Journal of Oncological Science 2 (2016) 29–31

Contents lists available at ScienceDirect

Journal of Oncological Science

journal homepage: https://www.elsevier.com/locate/jons

Case report

Association between efficacy and skin rash following treatment with the lapatinib in metastatic breast cancer

Suleyman Temiz [a, *], Serap Kaya [a], Gokhan Erbag [b], Gorkem Aksu [c], Kazım Uygun [a]

[a] Kocaeli University, Medical Faculty, Deparment of Medical Oncology, Turkey
[b] Kocaeli University, Medical Faculty, Department of Internal Medicine, Turkey
[c] Kocaeli University, Medical Faculty, Deparment of Radiation Oncology, Turkey

ARTICLE INFO

Article history:
Received 26 February 2016
Received in revised form
21 March 2016
Accepted 20 April 2016
Available online 20 July 2016

Keywords:
Lapatinib
Acneiform rash
Tumor response
Drug efficacy

ABSTRACT

Epidermal growth factor receptor (EGFR) is overexpressed in several solid human tumor types, such as colorectal, breast and lung cancers. There are strong evidences that EGFR inhibitors have an increased risk of dermatological side effects arise during the treatment of these agents. Lapatinib is an EGFR inhibitor approved for the treatment of patients with recurrent HER2-positive advanced or metastatic breast cancer. Herein, we report a 35 year old female patient, who had lung metastasis associated with breast cancer, with the presence of acneiform eruption in her face and metastatic lesions which did not progress for 17 months while she was having the lapatinib treatment for her metastatic lesions. As it is occur in all other EGFR inhibitors, the development of acneiform eruption during the lapatinib treatment might be an indicator of better and longer drug response.

1. Introduction

While the overexpression of the epidermal growth factor receptor (EGFR) is an indicator of bad prognosis; head and neck, breast, colorectal and lung cancers are the tumor types in which EGFR is overexpressed.[1,2] The most frequent side-effect of EGFR inhibitors, which are used for the treatment of these tumors, is the acneiform eruption.[3,4] Lapatinib, an EGFR inhibitor is approved for the treatment of patients with recurrent HER2-positive advanced or metastatic breast cancer.[5] The most frequently reported dermatologic event (DEs) of lapatinib is rash.[6] It is known that there is a significant correlation between the acneiform eruption due to use of EGFR inhibitor and the tumor response.[7,8] In this case, we reported a phenomenon of breast cancer treatment indicating a significant association between the acneiform eruption due to use of lapatinib inhibitor and the tumor response.

2. Case report

Right modified radical mastectomy and axillary lymph node dissection were applied in 2003 to the 35-year-old female patient who was diagnosed with invasive ductal carcinoma in the evaluation due to palpable mass in the right breast. It was detected that the diameter of the tumor is 2 cm and there is carcinoma metastasis in the four of the axillary lymph nodes (T2N2M0). It was found that estrogen and progesterone receptor were negative and HER2 was positive. The patient was taken to follow-up after receiving 6 cycles of adjuvant fluorouracil, doxorubicin and cyclophosphamide therapy. Multiple metastases, the largest of which was 3 cm, were detected in both lungs in computed tomography of the thorax which was applied in February 2006 due to the increase in Ca 15.3 level (Fig. 1). Despite the variety of chemotherapeutic drugs between February 2006 and March 2009, the disease progressed and lung metastases were developed (Table 1). Thus, lapatinib and capecitabine treatments were initiated in April 2009. Grade II–III acneiform rashes were occurred in the face skin in the 14TH day of the treatment (Fig. 2). Treatment was continued without decreasing the drug dose and the lung metastases were regressed

* Corresponding author. Yahya Kaptan Mah, Hanlı Sok, Armadakent-5 Sitesi B/A Blok K:1 D:1, Kocaeli, Turkey. Tel.: +90 262 3038841; fax: +90 262 3038001.
E-mail address: drstemiz@yahoo.com (S. Temiz).
Peer review under responsibility of Turkish Society of Medical Oncology.

