

# Successful treatment of epidermal growth factor receptor inhibitor–induced alopecia with doxycycline

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## INTRODUCTION

Both scarring and nonscarring alopecias have been described with the long-term use of epidermal growth factor receptor (EGFR) inhibitors. Current treatments revolve around anti-inflammatory agents such as topical corticosteroid ointments, creams, and intralesional injections to reduce follicular inflammation. Unfortunately, none of these therapies are universally effective. Here, we describe a case of erlotinib-induced alopecia refractory to intralesional and topical corticosteroids that was successfully treated with doxycycline as a novel treatment approach for EGFR inhibitor–associated alopecia.

## CASE REPORT

A 77-year-old woman with a 4-year history of non–small cell lung cancer (NSCLC) was started on the EGFR inhibitor, erlotinib (initial dose of 150 mg daily), for recurrence of her EGFR-mutated NSCLC after adjuvant chemotherapy. She experienced a papulopustular eruption on her face and chest within 2 weeks after initiating erlotinib therapy, which resolved after a month of minocycline and dose reduction of her erlotinib to 100 mg daily. She otherwise tolerated erlotinib without further dermatologic concerns. However, 5 months after initiating erlotinib, a localized asymptomatic alopecia developed over her right parietal scalp. Physical examination revealed a 5- x 3-cm area of alopecia with peripheral crusting and scale that was clinically consistent with an erosive pustular form of EGFR inhibitor–associated alopecia.

After her diagnosis, the patient received multiple therapies including intralesional triamcinolone injections every 8 weeks, daily topical triamcinolone

### Abbreviations used:

EGFR: epidermal growth factor receptor  
 NSCLC: non–small cell lung cancer

acetone cream 0.1%, and daily topical clobetasol solution for 1 year, all of which were unsuccessful. Her alopecia worsened despite treatment and spread to her left parietal scalp. At the peak of involvement, she exhibited an 8- x 8-cm area of hair loss with erythema, yellow crusting, and scale over her bilateral parietal scalp areas (Fig 1).

Because of her continued scalp inflammation, lack of improvement on skin-directed corticosteroids, and a culture swab that grew *Staphylococcus aureus*, the patient was started on 100 mg of oral doxycycline twice daily with discontinuation of her other skin therapies. She reported dramatic improvement of her alopecia with regression of the lesions, evidence of hair partial regrowth, and resolution of crusting within 1 to 2 weeks of starting the medication. Doxycycline was decreased to 50 mg twice a day 6 weeks after initiating treatment. Physical examination found diminishing areas of noninflamed scarring alopecia with partial hair regrowth on the right parietal scalp and no associated serous drainage or crust (Fig 2).

At her 6-month follow-up visit after initiating doxycycline, there were no signs of relapse of her alopecia and no evidence of recurrence of the scalp crust and drainage. Given the favorable results of her doxycycline and erlotinib regimen, her doxycycline was discontinued after a total 6-month treatment course, and over 3 months after discontinuation the improvement has been maintained. She was able to continue her erlotinib at 100 mg throughout without

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**Fig 1.** A case of EGFR inhibitor–induced alopecia in a 77-year-old woman. Examination of her scalp found biparietal scalp alopecia with peripheral crusting and scale despite treatment with topical steroids and bimonthly intralesional triamcinolone injections.



**Fig 2.** Successful treatment of EGFR inhibitor–induced alopecia with oral doxycycline. There was significant improvement of her alopecia 3 months after initiating oral doxycycline, 100 mg twice daily for 6 weeks followed by 50 mg twice daily for an additional 4.5 months, with hair partial regrowth extending to the periphery on the right parietal and left parietal scalp and resolution of serous drainage and crusting.

a change in dosage and was satisfied with the outcome of her treatment.

## DISCUSSION

EGFR overexpression is a common feature of several different types of cancers, including lung, pancreas, breast, and colon, and correlates with both cancer progression and worsening prognosis.<sup>1</sup> EGFR inhibitors are antibodies or small molecules developed to target EGFR overexpression and slow the progression of malignancy. Because the EGFR signaling cascade is also highly involved in the homeostasis of epidermal keratinocytes and hair follicles in the skin,<sup>2</sup> a variety of cutaneous side effects from EGFR inhibitor administration has been

reported. The most common of these side effects include acneiform eruption (85% of patients), xerosis (35%), paronychia (10%–15%), and mucositis (rare).<sup>3</sup> These cutaneous manifestations are a source of significant physical and emotional discomfort for patients.

