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CASE REPORT

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Radiotherapy can be a Cofactor in the Development and Severity of Lapatinib-Capecitabine-Related Skin Rash

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ABSTRACT

Skin rash induced by concurrent radiotherapy during lapatinib-capecitabine (LC) treatment has been rarely reported. We aim to draw attention to the potential of radiotherapy to act as a cofactor in the development of LC-related skin rash.

Herein, we report a case with a drug-related skin rash triggered by radiotherapy during LC treatment.

A 31-year-old woman with inflammatory metastatic breast cancer presented with a skin rash during LC treatment combined with radiotherapy. She was started on LC treatment, and palliative whole cranial radiotherapy was applied 3 days later. Three days after the radiotherapy, acneiform lesions started from the scalp and a maculopapular rash developed on the trunk and extremities. LC treatment was interrupted and skin lesions regressed rapidly with topical dermatological care, oral H1-antihistamine, and short-term oral steroid treatment. Although LC treatment was restarted alone in the follow-up, no recurrence was observed.

Radiotherapy may be a cofactor in the development and severity of skin toxicity during LC treatment. There is a need to elucidate whether the immunological mechanisms of skin eruptions occurring during concomitant chemoradiotherapy are due to the radiosensitizing effects of biological agents or exacerbation by radiotherapy.

Keywords: Lapatinib, capecitabine, radiotherapy, skin rash, drug allergy

INTRODUCTION

Lapatinib is a dual tyrosine kinase inhibitor that inhibits human epidermal growth factor receptor type 1 (EGFR1) and 2 (HER2). It is used in combination with capecitabine for treating HER2-positive metastatic breast cancer (1,2). Lapatinib-induced skin rash generally presents as acneiform or maculopapular rash, is mild to moderate in severity, and infrequently requires treatment intervention (2-5). Capecitabine is an oral antimetabolic chemotherapeutic agent widely used for various cancers. Capecitabine-related skin toxicity generally presents as a hand-foot syndrome that is mild to moderate in severity (6,7).

To the best of our knowledge, skin rash induced by concurrent radiotherapy during lapatinib-capecitabine (LC) treatment has been rarely reported. Herein, we report a metastatic breast cancer case with a drug-related skin rash triggered by radiotherapy during LC treatment. We aim to draw attention to the potential of concurrent radiotherapy to act as a cofactor in the development of LC-related skin rash.

CASE REPORT

A 31-year-old woman with refractory metastatic breast cancer presented with a skin rash during LC treatment. Previously she was treated with various regimens includ-

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ing docetaxel, trastuzumab, trastuzumab emtansine, and pertuzumab without any response. As the serial imagings revealed progression and cranial metastases, the patient was started on LC treatment, and palliative whole cranial radiotherapy was applied 3 days later.

Three days after the radiotherapy, acneiform lesions appeared, starting from the scalp and spreading to the other sides (Figure 1A,B). In addition, a maculopapular rash developed on the trunk and extremities. Because the lesions were spreading and the patient's quality of life was impaired, LC treatment was interrupted and topical dermatological care, oral H1-antihistamine, and short-term oral steroid treatment (methylprednisolone, 0.5 mg/kg/day) were started and gradually tapered off within 3 weeks with rapid regression of the lesions. Although LC treatment was restarted in the follow-up, no recurrence was observed (Figure 1C). The onset of the rash after the radiotherapy and the absence of an exacerbation despite the restart of LC treatment supported the role of radiotherapy in the rash onset.

DISCUSSION

Lapatinib itself is a radiosensitizing agent, and its action is much more aggravated under the influence of radiotherapy (8). This case is presented to draw attention to how concurrent radiotherapy may act as a cofactor in developing LC-related rash, the true incidence of which is not fully known.

Tyrosine kinase inhibitors have been reported to have a strong radiosensitizing effect. Erlotinib with concurrent radiotherapy has improved outcomes compared with radiotherapy alone, particularly for brain metastases (9,10). Likewise, lapatinib has both antiproliferative and radiosensitizing effects in either EGFR- or HER2-overexpressing breast cell lines (8).

A pronounced skin rash may develop when certain biologic therapies are applied with concurrent radiotherapy. The combination of radiotherapy and cetuximab can cause a severe papulopustular rash (11). Likewise, cranial radiotherapy exacerbates the erlotinib-associated rash (12). Similar to our case, whole cranial radiotherapy with concurrent LC treatment caused the onset of acneiform rash in a patient with metastatic breast cancer (13).