http://dx.doi.org/10.1016/j.jons.2016.04.004

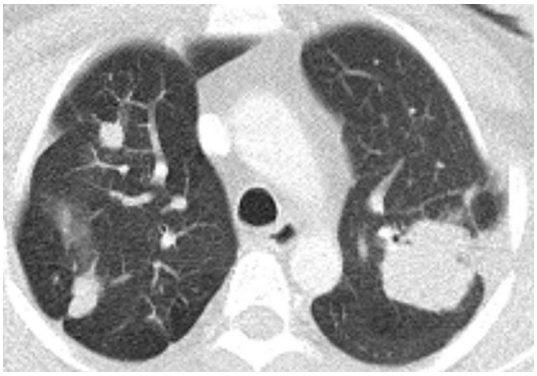

Fig. 1. Bilateral multipl lung metastases

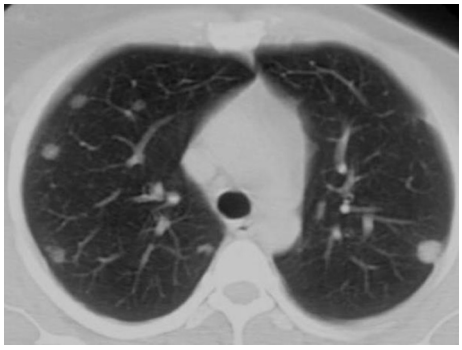

Fig. 3. Regressed lung metastases

in the follow-up (Fig. 3). Treatment was stopped in the 17TH month of treatment since a progression in the lung metastases was seen, and the rash completely disappeared (Fig. 4).

3. Discussion

EGFR inhibitors are generally well tolerated and do not have the severe systemic side-effects as usually seen with other cytotoxic drugs.[9,10] EGFR inhibitors are associated with specific dermatologic reactions, including a papulopustular rash (acneiform eruption) that affects primarily the face and upper trunk, pruritus, paronychia, xserosis and alopecia.[11,12] The most frequently reported DEs of lapatinib is rash. Most DEs developed between 1 and 14 days of starting treatment, with a median duration of 29 days.[6] Lapatinib-associated DEs appear to be clinically different from these associated with single–targeted EGFR agents. Rash associated with lapatinib tends to be localized most frequently on the trunk and infrequently on the face, whereas rash occurred on the face in 82% of the patients treated with cetuximab.[13] Grade II–III acneiform eruption occurred only in the face in the 14TH day of lapatinib and capecitabine treatment and rash continued during treatment in our case. There are conflicting results about correlation between tumor response and the presence or extent of skin rash as demonstrated with cetuximab.[7,8] In a randomized study of breast cancer patients who were treated with capecitabine or the combination of capecitabine and lapatinib, the incidence of skin rash was low and did not correlate to outcome.[14] On the other hand, another study reports that there is a significant correlation between tumor response and the rash which occurs during lapatinib treatment.[15] In our patient, rashes continued during the treatment and the duration in which the disease remained stable was increased significantly. In conclusion, considering this duration, the 17-month progression-free survival achieved by the treatment has led the acneiform rashes which evolved and continued during the treatment to be thought as a predictor of response to drug.

Table 1
Used chemotherapeutic drugs for the patient

Chemotherapeutic drugs	Number of the cycles given	Progression free time
DEC	6 cycles	7 months
CapT	6 cycles	6 months
Cap	6 cycles	5 months
DCap	6 cycles	5 months
GT	6 cycles	6 months
DT	6 cycles	6 months

D; Dosetaxel, E; Epirubicin, C; Cyclophosfamide, Cap; Capecitabine, T; Trastuzumab, G; Gemcitabine

