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Case Report

Long-term survival following molecular-targeted therapy for intramedullary non-small-cell lung cancer metastasis

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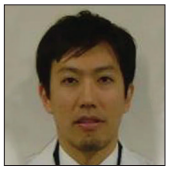

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ABSTRACT

Background: Intramedullary spinal cord metastases (ICSMs) are very rarely curable; these patients typically have very short-term survival rates. Here, a 22-year-old male with non-small-cell lung cancer (NSCLC) later developed ICSM twice; the first C4–C7 tumor responded well to surgery, radiation, and alectinib molecular-targeted therapy. The secondary ICSM C1 lesion seen years later (i.e., likely due to alectinib having been stopped) resolved once alectinib was again administered.

Case Description: A 22-year-old male with a limited smoking history presented with advanced non-small-cell lung cancer (NSCLC) treated with pulmonary surgery followed by radiotherapy and chemotherapy. Four years later, he developed cervical myelopathy attributed to a C4–C7 stage IV NSCLC ICSM (i.e., notably associated with an anaplastic lymphoma kinase [ALK] rearrangement). After cervical surgery and irradiation (40 Gy/20 fr) of the resection cavity, he was also given alectinib; the patient remained disease-free for the next 7 years, remaining on alectinib. However, 1 year after alectinib was discontinued, he experienced a newly occurrent C1 ICSM lesion; the alectinib was restarted, and his tumor regressed over the next 3 years. At present, 14 years after the original ICSM surgery, the patient remains disease free but continued alectinib (Karnofsky Performance Scale: 90%).

Conclusion: Although the prognosis for ICSM is generally poor, molecular-targeted therapies, such as alectinib, as administered in this case, may provide long-term survival for patients with ALK-positive NSCLC tumors.

Keywords: Intramedullary spinal cord metastasis, Molecular-targeted therapy, Non-small-cell lung cancer

INTRODUCTION

Intramedullary spinal cord metastasis (ICSM) is rarely curable. In a meta-analysis involving 284 patients, the median overall survival was 7.3 months.[5] The field of advanced non-small-cell lung cancer (NSCLC) treatment has experienced a paradigm shift with the discovery of genes with high mutation rates, providing a molecular basis to search for targeted therapeutic agents. Herein, a 22-year-old male originally underwent lung surgery for NSCLC (i.e., stage II lung adenocarcinoma harboring an anaplastic lymphoma kinase [ALK] rearrangement) followed by radiotherapy and chemoradiotherapy. Four years after the initial lung surgery for NSCLC, he developed cervical myeloradiculopathy attributed to a magnetic resonance (MR) documented C4–C7 ICSM. After cervical surgery and radiation therapy to the resection cavity, he was started on alectinib (i.e., an ALK inhibitor); it was continued for 7 postoperative years and then stopped. One year after stopping alectinib, the patient newly developed a C1 ICSM. He was restarted

on alectinib, and the tumor totally regressed over the next 3 years. Now, 14 years following the original diagnosis of an ICSM due to NSCLC, the patient remains disease free, and his long-term survival is largely attributed to the alectinib (i.e., molecular-based targeted therapeutic agents).