The potential etiopathological mechanisms involved in the synergistic effect of biologic agents and radiotherapy on skin rash are not well understood. Radiosensitizing effects of biological agents and potential systemic or inflammatory-based phenomena have been associated with this process (12).

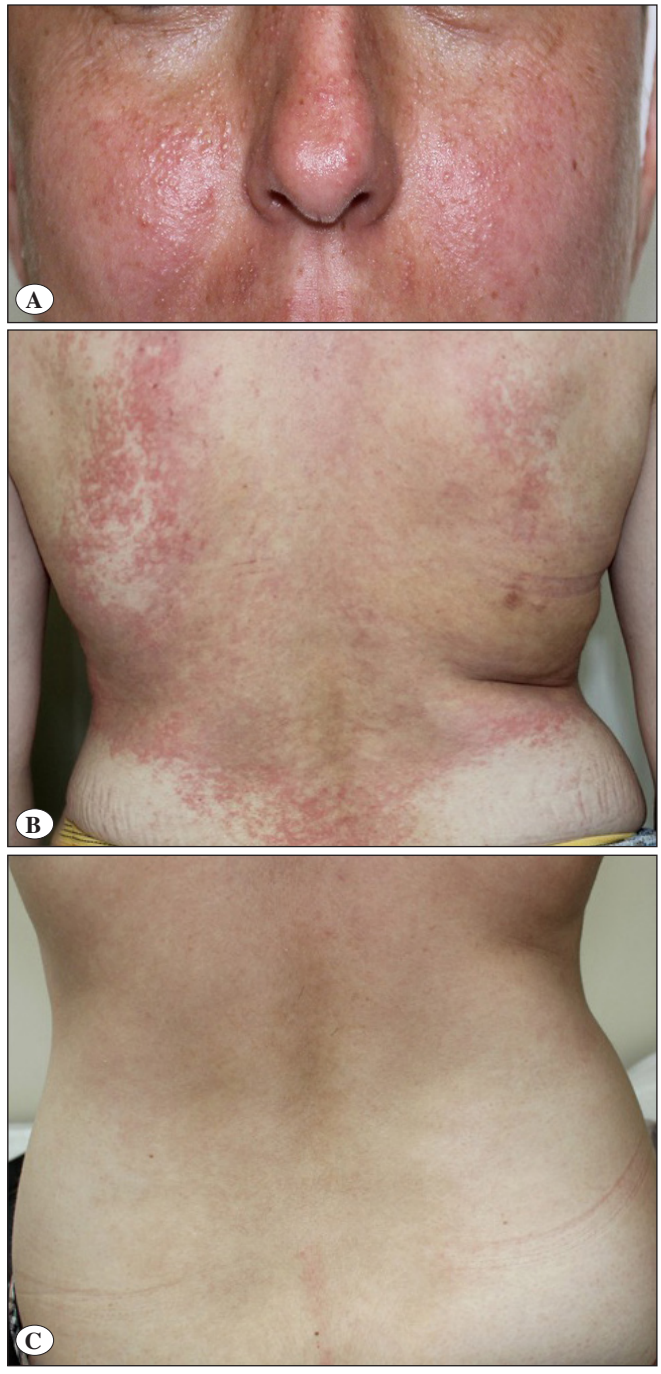

Figure 1. Photograph taken at the resolution phase of the skin rash that developed during LC+radiotherapy treatment. **A)** Acneiform lesions on the face, **B)** Maculopapular rash on the trunk, and **C)** No recurrence with the restart of LC treatment.

In conclusion, radiotherapy can be a cofactor in the development and severity of skin toxicity during LC treatment. This observation is important to contribute to clarifying the etiopathogenetic mechanisms of the skin rash related to LC. Physicians should be aware of the potential development of severe skin rash with concurrent radiotherapy during LC treatment.

Authorship Contributions

Concept: **Nilay Duman,** Design: **Nilay Duman,** Data collection or processing: **Nilay Duman, Meryem Demir, Sercan On, Zeynep Ozsaran,** Analysis or Interpretation: **Nilay Duman,** Literature search: **Nilay Duman, Meryem Demir,** Writing: **Nilay Duman, Meryem Demir, Sercan On, Zeynep Ozsaran,** Approval: **Nilay Duman, Meryem Demir, Sercan On, Zeynep Ozsaran.**

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