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Case Report

Erlotinib-Induced Papulopustular Eruption and Mucositis

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ABSTRACT

Erlotinib is an epidermal growth factor inhibitor that is used in the treatment of advanced stage cancers. Cutaneous reactions to erlotinib use have been observed. A 70-year-old male patient presented with the complaint of a rash on his nose and a lesion in the mouth. The patient history included a diagnosis of lung cancer and treatment with oral erlotinib 150 mg/day. The complaints developed on the third day of erlotinib treatment. A dermatological examination revealed numerous papulopustular lesions with an erythematous background on the nose. Yellow plaques and erosions were also observed on an erythematous area on the tongue. In the literature, anaphylaxis, acneiform rashes, xerosis, nail and hair changes, and mucosal changes have all been reported with erlotinib treatment. Presently described is a case of papulopustular lesions and mucositis appearing on the third day of erlotinib treatment. Practitioners should be aware of cutaneous side effects that may occur during erlotinib use.

INTRODUCTION

Erlotinib is an inhibitor of tyrosine kinase, which is an epidermal growth factor (EGFR). It is used in the treatment of locally advanced or metastatic non-small cell lung cancer.[1] When compared with traditional antineoplastic agents, an important advantage of erlotinib is that it has less systemic toxicity; however, the frequent development of cutaneous side effects during erlotinib treatment has been well documented.[2]

In this case study, a patient developed papulopustular eruptions and mucositis on the third day of erlotinib treatment. The objective of this report was to emphasize some of the potential cutaneous side effects of erlotinib use.

CASE REPORT

A 70-year-old male patient presented with the complaint of a rash on his nose and a lesion in the mouth. The patient history indicated a diagnosis of lung cancer and treatment with oral erlotinib 150 mg/day. The complaints developed on the third day of treatment. Dermatological examination revealed numerous papulopustular and some excoriated lesions with an erythematous background on the bridge of the nose extending toward the nasal wings (Fig. 1). Furthermore, a yellow plaque and scattered erosions were observed on an erythematous background on the tongue (Fig. 2). No other dermatological or systemic manifestations were detected. The laboratory test results were unremarkable. Nystatin oral suspension (4x1) was prescribed for the oral mucosa lesions and topical tetracycline hydrochloride ointment (2x1) for the lesions on the nose. On the 10th day of treatment, a marked regression in the lesions was observed.

DISCUSSION

Erlotinib is an oral EGFR tyrosine kinase inhibitor. It is a targeted drug used for the treatment of advanced (stage III and IV) non-small cell lung cancer.[1] Frequently, it induces papulopustular rash, nail and hair pathologies, and cutaneous reactions, such as xerosis. Apart from cuta-

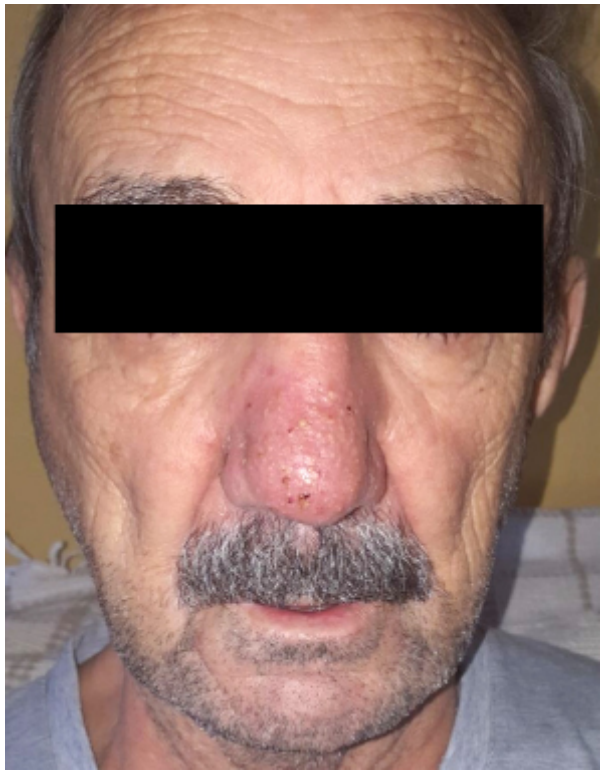

Figure 1. Papulopustular lesions on the face of the patient.

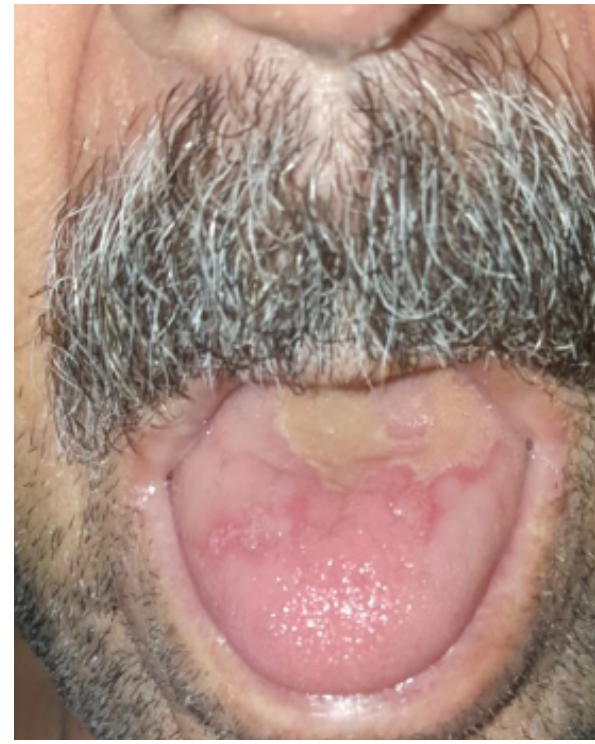

Figure 2. Yellow plaque and patchy areas of erosions on the surface of the tongue.