CASE DESCRIPTION

A 22-year-old male with a limited smoking history presented with Stage II lung NSCLC adenocarcinoma (i.e., harboring an ALK rearrangement) [Table1]. Following lung surgery, he was given four cycles of adjuvant chemotherapy (i.e., including cisplatin and gemcitabine). However, the disease progressed to involve the brain, for which he received whole-brain radiotherapy (40 Gy/20 fr); for the next 4 years, the patient experienced stable disease despite multiple brain lesions. However, 4 years later, he newly presented with right-sided cervical myeloradiculopathy (i.e., involving weakness of the right hand grip and right upper extremity numbness). The cervical MR revealed an ICSM extending from C4 to C7; the lesion was hyperintense on T2-weighted imaging and showed heterogeneous enhancement with gadolinium [Figure 1]. Following surgical resection, the ICSM pathology revealed an NSCLC tumor harboring an ALK rearrangement [Figure 2]. Postoperatively, he underwent adjuvant irradiation (40 Gy/20 fr) to the resection cavity and was also started on alectinib. Subsequently, he underwent surveillance MR scans every 6 months to monitor for disease recurrence/progression. For the next 7 years, he remained neurologically stable despite the continued presence of multiple metastatic cranial lesions; at this point, alectinib was stopped. However, 1 year after stopping alectinib, he developed a new ICSM at the C1 level [Figure 3a]. Over the next 3 years, with the repeated administration of alectinib, this secondary lesion resolved, and he remains in remission now 6 years after that [Figure 3b]. In short, the patient's overall survival is approximately 14 years following the original ICSM surgery (Karnofsky Performance Scale: 90%).

DISCUSSION

Molecular-targeted therapy for metastases in the central nervous system

We have summarized the characteristics of patients with ICSM from NSCLC who have achieved long-term survival [Table 2]. ALK gene rearrangements are found in approximately 5% of NSCLC cases. Although the majority of patients show initial dramatic responses to ALK inhibitors (i.e., average survival time of 70.3 months), they often relapse within 1 year because they develop resistance [Table 2].[1,2,3,6] A substantial portion of NSCLC cases harbor specific genetic alterations that affect tumor proliferation and survival, making them sensitive to inhibition of the corresponding activated oncogenic pathways. In this case, alectinib, a second-generation ALK inhibitor,

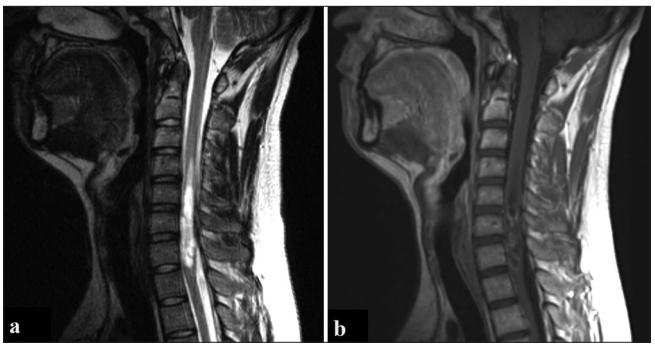
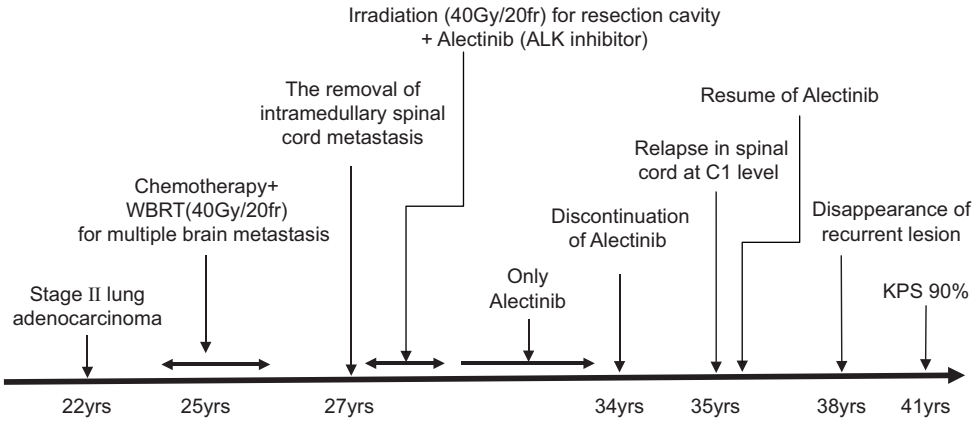


Figure 1: (a) Magnetic resonance imaging revealed an intramedullary spinal cord tumor extending from C4 to C7, appearing as a high-intensity area on T2-weighted imaging and (b) a gadolinium-enhanced heterogeneous mass on T1-weighted imaging.

