Erlotinib-induced purpuric papulopustular eruption treated with pulsed azithromycin

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Introduction

The overexpression of epidermal growth factor receptors (EGFRs) plays an important role in carcinogenic cellular processes in several tumor types. Erlotinib is one of the EGFR inhibitors that is administered for advanced stage cancer. EGFR inhibitors disturb the intracellular signal transduction by blocking receptor-ligand interaction.¹ Cutaneous toxicity including papulopustular eruption due to EGFR inhibitors is commonly observed.² However, purpuric lesions are rarely seen as an adverse cutaneous reaction. In this report, we described a patient with purpuric papular eruption secondarily infected with Staphylococcus aureus (SA) due to erlotinib therapy, who was successfully treated with pulsed azithromycin.

Case Report

A 73-year-old female patient was referred to our outpatient clinic for evaluation and treatment of a widespread acneiform eruption. She was put on erlotinib therapy for 3 months for the treatment of lung adenocarcinoma. The patient has developed nonpruritic papules and pustules widespread over the body except the face for the past 2 weeks. Bacterial culture obtained from a pustule on the back grew methicillin-sensitive Staphylococcus aureus (SA). Histopathological examination of a papule demonstrated vacuolar degeneration of basal layer, prominent walls of vessels, a mixed infiltration of eosinophils, and lymphocytes and erythrocyte extravasation. The eruption was successfully treated with two weekly pulses of azithromycin 500 mg for 3 consecutive days. This case demonstrated that erlotinib may cause purpuric papular eruption secondarily infected with SA. Routine bacterial culture should be performed from pustules before any treatment.

KEY WORDS: Cutaneous adverse reaction, epidermal growth factor receptor inhibitors, treatment

ABSTRACT

Erlotinib belongs to the targeted cancer treatments acting through epidermal growth factor receptor inhibition. Papulopustular eruption is the most common cutaneous toxicity. The pathogenesis of the rash is not clear. There is no consensus on treatment. In this report, we describe a 73-year-old female patient who was referred to our outpatient clinic for evaluation and treatment of a widespread acneiform eruption. She was put on erlotinib therapy for 3 months for the treatment of lung adenocarcinoma. The patient has developed nonpruritic papules and pustules widespread over the body except the face for the past 2 weeks. Bacterial culture obtained from a pustule on the back grew methicillin-sensitive Staphylococcus aureus (SA). Histopathological examination of a papule demonstrated vacuolar degeneration of basal layer, prominent walls of vessels, a mixed infiltration of eosinophils, and lymphocytes and erythrocyte extravasation. The eruption was successfully treated with two weekly pulses of azithromycin 500 mg for 3 consecutive days. This case demonstrated that erlotinib may cause purpuric papular eruption secondarily infected with SA. Routine bacterial culture should be performed from pustules before any treatment.
including complete blood count with differential, erythrocyte sedimentation rate, prothrombin time, partial thromboplastin time, liver and kidney function tests were within normal limits. Bacterial culture obtained from a pustule on the back grew methicillin sensitive SA. Histopathological examination of a papule demonstrated a mixed infiltration of eosinophils and lymphocytes and erythrocyte extravasation [Figure 4].

Depending on clinical and histopathological findings, the patient was diagnosed as having a purpuric papulopustular eruption due to erlotinib treatment complicated with staphylococcal infection. The severity of adverse cutaneous reaction was Grade 2 according to the National Cancer Institute Common Toxicity Criteria, version 3. The score of Naranjo’s et al. scale used for causality assessment was 3. The relationship between erlotinib and cutaneous eruption was considered “possible” using the WHO-UMC scale[8] and Naranjo’s et al. algorithm.[4]

The patient was started on pulse azithromycin therapy using a regimen of two weekly pulses of 500 mg for 3 consecutive days. Erlotinib was continued daily and the patient completely recovered after 2 weeks of therapy.

### Discussion

Cutaneous adverse reactions due to EGFR inhibitors are commonly observed. Skin toxicity has a waxing and waning nature during continued treatment. The occurrence of cutaneous adverse events, experiencing multiple adverse events, and more severe cutaneous lesions were found to be closely related to a better tumor response and overall survival.[5] The papulopustular reaction is the most common cutaneous adverse reaction of EGFR inhibitors, and the rash is observed in 50–100% of patients, in a dose-dependent manner.[6] The rash usually involves seborrheic areas, face, trunk, and sometimes extremities. Purpuric eruption is extremely rare.[7] In our case, the patient was presented with tiny pustules superimposed on purpuric papules.

The papulopustular eruptions due to EGFR inhibitors were classified as early and late phase reactions concerning the time of onset of the rash.[8] Involving of trunk without face, presence of pruritus, SA isolation in culture, and the long interval from erlotinib initiation to emerging eruption of our patient suggested that the rash was a late phase reaction. The pathogenesis of
As acneiform rash is not clear. A recent study described 7 patients with late phase rash secondarily infected by SA suggested that SA infection may be involved in the pathogenesis. The pustular component of rash seen in our patient may be a secondary infection on the purpuric inflammatory process triggered by erlotinib. We suggest that the immunocompromised state and cutaneous toxicity caused by erlotinib may lead to skin barrier impairment and overgrowth of SA in these cutaneous regions.

Prophylactic oral and topical treatments have been used to prevent acneiform eruptions due to EGFR inhibitors. Concurrent use of EGFR inhibitors with oral tetracycline has provided decreased incidence of moderate to severe folliculitis, not mild form until tetracycyle treatment was discontinued. Besides, topical preventive strategies such as topical minocycline and tazarotene cream were ineffective. There is no consensus on the treatment options of EGFR inhibitor related acneiform eruptions. In a recent study, 11 of 20 patients with acneiform eruption due to EGFR inhibitors who were resistant to previous tetracyclines, were treated with 500 mg azithromycin for 3 consecutive days per week for at least 2 weeks without performing bacterial cultures. This case was successfully treated with systemic azithromycin depending on the result of the bacterial culture of the pustule.

We suggest that treatment depending on bacterial culture and antibiotic susceptibility tests will be a better approach to the treatment of papulopustular eruption due to EGFR inhibitors.

Conclusion

Erlotinib may cause purpuric papular and pustular eruptions. Routine bacterial culture should be performed before any treatment since secondarily infection with SA may be associated.

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Conflicts of Interest

There are no conflicts of interest.

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