Symmetrical Drug-Related Intertriginous and Flexural Exanthema and Acneiform Eruption in a Patient with Metastatic Colorectal Cancer Treated with Cetuximab

Abstract

Over recent years, targeted therapy has become one of the most important innovations in cancer treatment. Agents targeting the epidermal growth factor receptor (EGFR) are administered in patients with advanced, recurrent or metastatic malignancy. We reported the case of a 74 year-old male patient with metastatic colorectal cancer who developed an SDRIFE and acneiform eruption during molecular target therapy with cetuximab and FOLFOX.

Keywords: *Acneiform eruption, cetuximab, skin toxicity, symmetrical drug-related intertriginous and flexural exanthema*

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Introduction

Over recent years, targeted therapy has become one of the most important innovations in cancer treatment. Agents targeting the epidermal growth factor receptor (EGFR) are administered in patients with advanced, recurrent, or metastatic malignancy.

Skin toxicity is one of the most common side effects of EGFR inhibitors (EGFRIs).[1]

Case Report

In August 2018, a 74-year-old male with colorectal cancer RAS wild type, with multiple liver metastases, received chemotherapy in accordance with the folinic acid, fluorouracil, and oxaliplatin (FOLFOX) scheme for 12 cycles, and cetuximab 250 mg/m^2 weekly until March 2019. Due to disease response, he continued weekly maintenance therapy with Cetuximab.

In May 2019, he was referred to our Plastic Surgery Unit due to the presence of a papulopustular eruption located at the mouth area, without mucosal involvement. Multiple superficial erosions with thin, light-brown to golden-yellow crusts, and vegetating lesions were observed [Figure 1a]. At the same time, he developed a symmetrical erythematous sharply demarcated erythema on the gluteal area [Figure 1b]. Patient history suggested a possible drug eruption. A microbiological culture of the crusting lesions of the mouth area showed the presence of *Staphylococcus aureus* and *Streptococcus anginosus*, whereas the gluteal skin resulted negative. We started a therapy which included cleansing, removal of crusts, application of wet dressings, and fusidic acid cream at the mouth area, with a complete resolution in 2 weeks [Figure 2a]. The gluteal area was treated with topical steroids and zinc oxide cream, with a complete resolution in 1 week [Figure 2b]. A prophylaxis with minocycline 100 mg daily for 8 weeks was also started.

Discussion

Cetuximab is a part of the EGFRIs used in metastatic or nonresectable colorectal cancer with EGFR and without RAS (wild-type) mutations.[2]

It is generally better tolerated than conventional chemotherapy. The main side effects are acneiform eruptions, xerosis, pruritus, paronychia, hair abnormalities, mucositis, trichomegaly, hypertrichosis, alopecia, photosensitivity, and urticarial.[1] Moreover, we recently highlighted the appearance of intertrigo such as eruption during therapy with cetuximab.[3]

How to cite this article: Coppola R, Santo B, Silipigni S, Panasiti V. Symmetrical drug-related intertriginous and flexural exanthema and acneiform eruption in a patient with metastatic colorectal cancer treated with Cetuximab. Clin Cancer Investig J 2021;10;331-2.

Submitted: 24-Jan-2021
Revised: 17-May-2021
Accepted: 05-Jun-2021
Published: 11-Dec-2021

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Access this article online

Website: www.ccij-online.org

DOI: 10.4103/ccij.ccij_11_21

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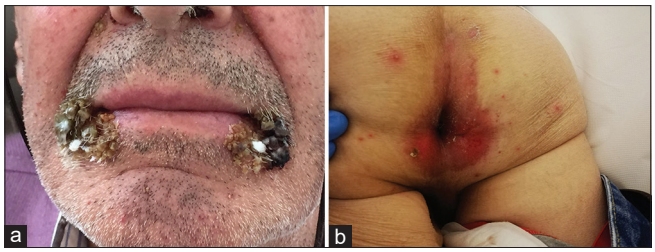

Figure 1: (a and b) Initial presentation

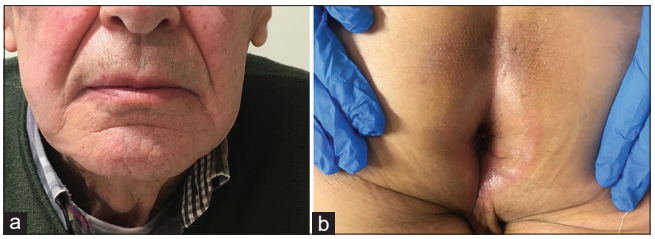

Figure 2: (a and b) Resolution after therapy

The alterations in EGFR signaling promote cell growth and inflammation, but the pathogenesis of these eruptions has not been fully elucidated. In fact, EGFR signaling has been shown to be critical to the normal development of skin and hair in human and mouse models.[4] Even if infections do not seem to be the driver factor, the disruption of the skin barrier can lead to secondary bacterial or viral infections, most frequently with *S. aureus*, although in our patient *Streptococcus anginosus* was also detected.[5]

Symmetrical Drug-related Intertriginous and Flexural Exanthema (SDRIFE) is a symmetrical erythematous rash of the gluteal and intertriginous areas observed after exposure to beta-lactam, in particular amoxicillin, although there are many reports of other systemic drugs also implicated.[6]

The clinical course usually is benign and self-limited; however, it could progress to a generalized maculopapular exanthema if the eliciting drug is not withdrawn.[7] Treatment of SDRIFE consists of discontinuation the triggering drug. In addition, antihistamines and topical/systemic glucocorticosteroids can be used,[8-10] especially when it comes to life-saving therapies such as cancer therapy.

There are only two published cases regarding SDRIFE in association with Cetuximab and FOLFOX,[11] and one case in a patient treated with gefitinib.[12]

In our opinion, the development of a SIDFRE-like reaction during oncologic treatment is now being carefully evaluated due to increased awareness of this eruption as a potential cutaneous adverse effect of EGFRI.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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