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Alectinib-Induced Alopecia in a Patient with Anaplastic Lymphoma Kinase-Positive Non-Small Cell Lung Cancer

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Key Words
Hair loss · Brain metastasis · Crizotinib · Anaplastic lymphoma kinase

Abstract
Alectinib, a novel alternative anaplastic lymphoma kinase (ALK) inhibitor, is highly effective against ALK-positive non-small cell lung cancer (NSCLC) and is well tolerated. Molecular targeted agents generally have little contribution to alopecia. We encountered a case of alopecia that developed gradually over 2 months after initiation of alectinib administration for the treatment of ALK-positive NSCLC. The patient had no history of alopecia in previous treatments of cisplatin + pemetrexed and crizotinib. The present case indicates that alopecia should be taken into consideration as toxicity during alectinib treatment, which could adversely affect the psychological and emotional condition and quality of life even in patients treated with specific molecular targeted agents.

Introduction

Alopecia (hair loss) is a psychologically and emotionally distressing side effect of cancer chemotherapeutic drugs. Chemotherapy, especially cytotoxic chemotherapy-induced alopecia, can result in anxiety, depression, a negative body image, lowered self-esteem, and a reduced sense of well-being [1, 2]. In particular, female cancer patients consider hair loss to be

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the most traumatic aspect of chemotherapy, and 8% would decline treatment due to fear of hair loss [1–4]. The incidence and severity of chemotherapy-induced alopecia are variable and vary between particular chemotherapeutic protocols. However, alopecia has generally been uncommon in patients treated with molecular targeted agents.

Here, we report a case of alopecia that developed gradually over 2 months after initiation of alectinib, a second-generation anaplastic lymphoma kinase (ALK) inhibitor, for the treatment of ALK-positive non-small cell lung cancer (NSCLC).

Case Presentation

A 54-year-old female, diagnosed with advanced ALK-positive NSCLC, was admitted to our hospital because of appetite loss and vomiting. Brain CT revealed multiple brain metastases. She had been treated with cisplatin + pemetrexed as first-line therapy and was subsequently treated with crizotinib. Crizotinib treatment was effective but was discontinued several times because of taste alteration. She developed brain metastasis 9 months after initiation of crizotinib treatment. Whole-brain radiotherapy was planned, but she developed dyspnea and orthopnea, resulting in cardiac tamponade before this could be performed. Pericardiocentesis with echocardiographic guidance was performed, and cytological examination revealed ALK-positive NSCLC. After catheter drainage, alectinib (300 mg twice daily) was initiated. The patient was successfully treated, and chest radiographs showed disappearance of pericardial effusion and significant tumor reduction in the primary lesion. In addition, multiple brain metastases also disappeared after initiation of alectinib treatment without brain radiation therapy. Alectinib therapy was continued without any toxicity, but the patient became aware of hair loss 2 months after initiation of the therapy. Although the severity of the adverse event was grade 1 according to the Common Toxicity Criteria for Adverse Events ver. 4, severe alopecia was observed 3–4 months after initiation of alectinib therapy (fig. 1). There were no patches of erythema or scales on her scalp. The alopecia remained during alectinib treatment over 8 months. She complained of no psychological or emotional distress except the alopecia and did not report any changes in lifestyle. In addition, there have been no cutaneous adverse events or abnormalities in laboratory data during alectinib treatment.

Discussion

Alectinib is a second-generation ALK inhibitor with potent in vitro activity against both wild-type and mutated ALK, including mutations that confer resistance to crizotinib [5]. Several recent clinical trials showed that alectinib was effective in patients resistant to crizotinib [6], as well as crizotinib-naive patients [7].

There have been no previous reports of alopecia or hair loss in clinical trials of first-line settings using alectinib and crizotinib in patients with ALK-positive NSCLC [6–8]. In the PROFILE1007 clinical trial [9], which showed superior efficacy of crizotinib to standard chemotherapy in previously treated advanced NSCLC with ALK rearrangement, the rate of alopecia was reported to be 8% with crizotinib. Although the event was not reported in detail, these findings may be reflected by prior chemotherapy or whole-brain irradiation. Indeed, the symptom score of alopecia was improved in the crizotinib group compared with deterioration in the chemotherapy group (pemetrexed or docetaxel). The present case developed brain metastasis, but whole-brain radiation therapy was not performed. In addition,

there were no other additive agents that could have contributed to alopecia. Therefore, alopecia in the present case was most likely due to the alectinib therapy. There are no previous case reports of the clinical presentation of alopecia in PubMed based on a search using the terms 'hair loss' or 'alopecia' and 'crizotinib' or 'alectinib.' Therefore, this is the first case report of ALK-positive NSCLC showing alopecia during alectinib therapy. We highlight the present case to alert physicians to the possibility of alopecia developing from the use of alectinib.

Alectinib has a more favorable toxicity profile compared to crizotinib [6–10]. Alectinib was approved for use in Japan in 2014. Due to the rarity of ALK-positive NSCLC, there has been limited clinical experience with this regimen for such cases. In particular, as the side effects of ALK-targeting inhibitors are unique, strategies are required to minimize the toxicity as well as maximize the efficacy of ALK inhibitors.

In conclusion, the present case demonstrated that alopecia may occur in patients treated with ALK inhibitors. Although an extremely rare clinical manifestation, we should be aware of the possibility of alopecia as an adverse event in patients treated with alectinib.

Statement of Ethics

Written informed consent was obtained from the patient for the publication of this case report and accompanying images.

Disclosure Statement

There are no potential conflicts of interest associated with this report.

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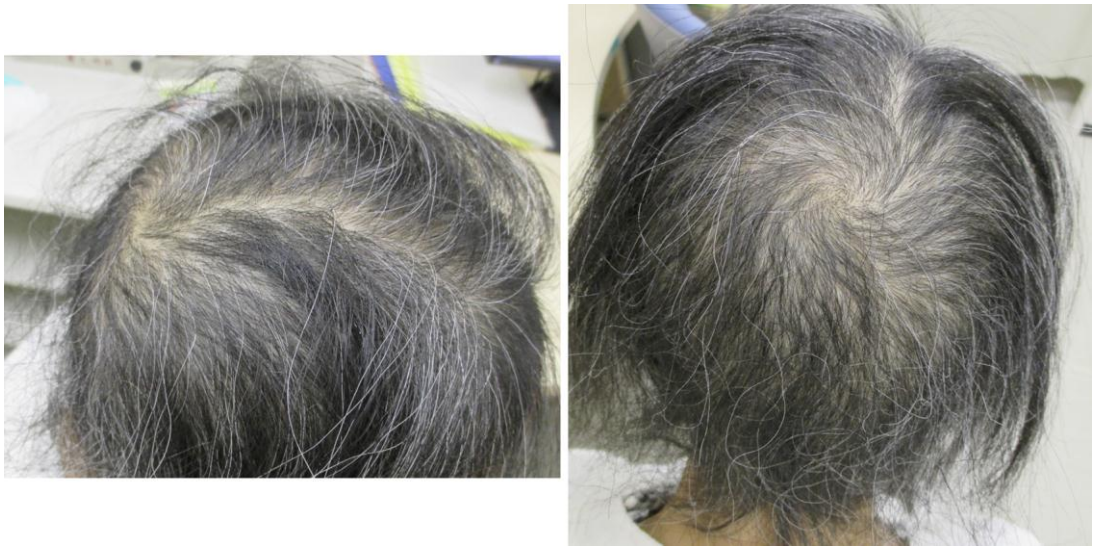

Fig. 1. Photograph of alopecia taken 4 months after initiation of alectinib treatment.