Table 1: Patient's timeline.



WBRT: Whole brain radiotherapy, ALK: Anaplastic lymphoma kinase, KPS: Karnofsky Performance Scale

Table 2: Summary of patients with intramedullary spinal cord metastasis from non-small-cell lung cancer who have achieved long-term survival.

	Age/Gender	Survival time (months)	Genetic alteration	Molecular-targeted therapy
Hata *et al*. (2012)	35/M	84M	EGFR	Gefitinib
Gainor *et al*. (2013)	31/M	31M	ALK	Crizotinib
Biya *et al*. (2015)	42/M	34M	ALK	Crizotinib Ceritinib
Kodama *et al*. (2022)	40/M	132M	ALK	Crizotinib Alectinib Ceritinib Lorlatinib
Our case (2024)	23/M	168M	ALK	Alectinib

ALK: Anaplastic lymphoma kinase, EGFR: Epidermal growth factor receptor

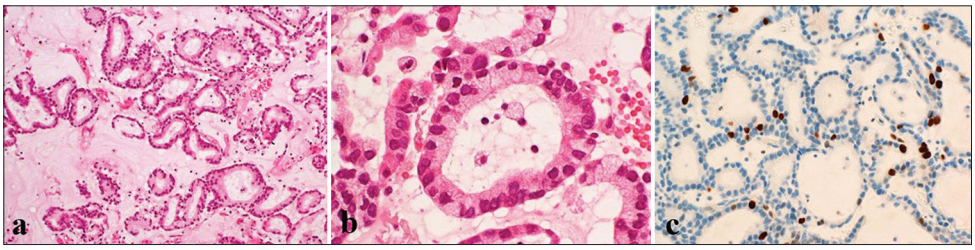


Figure 2: (a: ×200; b: ×400) Hematoxylin and eosin staining of the resected specimen revealed adenocarcinoma. (c) The MIB-1/Ki-67 labeling index was 14.3%.

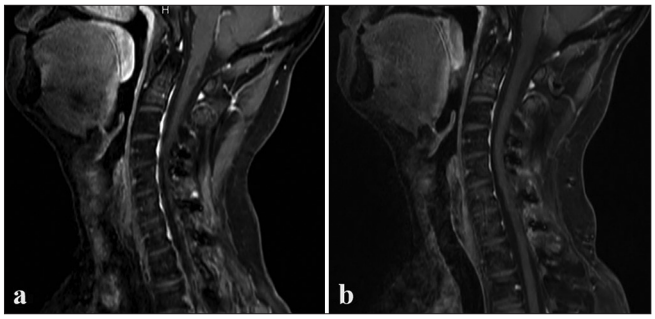


Figure 3: (a) When alectinib was discontinued, the patient had a relapse in the spinal cord at the C1 level after 1 year. (b) Alectinib administration was subsequently restarted, and the recurrent lesion disappeared after 3 years.

showed promising efficacy against ALK-positive NSCLC. Notably, alectinib can penetrate the blood-brain barrier at a high rate to exert clinical efficacy against central nervous system lesions.[8] In a previous study on brain metastases from NSCLC treated by conventional standard chemoradiotherapy, the median survival ranged from 3 to 14.8 months.[9] In another study involving 90 patients with NSCLC/ALK-rearrangement and brain metastases, Johung *et al*. documented a median survival of 49.5 months (i.e., likely due to the efficacy of modern ALK inhibitors).[4] Although recent studies have suggested that the responses to ALK inhibitors differ according to ALK rearrangement variants,[7] the present patient is presently in complete remission with continued molecular-targeted therapy 14 years following the original NSCLC surgery.

CONCLUSION

Although the prognosis for ICSM/NSCLC tumors is generally poor, molecular-targeted therapy with alectinib in a patient with a tumor showing ALK-positive gene rearrangement has, thus far, survived 14 years following the original NSCLC surgery.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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