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Letter

**Cetuximab-induced Crusted Pustular Eruption with Patchy Alopecia**

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**Abstract**

A 52-year-old man with recurrent metastatic rectal carcinoma being treated with cetuximab presented to the emergency department with a diffuse papulopustular eruption on the face, scalp, chest, and groin, accompanied by patchy alopecia of the scalp and facial hair.

**Keywords:** cetuximab, epidermal growth factor receptor inhibitor (EGFR inhibitor), cetuximab adverse effects

**Case synopsis**

A 52-year-old man with recurrent metastatic rectal carcinoma presented to the emergency department (ED) with nephrolithiasis and a diffuse pustular eruption. His prior treatments included colon resection, radiation therapy, and chemotherapy with oxaliplatin, 5-fluorouracil, and leucovorin. Owing to his extensive metastatic disease and lack of a KRAS mutation, a second cycle of cetuximab was initiated three weeks prior to his presentation. Thus far, the patient had demonstrated a favorable response with lesion size reduction in both liver and pulmonary metastases.



## Figure 1,2. Papulopustular eruption.

On physical examination, the patient exhibited a severe, diffuse follicular papulopustular eruption with honey-colored crusting, most prominent on the sebaceous areas of the face (Figure 1,2). A similar papulopustular eruption with crusting was also seen on the scalp, chest, and groin.



Figure 3,4. Papulopustular reaction and patchy alopecia of scalp and facial hair bearing areas

Furthermore, the patient demonstrated patchy alopecia of the scalp (Figure 3) as well as patchy alopecia of the facial hair (Figure 4).

The eruption began initially on his face approximately two weeks into cetuximab treatment and peaked in severity near the end of the four-week cycle (at time of presentation). Based on his previous cycle of cetuximab, he said it would regress approximately two weeks after treatment cessation. Subjectively, the eruption was mildly pruritic, but more bothersome to the patient from a cosmetic standpoint. A pustule on the face was cultured positive for methicillin-sensitive *Staphylococcus aureus*. Despite offering both topical (mupirocin) and oral (doxycycline) antibiotics to manage the eruption, the patient declined any treatment for the eruption because he was satisfied with the efficacy of cetuximab and predicted the eruption would subside within a few weeks of completing the treatment cycle, as it had during the previous cycle. He was also comforted by the thought that the skin eruption was evidence of internal response to the cetuximab.

## Discussion

Epidermal growth factor receptor (EGFR) inhibitors are currently used to treat solid tumors, including colon carcinoma, lung carcinoma, breast carcinoma, and head and neck squamous cell carcinoma. Current EGFR inhibitors include cetuximab, erlotinib, and gefitinib.

The EGFR inhibitors are associated with several dermatologic side effects, including a pustular or maculopapular follicular eruption (often called "acneiform"), xerosis, paronychia, pruritus, alopecia, and alterations in hair [1]. The most common of these adverse effects is the pustular eruption [2]. Interestingly, the eruption is thought to serve as visible evidence of both anti-tumor activity and treatment efficacy [2]. The mechanism of the eruption is thought to be formation of productive dimerization complexes, which disrupt the normal development of the hair follicle, followed by an inflammatory response that leads to the clinical presentation [3]. A potential explanation of why these complexes form in the presence of an EGFR inhibitor, but not HER2 receptor therapies, is that in human keratinocytes, EGFR homo-dimers are the predominant isoform [4].

Patients often present with monomorphous follicular papules and pustules (without comedones) of the scalp, face, and upper trunk. The eruption usually begins 1-3 weeks after beginning treatment with an EGFR inhibitor. Secondary infection is not uncommon, usually with *Staphylococcus aureus*, which presents as honey-colored crusts and oozing [5].

Histopathology shows a superficial purulent folliculitis with disordered differentiation and focal parakeratosis[6], but no comedones [5].

The eruption usually resolves without scarring once the EGFR-inhibitor is discontinued [7]. If a patient is interested in treatment, regimens are chosen based on the severity of the eruption, ranging from topical medications to oral antibiotics, in conjunction with

antihistamines if pruritus is present [8]. Successful reported therapies include benzoyl peroxide, topical erythromycin [6], doxycycline, and minocycline [9], among others.

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