

Acneiform Reaction to Erlotinib

Peter C. Schalock and Kathryn A. Zug

Erlotinib is a reversible inhibitor of epidermal growth factor receptor (EGFR) tyrosine kinase (TK) newly approved for the treatment of refractory, locally advanced, or metastatic nonsmall cell lung cancer. Acneiform skin reactions with EGFR inhibitors are common, with a dose-dependent skin reaction being seen in 50 to 100% of patients. This case illustrates the typical skin reaction seen with EGFR-TK inhibitors and illustrates the lack of reaction in skin with sebaceous glands that have been destroyed by radiation. Discussion of this skin reaction in the literature of dermatology is limited; this case illustrates a pattern of reaction that may suggest a mechanism for this skin reaction pattern to erlotinib.

Case Report

A 54-year-old man with recurrent and metastatic non-small cell lung cancer presented with a 1-week history of a progressive pruritic "rash" on his chest, back, neck, and face. He had been given clindamycin gel by his oncologist, which was not helpful. Other medications included erlotinib 150 mg and bexarotene 750 mg by mouth daily, starting 3 weeks prior to presentation. Skin examination revealed follicular-based pustules with surrounding erythema on the upper chest, back, neck, and face. Of note, the central chest and back had sparing, with a sharp cutoff in the area that had been previously irradiated for the patient's lung carcinoma. A skin biopsy specimen revealed acute neutrophilic folliculitis. The periodic acid-Schiff stain reaction was negative. The patient was treated with doxycycline 100 mg by mouth twice daily and topical clindamycin 1%/benzoyl peroxide 5% gel. He was pleased by significant improvement at numerous follow-up visits.

Discussion

Erlotinib is a reversible inhibitor of epidermal growth factor receptor (EGFR) tyrosine kinase. It is used in the treatment of refractory, locally advanced, or metastatic non-small cell lung cancer. EGFR is highly expressed in tumors of the head/neck, breast, brain, lung, cervix, and gastrointestinal tract. Overexpression of EGFR plays a significant role in tumor

growth and progression. Erlotinib inhibits EGFR-dependent proliferation of tumor cells in vivo and blocks cell cycle progression in the G1 phase of cell division. Its use has been associated with improved survival benefit with the significant morbidity of other cytotoxic chemotherapy agents. The use of erlotinib has been associated with dose-dependent skin reactions, the most common being an acneiform eruption.¹

Acneiform skin reactions to EGFR inhibitors are common; a dose-dependent skin reaction is seen in 50 to 100% of patients.¹ There may be a correlation between skin reaction and tumor response; some authors suggest that titrating the dose to skin reaction may be beneficial.² Other reaction patterns include a seborrheic dermatitis or rosacea-like patterns, xerosis, paronychia, and hair changes. The cutaneous findings of EGFR inhibitors are discussed in detail in a recent review.³

Treatment of the acneiform reaction is similar to acne therapy. For mild cases, topical antiacne or antirosacea medications are helpful. For moderate cases, a 3-month course of a tetracycline derivative by mouth is recommended. In severe cases, open wet dressings plus topical and oral therapy are recommended. A delay or discontinuation of the medication should be considered.⁴ The use of retinoids is controversial. Some authors believe retinoids should not be used for the EGFR inhibitor reaction, because of a different mechanism for acne formation³ although others believe topical retinoids or isotretinoin may be helpful.⁴

The mechanism of acneiform skin reaction is unknown but is hypothesized to be related to a yet unknown function of EGFR within the sebaceous/follicular unit. There are no precursor comedones as seen in acne. Further research into the interaction of EGFR and the follicular unit is needed.

From the Department of Dermatology, Harvard Medical School, Boston, MA, and the Department of Medicine (Dermatology), Dartmouth Medical School, Hanover, NH.

Address reprint requests to Peter C. Schalock, MD, Massachusetts General Hospital, Department of Dermatology/BAR622, 55 Fruit St., Boston, MA 02114. E-mail: schalock@gmail.com

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Use of erlotinib and other EGFR inhibitors (cetuximab, panitumumab, gefitinib) within oncology is increasing. Dermatologists should be aware of the typical skin findings seen with this class of medications and should be facile in the variations in treatment of the acneiform reaction.

References

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