of patients have opportunities for targeted therapy. The clinical application of ALK-TKIs is primarily dependent on the positivity of the *ALK* gene, independent of the molecular characteristics of the fusion partner. Patients with ALK rearrangements have poor responses to conventional cytotoxic chemotherapy, but ALK inhibitors such as ceritinib, crizotinib, and alectinib may affect treatment efficacy and improve outcomes in these patients. On the other hand, it is important to note that tumor biopsy specimens taken from patients with advanced

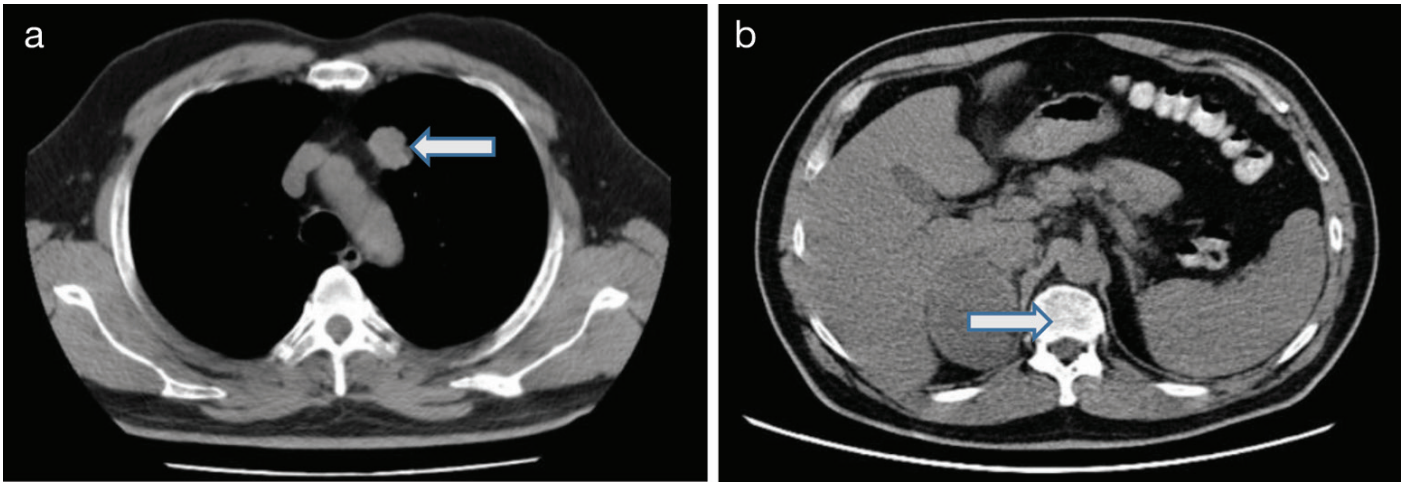

Figure 1. (a) Baseline radiological evaluation of the primary tumor. Computed tomography (CT) revealed a 2.9x2.2 cm mass in the left upper lung. b) Baseline radiological evaluation of right isolated adrenal metastasis (11x8x5 cm) (PET/CT).

PET: Positron emission tomography.

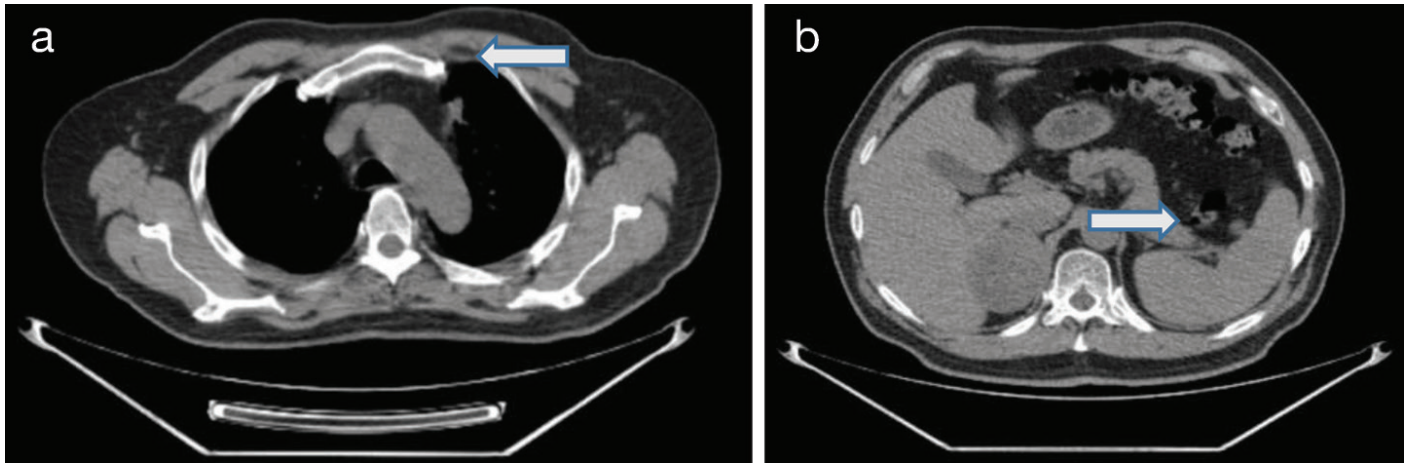

Figure 2. (a) Radiological evaluation of primary tumor after 4 cycles of chemotherapy (1.6x1.1 cm) (PET/CT). b) Radiological evaluation of isolated adrenal metastasis after 4 cycles of chemotherapy (10x7.5x5.5 cm) (PET/CT).

