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Intertrigo-Like Eruption Induced by Cetuximab: A Novel EGFR Inhibitor-Associated Toxicity

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ABSTRACT

Targeted therapy has emerged as one of the most significant developments in cancer treatment in recent years. Patients with advanced, recurring, or metastatic cancer are treated with agents that target the epidermal growth factor receptor (EGFR). One of the most prevalent adverse reactions of EGFR inhibitors is skin damage. We report on a 70-year-old male patient with metastatic colorectal cancer who experienced an intertrigo-like eruption while receiving topical corticosteroid treatment as part of molecular target therapy with cetuximab. After being diagnosed in 2014, the patient had surgery. The surgical anastomosis (total dose = 50.4 Gy/dose per fraction = 1.8 Gy) and pelvic lymph nodes (total dose = 45 Gy; dose per fraction = 1.8 Gy) were treated with adjuvant radiochemotherapy in 2014. He then underwent four cycles of chemotherapy using the folinic acid, fluorouracil, and oxaliplatin scheme. The patient began chemotherapy in 2016 using the folinic acid, fluorouracil, and irinotecan scheme in conjunction with cetuximab 250 mg/sq. m weekly (for 6 cycles) due to the development of the illness as seen by fluorodeoxyglucose-positron emission tomography/CT. Owing to the stability of his condition, he resumed weekly cetuximab maintenance therapy, which is currently continuing with a partial response. After four weeks, a full remission was achieved. According to the results of this study, it might be beneficial to think about premedication with corticosteroids for individuals who have already experienced an episode of intertrigo-like eruption.

Keywords: Cetuximab, Intertrigo-like eruption, Skin toxicity, EGFR

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Introduction

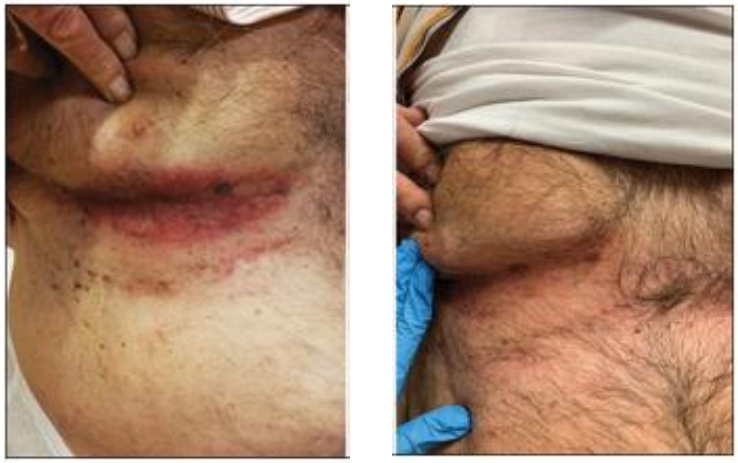
One of the most significant advancements in the treatment of cancer is targeted therapy. Patients with improved, recurring, and metastatic cancer are treated with agents that target the epidermal growth factor receptor (EGFR). One of the most frequent adverse effects of EGFR inhibitors is skin damage [1]. We describe a 70-year-old man with metastatic colorectal cancer who experienced an intertrigo-like eruption while receiving cetuximab treatment.

Case report

After being diagnosed in 2014, the patient had surgery. The surgical anastomosis (total dose = 50.4 Gy/dose per fraction = 1.8 Gy) and pelvic lymph nodes (total dose = 45 Gy; dose per fraction = 1.8 Gy) were treated with adjuvant radiochemotherapy in 2014. He then underwent four cycles of chemotherapy using the folinic acid, fluorouracil, and oxaliplatin scheme. The patient began chemotherapy in 2016 using the folinic acid, fluorouracil, and irinotecan scheme in conjunction with cetuximab 250 mg/sq. m weekly (for 6 cycles) due to the development of the illness as seen by fluorodeoxyglucose-positron emission tomography/CT. Owing to the stability of his

condition, he resumed weekly cetuximab maintenance therapy, which is currently continuing with a partial response.

