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Case Presentation

Erlotinib-induced trichomegaly of eyelashes in lung cancer treatment: epidermal growth factor receptor inhibitor side effect

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Abstract

Erlotinib is one of the epithelial growth factor receptor tyrosine kinase inhibitors that have been developed and extensively employed in the treatment of non-small cell lung cancer, particularly in individuals with activating epithelial growth factor receptor mutations. This report presents a case of erlotinib induced eyelash trichomegaly and irritation, a rare side effect in a woman who received erlotinib for lung adenocarcinoma. Following the detection of an epithelial growth factor receptor mutation in tumor tissue from a non-small cell lung cancer in a nonsmoking woman, the patient was initiated on erlotinib therapy. After several months, she experienced significant overgrowth of both eyelashes, leading to vision problems. Dermoscopy findings revealed an increase in the length and thickness of the eyelashes associated with inflammation of the eyelid's edges. It has been hypothesized that the inhibition of epithelial growth factor receptor signaling by epithelial growth factor receptor tyrosine kinase inhibitors could alter the growth pattern of hair, potentially leading to the induction of abnormal hair growth, such as trichomegaly, which has been reported only in a small number of case reports.

the treatment of non-small cell lung cancer, particularly in individuals with activating EGFR mutations.²

Erlotinib inhibits the activity of purified EGFR tyrosine kinase and EGFR autophosphorylation in intact tumor cells. This effect is involved in cellular proliferation, apoptosis, cell cycle alterations, and metastatic potential.³

EGFR is expressed in basal and suprabasal layers of the epidermis, in sebaceous glands, and in the outer root sheath of the hair follicles,⁴ which may explain the cutaneous side effects of erlotinib, including acneiform skin rash, pruritus, xerosis, skin fissures, telangiectasias, paronychia and hair changes.⁵

Trichomegaly of the eyelashes or excessive overgrowth of eyelashes, although rarely documented as an uncommon adverse effect of EGFR inhibitor therapy,⁶ typically does not constitute a limiting factor in drug administration. Its potential to induce cosmetic changes or ocular discomfort owing to elongated lashes requires careful consideration in the clinical management of patients receiving EGFR inhibitor therapy.

EGFR TKI-associated eyelash trichomegaly has been rarely reported in the literature and its incidence remains unknown.⁷

This report presents a case of erlotinib induced eyelash trichomegaly in a woman who received erlotinib for lung adenocarcinoma. To the best of our knowledge, few cases have been reported in the literature, and this is the first case of trichomegaly associated with erlotinib treatment reported in Africa.

Introduction

Lung cancer remains the leading cause of cancer-associated deaths worldwide accounting for the highest mortality rates among both men and women.¹ The epithelial growth factor receptor (EGFR) tyrosine kinase inhibitors (TKI) have been developed and extensively employed in

Case Synopsis

A 50-year-old woman with no history of smoking was referred to our department with a chief complaint of excessive overgrowth of both eyelashes and ocular irritation. She had previously been diagnosed with lung adenocarcinoma. After receiving first-line treatment for two cycles, EGFR mutation was detected in tumor tissue by direct sequencing test. Subsequently, treatment was switched to

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Figure 1. Trichomegaly of both eyelashes with eyelid inflammation.



Figure 2. Dermoscopic examination revealed an elongation of both eyelashes, measuring around 17mm, and was associated with inflammation of the eyelid's edges.

the second-line therapy consisting of erlotinib monotherapy, 150mg once daily.

During the erlotinib treatment, the patient developed a moderate acneiform rash characterized by erythematous papulopustular lesions affecting the face and neck, which was managed with erythromycin gel and benzoyl peroxide. Within three weeks, there was a significant improvement and regression of the skin lesions. In addition, after several months of treatment, the patient experienced significant overgrowth of both eyelashes, showing increased length and thickness resulting in vision problems.

Regarding the dermoscopy findings, we noted an increase in the length and thickness of the eyelashes associated with inflammation of the eyelid's edges (**Figures 1, 2**).

There was no evidence of androgen-stimulated hair growth. The patient was not taking any additional medications, and her family history was insignificant.

If the patient's quality of life remains unaffected by this side effect and as there is no targeted treatment for these symptoms, no intervention is deemed necessary. However, given our patient's visual impairment, trimming may be considered.