PET: Positron emission tomography, CT: Computed tomography.

NSCLC generally tend to be small, and it is unclear whether these specimens accurately represent tumor histology. Therefore, it is not possible to exclude the possibility that certain cells with ALK rearrangements are present in tumors. In such a situation, patients will lose the opportunity to receive appropriate treatment unless tests for ALK rearrangement are performed. In our case, the biopsy was insufficient for molecular tests at the time of diagnosis.

Local ablative therapies, surgery, or stereotactic radiotherapy (SABR) are now known to be an integral component in the treatment of oligometastatic disease in NSCLC (7,8). The NCCN guidelines suggest that local therapy (RT, SABR, or surgery) for primary and oligometastatic lesions should be used for the management of patients without progression on systemic chemotherapy.

Regarding adjuvant targeted therapy, previous trials (5,6) have explored the administration of oral TKIs for epidermal growth factor receptor-positive NSCLC patients and the results were encouraging. However, no randomized controlled trials have been reported for patients with ALK-positive locally advanced NSCLC. Our patient was oligometastatic and suitable for surgery. He then received adjuvant brigatinib therapy. Results supporting adjuvant therapy were obtained in patients with ALK rearrangement.

In summary, a patient with lung adenocarcinoma with ALK-rearranged isolated adrenal metastasis was treated with adjuvant brigatinib after sequential surgery, and 23 months of DFS was achieved. Our case is the first case in which brigatinib was used after metastasectomy and primary tumor surgery. The case reported here represents the use of adjuvant therapy of ALK inhibitors in ALK-positive oligometastatic NSCLC in eligible patients.

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Footnotes

Authorship Contributions

Surgical and Medical Practices: O.Y., A.İ.T., Concept: O.Ü., A.Ö., Design: O.Ü., A.Ö., Data Collection or Processing: O.Ü., N.A., Analysis or Interpretation: O.Ü., N.A., A.Ö., Literature Search: O.Ü., Writing: O.Ü.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Siegel RL, Miller KD, Wagle NS, Jemal A. Cancer statistics. CA Cancer J Clin. 2023; 73: 17-48.
2. Kwak EL, Bang YJ, Camidge DR, Shaw AT, Solomon B, Maki RG, et al. Anaplastic lymphoma kinase inhibition in non-small-cell lung cancer. N Engl J Med. 2010; 363: 1693-703.
3. Ando K, Manabe R, Kishino Y, Kusumoto S, Yamaoka T, Tanaka A, et al. Comparative efficacy of ALK inhibitors for treatment-naïve ALK-positive advanced non-small cell lung cancer with central nervous system metastasis: a network meta-analysis. Int J Mol Sci. 2023; 24: 2242.
4. Zhong WZ, Chen KN, Chen C, Gu CD, Wang J, Yang XN, et al. Erlotinib versus gemcitabine plus cisplatin as neoadjuvant treatment of stage IIIA-N2 EGFR-mutant non-small-cell lung cancer (EMERGING-CTONG 1103): a Randomized Phase II Study. J Clin Oncol. 2019; 37: 2235-45.
5. Zhong WZ, Wang Q, Mao WM, Xu ST, Wu L, Shen Y, et al. Gefitinib versus vinorelbine plus cisplatin as adjuvant treatment for stage II-IIIA (N1-N2) EGFR-mutant NSCLC (ADJUVANT/CTONG1104): a randomised, open-label, phase 3 study. Lancet Oncol. 2018; 19: 139-48.
6. Yue D, Xu S, Wang Q, Li X, Shen Y, Zhao H, et al. Erlotinib versus vinorelbine plus cisplatin as adjuvant therapy in Chinese patients with stage IIIA EGFR mutation-positive non-small-cell lung cancer (EVAN): a randomised, open-label, phase 2 trial. Lancet Respir Med. 2018; 6: 863-73.
7. Coster JN, Groth SS. Surgery for locally advanced and oligometastatic non-small cell lung cancer. Surg Oncol Clin N Am. 2020; 29: 543-54.
8. Jasper K, Stiles B, McDonald F, Palma DA. Practical management of oligometastatic non-small-cell lung cancer. J Clin Oncol. 2022; 40: 635-41.