EGFR signaling is involved in the initiation of the anagen phase of the hair cycle and acts as an important regulator of the hair growth phase. Disruption of this phase with EGFR inhibitors leads to disorganized formation of the hair follicle and manifests as abnormalities such as finer, curlier, and more brittle hair and both scarring and nonscarring alopecia.<sup>3</sup> Alopecia is a late manifestation of EGFR inhibitor–associated dermatologic side effects, typically arising 2 to 3 months after initiation of the medication, and is characterized by significant inflammation of the scalp with recruitment of lymphocytes, plasma cells, neutrophils, and eosinophils on histologic examination.<sup>4</sup> This inflammation is thought to arise from inhibition of EGFR from its normal role of suppressing free radical synthesis, thus resulting in activation of the inflammatory cascade and leading to follicle destruction and alopecia.<sup>5</sup>

Current treatments for EGFR inhibitor–associated alopecia center on inflammation modulation with local anti-inflammatory agents, such as topical hydrocortisone, steroid shampoos, and steroid lotions,<sup>6</sup> none of which are universally effective. In a review of 11 cases of EGFR inhibitor–associated alopecia, Toda et al<sup>4</sup> concluded steroids alone were not an effective treatment and that reduction or discontinuation of the EGFR inhibitor was needed in most cases to prevent scarring. The clinical practice guidelines for the prevention and treatment of EGFR inhibitor–associated dermatologic toxicities similarly do not describe any established interventions to reduce or prevent alopecia.<sup>5</sup> Current recommended therapies are largely supportive and consist mainly of approaches to reduce inflammation and reduction or discontinuation of EGFR inhibitor therapy as a last resort. Unfortunately, for our patient, discontinuation of erlotinib was not a favorable option given its efficacy against her recurrent NSCLC.

Doxycycline, as a member of the tetracycline family, inhibits key proinflammatory mediators such as nitric oxide and the mitogen-activated protein kinase pathway.<sup>7</sup> These anti-inflammatory effects of doxycycline may contribute to its success in treating EGFR inhibitor–associated alopecia. In addition, doxycycline is a potent broad-spectrum antibiotic with good coverage of skin flora. Patients undergoing EGFR-inhibitor treatment frequently have superinfections at sites of toxicity. In one study, 84 of 221

(38%) patients had culture-positive *Staphylococcus aureus* superinfections after treatment with EGFR inhibitors.<sup>8</sup> *S aureus* infection has also been linked to exacerbations of EGFR inhibitor–induced skin eruptions, including that of a papulopustular eruption on the scalp with associated alopecia.<sup>9</sup> Minocycline, another tetracycline, was reported to help in one case of folliculitis decalvans–type alopecia associated with erlotinib<sup>10</sup>; however, within the tetracycline family, doxycycline has been linked to fewer severe toxicities and is safer in patients with renal impairment than minocycline.

The success of doxycycline in treating our patient’s EGFR inhibitor–associated alopecia may be a combination of its potent anti-inflammatory and antibiotic properties. Although further studies are required, doxycycline should be considered a potential therapeutic option for corticosteroid-resistant EGFR inhibitor–induced alopecia.

#### REFERENCES

1. Nicholson RI, Gee JM, Harper ME. EGFR and cancer prognosis. *Eur J Cancer*. 2001;37(Suppl 4):S9-S15.
2. Nanney LB, McKanna JA, Stoscheck CM, Carpenter G, King LE. Visualization of epidermal growth factor receptors in human epidermis. *J Invest Dermatol*. 1984;82(2):165-169.
3. Galimont-Collen AF, Vos LE, Lavrijsen AP, Ouwerkerk J, Gelderblom H. Classification and management of skin, hair, nail and mucosal side-effects of epidermal growth factor receptor (EGFR) inhibitors. *Eur J Cancer*. 2007;43(5):845-851.
4. Toda N, Fujimoto N, Kato T, et al. Erosive pustular dermatosis of the scalp-like eruption due to gefitinib: case report and review of the literature of alopecia associated with EGFR inhibitors. *Dermatology*. 2012;225(1):18-21.
5. Lacouture ME, Anadkat MJ, Bensadoun RJ, et al. Clinical practice guidelines for the prevention and treatment of EGFR inhibitor-associated dermatologic toxicities. *Support care cancer*. 2011;19(8):1079-1095.
6. Burtneess B, Anadkat M, Basti S, et al. NCCN Task Force Report: Management of dermatologic and other toxicities associated with EGFR inhibition in patients with cancer. *J Natl Compr Canc Netw*. 2009;7(Suppl 1):S5-S21. quiz S22-24.
7. Hoyt JC, Ballering J, Numanami H, Hayden JM, Robbins RA. Doxycycline modulates nitric oxide production in murine lung epithelial cells. *J Immunol*. 2006;176(1):567-572.
8. Eilers Jr RE, Gandhi M, Patel JD, et al. Dermatologic infections in cancer patients treated with epidermal growth factor receptor inhibitor therapy. *J Natl Cancer Inst*. 2010;102(1):47-53.
9. Wiznia LE, Choi JN. Unique presentations of epidermal growth factor receptor inhibitor-induced papulopustular eruption related to bacterial superinfection. *Dermatol Online J*. 2013;19(3):8.
10. Sillani C, Bin Z, Ying Z, Zeming C, Jian Y, Xingqi Z. Effective treatment of folliculitis decalvans using selected antimicrobial agents. *Int J Trichology*. 2010;2(1):20-23.