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Symmetrical Drug-Related Rash and Acneiform Lesions in a Metastatic Colorectal Cancer Patient on Cetuximab

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Abstract

Advancements in targeted therapy have significantly influenced modern cancer treatment. Among these, epidermal growth factor receptor (EGFR) inhibitors are widely utilized for managing metastatic, recurrent, and advanced malignancies. This report discusses a 74-year-old male diagnosed with metastatic colorectal cancer who experienced symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) alongside an acneiform eruption during cetuximab therapy in combination with FOLFOX chemotherapy. Examination revealed multiple superficial erosions accompanied by thin, light-brown to golden-yellow crusts and vegetating lesions. Concurrently, the patient exhibited a sharply demarcated symmetrical erythematous rash on the gluteal region. Given his medical history, a drug-induced reaction was suspected. Microbiological cultures from the crusted lesions around the mouth confirmed the presence of *Staphylococcus aureus* and *Streptococcus anginosus*, while cultures from the gluteal area were negative. The patient underwent treatment involving lesion cleansing, crust removal, wet dressings, and the application of fusidic acid cream to the affected mouth area, leading to complete resolution within two weeks. The erythema on the gluteal region was managed with topical steroids and zinc oxide cream, which resolved within one week. Additionally, prophylactic therapy with minocycline at a dosage of 100 mg per day was initiated for eight weeks.

Keywords: Cetuximab, Acneiform eruption, Skin toxicity, Symmetrical drug-related intertriginous and flexural exanthema

Introduction

The landscape of cancer treatment has evolved significantly with the introduction of targeted therapies in recent years. Among these, epidermal growth factor receptor (EGFR) inhibitors are frequently prescribed for patients with recurrent, or metastatic malignancies. However, a prevalent adverse effect associated with EGFR inhibitors (EGFRIs) is skin toxicity.

This report discusses a 74-year-old male diagnosed with metastatic colorectal cancer who experienced symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) alongside an acneiform eruption during cetuximab therapy in combination with FOLFOX chemotherapy.

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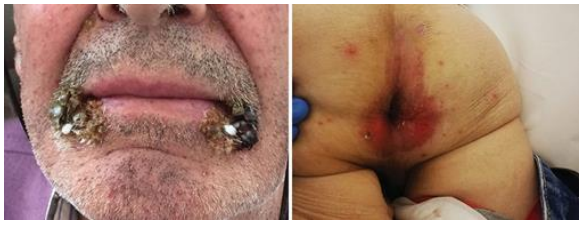
Case Report

In August 2018, a 74-year-old male diagnosed with RAS wild-type colorectal cancer with several liver metastases began chemotherapy following the fluorouracil, folinic acid, and oxaliplatin (FOLFOX) regimen for 12 cycles. Alongside this, he received weekly doses of cetuximab at 250 mg/m² until March 2019. Because of a favorable response to treatment, he continued with cetuximab as maintenance therapy every week.

By May 2019, we referred him to our plastic surgery unit for evaluation of a papulopustular eruption around the mouth, which did not extend to the mucosa. Examination revealed multiple superficial erosions accompanied by thin, light-brown to golden-yellow crusts and vegetating lesions **(Figure 1a)**. Concurrently, the patient exhibited a

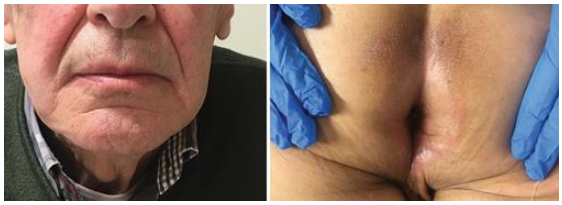
sharply demarcated symmetrical erythematous rash on the gluteal region **(Figure 1b)**. Given his medical history, a drug-induced reaction was suspected. Microbiological cultures from the crusted lesions around the mouth confirmed the presence of *Staphylococcus aureus* and *Streptococcus anginosus*, while cultures from the gluteal area were negative.

The patient underwent treatment involving lesion cleansing, crust removal, wet dressings, and the application of fusidic acid cream to the affected mouth area, leading to complete resolution within two weeks **(Figure 2a)**. The erythema on the gluteal region was managed with topical steroids and zinc oxide cream, which resolved within one week **(Figure 2b)**. Additionally, prophylactic therapy with minocycline at a dosage of 100 mg per day was initiated for eight weeks.



(a) (b)

Figure 1. (a and b) Initial presentation



(a) (b)

Figure 2. (a and b) Resolution after therapy

Discussion

Cetuximab belongs to the class of EGFR inhibitors (EGFRIs) used in the treatment of metastatic or unresectable colorectal cancer in patients with EGFR expression and without RAS (wild-type) mutations [1]. Compared to traditional chemotherapy, cetuximab is generally associated with a more favorable tolerance profile. However, it can lead to several dermatological side effects, including acneiform eruptions, paronychia, hair abnormalities, xerosis, pruritus, mucositis, trichomegaly, hypertrichosis, photosensitivity, alopecia, and urticarial [2]. Additionally, recent observations have identified intertriginous eruptions as a possible reaction during cetuximab therapy [3].

EGFR signaling plays a crucial role in regulating cell proliferation and inflammatory responses, yet the exact mechanism behind these skin reactions remains unclear. Studies in both human and mouse models suggest that EGFR is essential for maintaining normal skin and hair development [4]. While infections are not necessarily the primary trigger, disruption of the skin barrier may increase susceptibility to secondary viral infections or bacterial, with *Staphylococcus aureus* being the most commonly implicated pathogen. However, in this particular case, *Streptococcus anginosus* was also found [5].

Symmetrical Drug-Related Intertriginous and Flexural Exanthema (SDRIFE) is characterized by a well-defined erythematous rash in intertriginous and gluteal regions following exposure to certain systemic medications, most notably beta-lactam antibiotics such as amoxicillin. However, various other systemic drugs have also been associated with this reaction [6]. The condition is generally benign and self-limiting, though failure to discontinue the causative drug can lead to a more widespread maculopapular exanthema [7]. Managing SDRIFE primarily involves stopping the triggering medication. In cases where treatment continuation is necessary, supportive therapy with antihistamines and topical or systemic glucocorticosteroids may be beneficial [8-10]. This approach is particularly relevant in cancer patients undergoing critical life-sustaining treatments.

To date, only two documented cases have linked SDRIFE to a combination of Cetuximab and FOLFOX [11], along with a single report in a patient receiving gefitinib [12]. Given the increasing awareness of SDRIFE as a potential dermatological side effect of EGFRIs, we believe that such reactions should now be more closely monitored and evaluated in oncology settings.

Declaration of Patient Consent

The authors confirm that all necessary patient consent forms have been obtained. The patient(s) has/have provided consent for the publication of their images and clinical details in this journal. They acknowledge that while their names and initials will not be disclosed and efforts will be made to maintain their anonymity, complete confidentiality cannot be assured.

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Conflict of Interest: None

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Ethics Statement: None

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