neous side effects, telangiectasia, hyperpigmentation, exacerbation of radiation dermatitis, oral aphthous ulcers, vasculitis, necrolytic migratory erythema, and temporary acantholytic dermatosis have also been reported.[3–5]

In our patient, on the third day of erlotinib treatment, papulopustular eruptions on the nose and an eroded, yellow, plaque lesion were observed. Though in some sources erlotinib-induced papulopustular lesions have been described as acneiform lesions, in this case, since comedones, nodules, or cystic lesions were not observed, the term papulopustular lesion was more appropriate. The etiopathogenesis of erlotinib-induced eruptions is not fully known; however, it may be related to a disruption of the balance between differentiation and maturation in keratinocytes, eccrine and sebaceous glands, and hair follicle cells due to dose-related inhibition of EGFR.[6] Follicular occlusion and secondary inflammation occurring following inhibition of EGFR has been suggested in the pathogenesis of papulopustular eruptions. In addition to aseptic suppurative folliculitis, deterioration of the epidermal structure may increase the tendency for secondary infection. Generally, lesions are localized in seborrheic areas, such as the face, scalp, upper parts of the trunk, and the back. The incidence of papulopustular lesions reportedly increases with exposure to ultraviolet light, and sun protection creams fail to prevent the development of these lesions. Symptoms including itching, burning pain, and stinging may accompany other clinical manifestations.[6,7]

Because of the rapid turnover of oral cavity cells as a result of cancer treatment, the side effects of mucositis and somatitis are frequently observed. Mucosal side effects may be important indications for the postponement or termination of cancer treatments. The relationship between targeted cancer treatments and adverse mucosal effects has been well reported. The dose, route of administration, and the use of multiple chemotherapeutic agents may influence the development of mucosal side effects. Among erlotinib-induced mucosal manifestations, oral aphthae, xerostomy, geographic tongue, vulvovaginitis, balanitis, genital aphthae, conjunctivitis, and keratitis have been reported.[8] In the presence of mucositis, the development of bacterial, fungal, or viral infections facilitated by the immunosuppressive condition of the patient should be thoroughly investigated.[9]

Treatment of papulopustular lesions primarily involves moisturizing the skin and the use of sun protection products. Topical metronidazole, clindamycin, or salicylic acid may be used for clinically mild lesions, and for moderate or severe lesions, systemic tetracycline may be recommended.[10] Topical retinoids and topical vitamin D analogues are not effective.[9] In the event of itching, systemic antihistamines may be used. Oral isotretinoin treatment is not recommended due to potential side effects of eczema, xerosis, and paronychia. In cases of very severe acneiform eruptions, a reduction in the dose of erlotinib or deferral of the treatment may be considered.[10,11] Erlotinib treatment

frequently induces mild or moderately severe skin manifestations; however, in 1% of patients cessation of erlotinib treatment due to its side effects has been reported.[6]

In conclusion, it should be remembered that in patients using erlotinib, skin lesions may be related to the drug treatment. Early diagnosis and treatment of skin lesions developing secondary to erlotinib use may be important with respect to the patient's continuation with treatment.

Informed Consent

Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: Z.A.S., E.A.K.; Design: Z.A.S., E.A.K.; Data collection &/or processing: E.A.K.; Analysis and/or interpretation: Z.A.S., E.A.K.; Literature search: E.A.K.; Writing: E.A.K.; Critical review: Z.A.S., E.A.K.

Conflict of Interest

None declared.

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Erlotinib Kullanımına Bağlı Gelişen Papülopüstüler Erupsiyon ve Mukozit Olgusu

Erlotinib ileri dönem kanser tedavisinde kullanılan bir epidermal büyüme faktörü inhibitörüdür. Erlotinibe bağlı kutanöz reaksiyonlar izlenebilir. Yetmiş yaşında erkek hasta burun bölgesinde döküntü ve ağız içinde yara şikayetiyle başvurdu. Hastanın öyküsünde akciğer kanseri tanısı ile oral erlotinib 150 mg/gün tedavisi başlandığı ve tedavinin üçüncü gününde bu şikayetlerinin geliştiğini öğrendik. Dermatolojik muayenede burun üzerinde eritemli zeminde çok sayıda papulopüstüler lezyonlar ve dil üzerinde eritemli zeminde sarı renkli plak, yer yer erozyonlar izlendi. Literatürde erlotinib kullanımına bağlı anafilaksi, akneiform döküntü, kseroz, tırnak ve saç değişiklikleri, mukozal değişiklikler bildirilmiştir. Burada erlotinib kullanımı sırasında oluşabilecek kutanöz yan etkilere dikkat çekmek amacıyla tedavinin üçüncü gününde papülopüstüler döküntüleri ve mukozit gelişen bir hasta sunulmuştur.

Anahtar Sözcükler: Epidermal büyüme faktörü; kutanöz reaksiyon; mukozit; papülopüstül; yan etki.