Erlotinib-induced Perioral Lesions Resembling Scleroderma

Dear Editor,

Erlotinib, an epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI), is currently used in the therapy of several solid malignancies. This agent has been associated with several dermatological side-effects, the most common being papulo-pustular acneiform rash. Herein we describe a unique skin effect in a patient treated with erlotinib for non-small cell lung cancer.

A 68-year-old Caucasian woman presented with complaints of an unusual perioral rash associated with redness and pain. A "feeling of tension" that interfered with chewing was described by the patient. She denied myalgias, arthralgias, shortness of breath, or other skin lesions. The patient also denied self-infliction of wounds, physical abuse, or trauma. Three months before this presentation, she was diagnosed with metastatic lung adenocarcinoma in the liver and adrenal glands, which carried an exon 21 L858R EGFR-TK mutation. A month after the diagnosis, the patient was started on erlotinib 150 mg PO daily, which she had continued up to the time the perioral skin lesions commenced. Besides erlotinib, the patient denied any other new medications. At the start of perioral skin lesions, a restaging computed tomography (CT) scan showed a decrease in size of all metastatic site lesions, consistent with a partial response to erlotinib. Other comorbidities included peptic ulcer disease and hypertension. The patient had a 5-pack year history of tobacco smoking in her early 20s.

Skin examination showed convergent erythematous perioral lesions with a cut-like appearance, some having healed with crusts and others with hyperkeratotic scars (Figure 1, A, B). Physical examination was further remarkable for a grade 1 papulo-pustular acneiform rash involving the face (Figure 1, B) and grade 1 xerosis of the face (Figure 1, A, B) and both hands. Complete blood count, comprehensive metabolic panel, C3 and C4 complement fractions, C-reactive protein, as well as antinuclear, anti-DNA, anti-protein-A and -B, and anti-SCL-70 antibodies were within normal range.

The patient was advised to apply colloidal oatmeal lotion to the lesions three times per day. She reported a moderate improvement in skin lesions and decreased anxiety about their appearance. Erlotinib was continued at the same dose. The most recent re-evaluation CT scan showed a continued clinical response of lung cancer to erlotinib.

Causality between EGFR-TKIs and various skin lesions is well-documented (1-3). The most commonly seen manifestation in this context is papulo-pustular, acneiform rash involving the face, neck, and torso, with an incidence of 70-80% (1). The dermatologic toxicity of erlotinib to the fingernails and distal phalanges includes xerosis, paronychia, and finger fissures (4).

The skin toxicity of erlotinib is thought to be due its complex effects on keratinocyte growth and differentiation (5,6). The present patient's perioral deep, cut-like

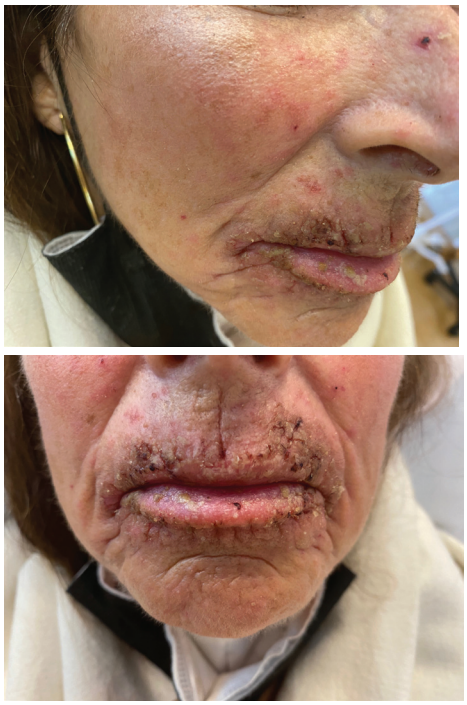

Figure 1. Convergent flesh-colored perioral lesions, some having healed with crusts and others with hyperkeratotic scars, and xerosis of face. A) Frontal view. B) Oblique view, also showing several papulo-pustular acneiform lesions affecting facial skin.

lesions penetrated into the deep dermis (Figure 1, A, B). Xerosis might have preceded these lesions, as they improved with colloidal oatmeal lotion. However, a unique feature in our patient was the perioral localization resembling scleroderma (Figure 1, A, B).

The present patient's lesions presented a clinical question: was she engaging in self-injury, or did her wounds represent a side-effect of erlotinib? Although these lesions had the appearance of cuts, they were not consistent with a non-suicidal self-injury (NSSI) (7). The patient denied any history of psychiatric disorders or previous episodes of self-injury. In addition, unlike injuries seen in patients who engage in NSSI, the cuts were bilateral and symmetric. Our patient was compliant with the topical treatment, and her lesions improved accordingly.

We postulate that erlotinib was the etiologic agent that caused the described deep, cut-like lesions, as it was the only new agent that the patient was taking at that time. She experienced this effect after two months of taking erlotinib. In addition, the patient experienced other side-effects of this agent, including papulopustular acneiform rash and xerosis. Furthermore, the medical literature supports the use of colloidal oatmeal lotion to alleviate skin manifestations due to EGFR TKIs (8), consistent with the positive response in our case. The causal relationship between erlotinib and scleroderma-like lesions in our patient was rated as probable according to the Naranjo Adverse Drug Reaction Probability Scale that yielded a score of 8.

This cutaneous toxic effect of erlotinib has not been previously reported in the medical literature. Although some authors showed dose-dependent improvement in other skin effects due to this class of pharmaceuticals (1), no interruption or dose reduction of erlotinib was required in our case. Awareness of erlotinib-induced scleroderma-like lesions is important to provide reassurance to the patient, continue anticancer therapy, and avoid unnecessary costly work-up or referrals to dermatology or psychiatry specialists.

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Received: December 31, 2023
Accepted: March 5, 2024