Case Discussion

Hypertrichosis of the eyelashes, known as trichomegaly, is characterized by increased length, thickness, stiffness, curling, and pigmentation of existing eyelashes.⁸ The diagnosis is established through clinical findings if eyelashes exceed 12mm.⁹

Trichomegaly was initially identified in congenital disorders, such as Oliver-McFarlane syndrome,¹⁰ Cornelia de Lange syndrome,¹¹ or familial hypertrichosis.¹² However, it also emerges as an acquired condition associated with specific drugs such as phenytoin, cyclosporin, diazoxide, minoxidil, streptomycin, penicillamine, interferon 2α, and latanoprost.⁶ It also may occur in diseases, including human immunodeficiency virus type 1,¹³ vernal keratoconjunctivitis,¹⁴ atopic dermatitis,¹⁵ uveitis,¹⁶ dermatomyositis,¹⁷ and systemic lupus erythematosus¹⁸ (**Table 1**).

In cancer patients, discerning trichomegaly from acquired hypertrichosis lanuginosa is essential. This rare paraneoplastic syndrome manifests as the abnormal growth of lanugo-type hair, primarily on the face and neck, often alongside the progression of an internal malignancy.²⁹

EGFR tyrosine kinase inhibitors (EGFR-TKIs) have been developed and widely employed in the management of non-small cell lung cancer patients.³⁰ Erlotinib is one of the EGFR-TKIs and used for patients with activating mutations in the EGFR genes.

Clinicians often encounter a spectrum of cutaneous side effects associated with EGFR-TKIs, including acneiform rash, pruritus, and less commonly, xerosis, paronychia, skin fissures, and telangiectasia⁵ (**Table 2**).

EGFR is located in the hair follicle, particularly in its outer root sheath, where it exerts a pivotal influence on regulating the hair cycle.³³ It has been hypothesized that the inhibition of EGFR signaling by these drugs could alter the growth pattern of hair, potentially leading to the induction of abnormal hair growth, such as trichomegaly. In such cases, trichomegaly typically occurs after approximately two months of treatment and reverses upon discontinuation of the medication.

Erlotinib-associated eyelash trichomegaly has been reported only in a small number of case reports,^{34,35} with no previous mention of dermoscopy findings. To the best of our knowledge, erlotinib-induced trichomegaly has never been reported in Africa.

Trichomegaly is not a drug-limiting side effect. However long eyelashes often cause eyeball irritation and corneal epithelial defects, including erosions,³⁶ irritation,³⁴ infection, and ulcers.³⁷

Eyelash trimming with scissors or epilation can be effective and safe therapeutic options.

Conclusion

Eyelash trichomegaly is a rare, EGFR TKI-associated effect. Although trichomegaly of the eyelashes may occasionally lead to ocular adverse effects, a significant num-

Table 1. *Reported causes of trichomegaly.*

Congenital conditions associated with eyelash trichomegaly Oliver-McFarlane syndrome¹⁹ Cornelia de Lange syndrome¹¹ Familial hypertrichosis¹² Acquired conditions associated with eyelash trichomegaly Hair disorders: Alopecia Areata²⁰ Connective tissue disorders: Dermatomyositis,¹⁷ systemic lupus erythematosus¹⁸ Allergic conditions like allergic rhinitis, atopic dermatitis¹⁵ Infections: HIV¹³ Ocular diseases: Uveitis,¹⁶ vernal keratoconjunctivitis¹⁴ Miscellaneous disorders: Anorexia nervosa, malnutrition, hypothyroidism, porphyrias, pregnancy Paraneoplastic syndrome Renal cell cancer²¹ Drugs associated with eyelash trichomegaly Latanoprost,²² bimatoprost²³ Epidermal growth factor receptor inhibitors: cetuximab,²⁴ Panitumumab; tyrosine kinase Inhibitors: erlotinib,²⁵ gefitinib²⁶ Interferon-α2b²⁷ Cyclosporine,¹⁴ tacrolimus²⁸ Topiramate⁸

Table 2. *Adverse mucocutaneous effects owing to erlotinib.*

Acneiform eruption³¹ Seborrheic dermatitis³² Paronychia Mouth ulcers Xerosis Pruritus Paronychia Hair changes Blepharitis Skin fissures Angular cheilitis Telangiectasias

ber of affected individuals perceive the alteration in eyelash length as a cosmetic enhancement to their appearance. Simple measures can be taken to shorten or remove the elongated eyelashes if needed. Usually, once the treatment is stopped, the eyelashes return to their normal length.

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Potential conflicts of interest

The authors declare no conflicts of interest

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