He acquired many glossy, well-defined erythematous macules throughout the therapy that affected the scrotum, inguinal area, and bra area (pillar axillary and submammary region). The lesions (skin toxicity grade 2 by NCI/GOG standards) produced a burning sensation but did not impede regular daily activities. There were no further mucosal lesions or palmoplantar involvements found. Fungal cultures and skin scrapings examined under a microscope showed no signs of infection. Based on the patient's medical history, cetuximab may cause an intertrigo-like eruption. Clobetasol BID for three weeks was a topical corticosteroid treatment that was launched. It was advised to wear loose clothing, stay away from sharp things, and wear tight shoes. After four weeks, the lesions were completely remitted in response to therapy **(Figure 1)**. The oncologists were shown the situation and chose to proceed with the treatment.



a) b)

Figure 1. Clinical presentation before and after 4 weeks of treatment.

Results and Discussion

Cetuximab is an EGFR-targeting medication used to treat colorectal cancer that has spread or is incurable, has EGFR expression, and does not have RAS (wild-type) mutations [2]. One of the main adverse effects of cetuximab therapy is skin responses, which include urticarial, xerosis, pruritus, paronychia, acneiform rash, mucositis, hair abnormalities, increased growth of facial hair or eyelashes, and photosensitivity. These skin conditions have been dubbed papulopustular and/or paronychia, regulatory anomalies of hair development, itching, and dryness because they are linked to acneiform eruptions and are caused by EGFR syndrome inhibitors [1]. The National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03 is the most widely used grading method to determine the grade of skin toxicity caused by cetuximab. It considers the body surface area affected by the response, represented as a percentage [3].

Not yet; cetuximab has been linked to intertrigo-like eruptions. In individuals receiving pegylated liposomal doxorubicin, it has been documented as cutaneous toxicity [4].

It is uncertain what causes EGFR inhibitors to cause skin toxicity. The outer layers of hair follicles, pilosebaceous glands, and undifferentiated, actively growing basal and suprabasal keratinocytes in the epidermal layer are the usual sites for EGFR expression. By controlling keratinocyte proliferation, differentiation, migration, and survival, EGFR is essential for preserving epidermal homeostasis [5].

Lower basal keratinocyte proliferation, growth arrest, and keratinocyte death are the outcomes of cetuximab's downregulation of phosphorylated EGFR in basal and suprabasal keratinocytes as well as the outer layer of hair follicles. The EGFR inhibitors then cause the overexpression of inflammatory chemokines and cytokines, including interleukin-1 and tumor necrosis factor-alpha, which attract granulocytes, mast cells, and macrophages [6]. Acneiform eruptions may be explained by the impact of EGFR inhibitors on inflammation and keratinocyte proliferation. In a patient receiving cetuximab, this is the first instance of an intertrigo-like eruption. We believe that local microtrauma in anatomical regions such as the axillary folds, the abdominal belt, and the inguinal areas

results in vascular injury, extravasation of molecules in the epidermis, and local inflammation with erythema, edema, desquamation, and painful erosions. Keratinocytes are also directly impacted by EGFR inhibitors.
The most frequent adverse reaction to EGFR inhibitors is skin toxicity [1]. A dosage decrease is recommended for people who experience severe skin eruption (Grade 3). It is advised to take conservative precautions such as using moisturizing lotions and avoiding pressure, heat, and trauma [7]. Acneiform eruption has been treated using premedications. There are currently no established preventative or curative measures for intertrigo-like eruptions. Topical steroids were required in our patient to heal the lesions, reduce the symptoms, and enhance quality of life. According to the results of this study, it might be beneficial to think about premedication with corticosteroids for individuals who have already experienced an episode of intertrigo-like eruption.

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Conflict of Interest: None

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Ethics Statement: The authors attest to having acquired all necessary patient permission documents. According to the form, the patient or patients have consented to the publication of their photos and other clinical data. The patients are aware that although every attempt will be made to hide their identities, anonymity cannot be ensured, and that their names and initials will not be published.

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