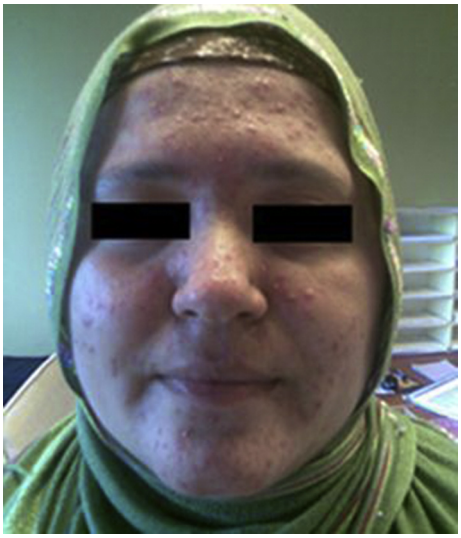

Fig. 2. The acneiform rash evolved during the lapatinib treatment

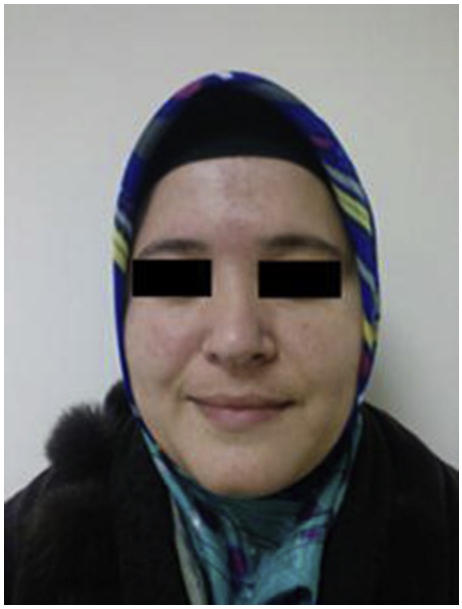

Fig. 4. Appearance one month after the treatment

Conflict of interest

There is no conflict of interest.

References

1. Dei Tos AP, Ellis I. Assessing epidermal growth factor receptor expression in tumours: What is the value of current test methods? *Eur J Cancer*. 2005;41:1383–1392.
2. Itakura Y, Sasano H, Shiga C, et al. Epidermal growth factor receptor overexpression in esophageal carcinoma. An immunohistochemical study correlated with clinicopathologic findings and DNA amplification. *Cancer*. 1994;74:795–804.
3. Rowinsky EK, Schwartz GH, Jared A, et al. Safety, pharmacokinetics, and activity of ABX-EGF, a fully human anti-epidermal growth factor receptor monoclonal antibody in patients with metastatic renal cell cancer. *J Clin Oncol*. 2004;22:3003–3015.
4. Tan AR, Yang X, Hewith SM, et al. Evaluation of biologic and points and pharmacokinetics in patients with metastatic breast cancer after treatment with erlotinib, an epidermal growth factor receptor tyrosine kinase inhibitor. *J Clin Oncol*. 2004;22:3080–3090.
5. Tykerb [package insert] GlaxoSmithKline, Research Triangle Park, NC 2007.
6. Lacouture ME, Laabs SM, Koehler M, et al. Analysis of dermatologic events in patients with cancer treated with lapatinib. *Breast Cancer Res Treat*. 2009;114:485493.
7. Perez-Soler R. Can rash associated with HER1/EGFR inhibition be used as a marker of treatment outcome? *Oncology*. 2003;11(Suppl 12):23–28.
8. Mohammed MK, Ramalingam S, Lin Y, et al. Skin rash and good performance status predict improved survival with gefitinib in patients with advanced non-small cell lung cancer. *Ann Oncol*. 2005;16:780–785.
9. Cunningham D, Humblet Y, Siena S, et al. Cetuximab monotherapy and cetuximab plus irinotecan in irinotecan-refractory metastatic colorectal cancer. *N Engl J Med*. 2004;351:337–345.
10. Kris MG, Natale RB, Herbest RS, et al. Efficacy of gefitinib, an inhibitor of the epidermal growth factor receptor tyrosine kinase, in symptomatic patients with non-small cell lung cancer. *JAMA*. 2009;2003:2149–2158.
11. Perez-Soler R, Saltz L. Cutaneous adverse effects with HER1/EGFR-targeted agents: Is there a silver lining? *J Clin Oncol*. 2005:5235–5246.
12. Agero AL, Dusza SW, Benvenuto-Andrade C, et al. Dermatologic side effects associated with the epidwermal growth receptor inhibitors. *J Am Acad Dermatol*. 2006;55:657–670.
13. Jacot W, Bessis D, Jorda E, et al. Acneiform eruption induced by epidermal growth factor inhibitors in patients with solid tumours. *Br J Dermatol*. 2006;151:238–241.
14. Ramanathan RK, Belani CP, Singh DA, et al. A phase II study of lapatinib in patients with advanced biliary tree and hepatocellular cancer. *Cancer Chemother Pharmacol*. 2009;64:777–783.
15. Geyer CE, Forster J, Lindquist D, et al. Lapatinib plus capecitabine for HER2-positive advanced breast cancer. *N Engl J Med*. 2006;355:2733–2743.