Received: 24 January 2022 | Accepted: 25 February 2022

DOI: 10.1111/1759-7714.14383

CASE IMAGE

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Rare ashy dermatosis-like hyperpigmentation associated with osimertinib

Kazuhito Funai

First Department of Surgery, Hamamatsu University School of Medicine, Hamamatsu, Japan

Correspondence
Kazuhito Funai, First Department of Surgery, Hamamatsu University School of Medicine, 1-20-1 Handayama, Higashi-ku, Hamamatsu, Shizuoka 431-3192, Japan.
Email: kfunai@hama-med.ac.jp

Abstract

Osimertinib, a third-generation epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor (TKI), is the most reliable EGFR-TKI and is widely used as the first-line treatment for EGFR mutation-positive non-small cell lung cancer. Pigmentary changes caused by EGFR-TKIs are unusual, and to the best of my knowledge, hyperpigmentation with osimertinib has rarely been reported as a skin-related adverse event. Here, I report a case of osimertinib-associated ashy dermatosis-like hyperpigmentation on imaging. Although reducing the dose of osimertinib to 40 mg did not improve pigmentation, osimertinib use was continued due to its clinical and radiological benefit, which persisted for a long time.

KEYWORDS

ashy dermatosis-like hyperpigmentation, dermatological adverse event, epidermal growth factor receptor-tyrosine kinase inhibitor, lung adenocarcinoma, quality of life

CASE REPORT

A 77-year-old woman underwent lung wedge resection 3.5 years ago for multiple ground-glass nodules (GGNs) and was diagnosed with lung adenocarcinoma with a positive epidermal growth factor receptor (EGFR) mutation (L858R). During 30 months of surveillance, the GGNs grew constantly and became part-solid nodules. The patient was started on osimertinib therapy (80 mg/day) a year ago and experienced adverse events, including mild diarrhea, acneiform eruption, pruritus, and skin dryness, during the therapy. These adverse events were well managed. Approximately 3 months into osimertinib treatment, the patient noticed progressive skin darkening all over her body without any associated symptoms (Figure 1a,b). Dermatological examination revealed dark brown hyperpigmentation with mild itching throughout the body (Figure 1a,b), including the face. The differential diagnosis of ashy dermatosis-like hyperpigmentation includes intestinal parasites, enterovirus, human immunodeficiency virus, and hepatitis C; however, none of them was applicable in this case. A dermatologist diagnosed osimertinib-associated ashy dermatosis-like hyperpigmentation. Initially, dermatologists prescribed mild steroids for acneiform eruption and moisturizers for pruritus associated with skin dryness. Later, the dermatologist prescribed the strongest alternative steroid for hyperpigmentation of the trunk, along with an antihistamine; however, the treatment was ineffective. Although the therapeutic effect was sustained, the dose of osimertinib was reduced to 40 mg due to progressive hyperpigmentation. The pigmentation did not improve after reducing the dose of osimertinib. However, the antitumor effect was maintained and the multiple part-solid nodules in the lung remained in a contracted state.

DISCUSSION

This case highlights the appearance of osimertinib-associated ashy dermatosis-like hyperpigmentation on imaging. The dermatological adverse event profile of osimertinib, a third-generation EGFR-tyrosine kinase inhibitor (TKI) appears to be milder than that found for first- and second-generation agents.[1] Pigmentary changes caused by EGFR-TKIs are unusual, moreover, hyperpigmentation with osimertinib is a very rare adverse event,[2] unlike acne-like rashes and resistance to treatment. To the best of my knowledge, only three cases have been reported to date.[2,3] Two cases were induced by gefitinib and were thought

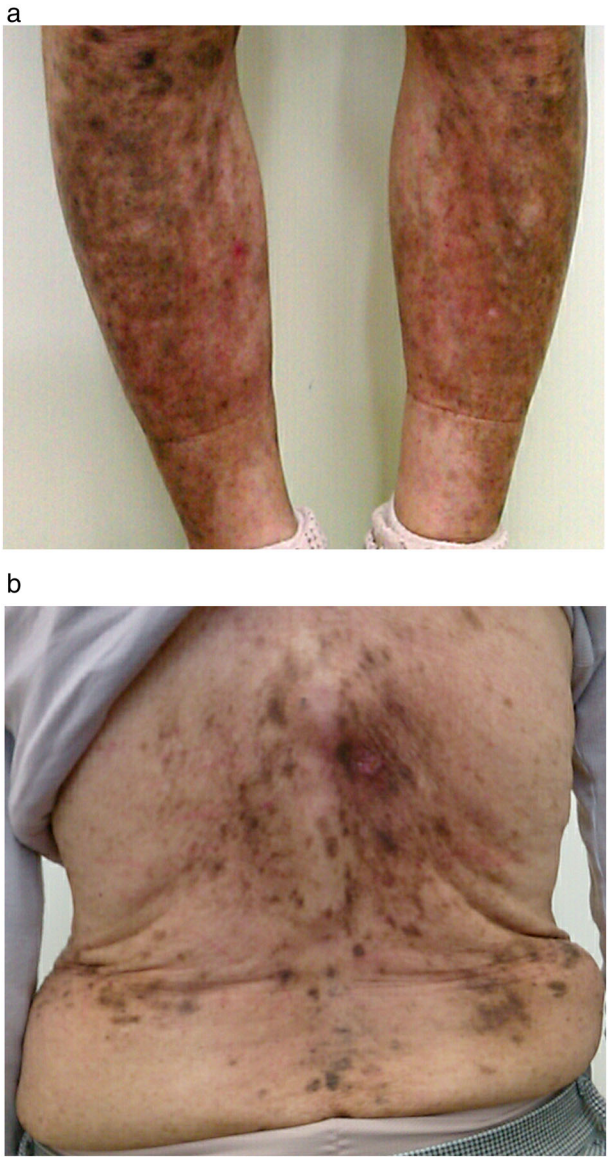

FIGURE 1 Progressive darkening of the skin diagnosed by a dermatologist as osimertinib-associated ashy dermatosis-like hyperpigmentation. Skin of the lower leg (a) and back (b)

to be due to post-inflammatory hyperpigmentation.[2] Both manifested as progressively multifocal hyperpigmented patches that developed after several months of gefitinib administration. The pigmentation followed severe acneiform eruptions.[2] In the third case, the patient experienced pigmentary changes 6 months after starting osimertinib treatment.[3] The ashy dermatosis-like hyperpigmentation did not arise on the previously inflamed skin, but rather, appeared de novo. Therefore, it was not considered as a post-inflammatory hyperpigmentation process.[3] However, in the current case, the ashy dermatosis-like hyperpigmentation was seen on the previously inflamed skin, following acneiform eruption, pruritus, and skin dryness. Therefore, it is considered to be similar to the case of gefitinib. The mechanism of ashy dermatosis-like hyperpigmentation is not clear.

Although osimertinib-associated ashy dermatosis-like hyperpigmentation is a benign condition and the overall prevalence is very low, there is a significant risk of reduction in the quality of life (QoL) of the patients. Since, many female patients receive TKIs in Japan, and hyperpigmentation, especially exposed parts such as a face, has a high risk of affecting their QoL. Not only lung cancer therapists but also dermatologists and physicians should observe this image to help them diagnose the disease more accurately in any future encounters.

CONFLICT OF INTEREST

The author has no conflicts of interest.

ORCID

Kazuhito Funai https://orcid.org/0000-0001-8609-3305

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How to cite this article: Funai K. Rare ashy dermatosis-like hyperpigmentation associated with osimertinib. Thorac Cancer. 2022;13:1436–7. https://doi.org/10.1111/1759-7714.14383