

CASE REPORT

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Trichomegaly of Eyelashes in Lung Cancer Following Treatment with Erlotinib

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Abstract

Erlotinib is widely used in the management and treatment of non-small cell lung cancer, pancreatic cancer and several other types of malignancies. It is one of the inhibitors of the epidermal growth factor receptor (EGFR) tyrosine kinase. Ocular side effects are rare compared to cutaneous toxicities which are more common. We are reporting a case of erlotinib induced trichomegaly in a 65-year-old Malay female who is suffering from metastatic adenocarcinoma of the lung. The patient started to notice coarse eyebrows and long eyelashes almost 1 year after initiation of treatment. The length of eyelashes is around 17mm. She was treated conservatively with frequent trimming of eyelashes and eyebrows since she was asymptomatic.

Keywords: Epidermal growth factor receptor inhibitors; Erlotinib; Trichomegaly

Introduction

Lung cancer is one of the most common cancers in Malaysia which is about 10% of all malignancies¹. Erlotinib is the first generation epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) used in the management of non-small cell lung cancer harbouring EGFR activating mutations². EGFR inhibitors are generally well tolerated. Yet side effects such as skin toxicities are commonly observed due to interference of epithelial growth factor receptor signalling in the skin. Patients usually complain of papulopustular rash, mucositis, pruritus, xerosis, paronychia and facial hirsutism³. Trichomegaly is defined as

an excessive increase in length (12mm and more), stiffness, thickness, curling and pigmentation of eyelashes. Erlotinib TKI associated eyelash trichomegaly is rare and the incidence rate is unknown⁴. There are multiple causes for trichomegaly such as congenital, familial, acquired and drugs.^{5,6} We report a rare case of trichomegaly in non-small-cell-lung cancer following treatment with Erlotinib.

Case Report

A 65-year-old Malay female non smoker presented with prolong cough for a month, fever and shortness of breath. Computed tomography (CT) scan of thorax revealed a large mass in right lower

lobe measuring 4.0cm x 2.5cm x 3.2cm. (AP x W x CC) and multiple small lung nodules seen in both lungs which was suggestive of metastasis. Subsequently CT-guided transthoracic lung biopsy was done. Immunohistochemical stains were positive for cytokeratin 7 (ck7), thyroid transcription factor (TTF), EGFR (epidermal growth factor receptor) and negative for cytokeratin 20 (ck 20). She was diagnosed as metastatic adenocarcinoma of lung.

Polymerase chain reaction-based DNA sequencing detected a mutation in exon 19 of the EGFR gene. She was started on systemic front line therapy with single agent Erlotinib in December 2018 (standard oral dose 150mg). The patient did not have any systemic side effects since started on Erlotinib. Patient only noticed overgrowing of long eyelashes and coarse eyebrows around one year after starting on regular treatment.

The length of the eyelashes was around 17 mm. Coarse and thick eyebrows were also noticed by the patient. Patient denies any visual disturbance or any ocular complication due to trichomegaly. She was treated conservatively. She did frequent trimming of eyelashes and eyebrows to prevent discomfort and ocular surface complications such as cornea abrasion. During the whole treatment, she did not receive, use or consume any other medications. According to the Naranjo algorithm or adverse drug reaction probability scale our patient score is five which shows Erlotinib is the probable cause for the symptoms.⁷ The subsequent assessment revealed the disease was progressing despite compliance to erlotinib. CT- thorax reported new soft tissue nodule seen adjacent to the previous lung mass. Erlotinib was discontinued by the oncology team in March 2022. Patient noticed there is no more overgrowing eyelashes and coarse eyebrows since then.



Fig 1.



Fig 2.

Discussion

Trichomegaly is known as hypertrichosis which is defined as excessive in length, stiffness, thickness, curling and pigmentation of eyelashes. The diagnosis is made based on clinical findings if eyelashes are measured more than 12 mm in length⁸. First terminal hair to appear is eyelashes during embryological development at 12 weeks of gestation. The nuclear factor of activated T-cells (NFAT) blocks stem cell activation in the bulge and suprabulbar region of the eyelash hair follicles. Trichomegaly occurs as a result of inactivation of NFAT⁹. EGFR is located in hair follicles at the outer root specifically and plays an important role in regulating hair cycle⁶. Signalling of EGFR acts as a stopper in the growth of eyelash hair follicle cycle. Any condition causing inhibition of EGFR may cause trichomegaly⁹. Inhibition of EGFR will cause dysregulation of keratin gene expression within the hair follicle activity which leads to abnormal hair growth. Erlotinib not only affects apoptosis and proliferation of cancer cells, but it also affects the progression of hair follicles from anagen to telogen phase and this ends abnormal hair growth¹⁰.

Congenital diseases such as Oliver-McFarlane syndrome, oculocutaneous albinism type I or familial hypertrichosis is reported to present with trichomegaly⁴. Certain diseases such as human immunodeficiency virus type 1, systemic erythematous lupus, alopecia areata, atopic dermatitis and some acquired conditions like uveitis, vernal keratoconjunctivitis, malnutrition may develop trichomegaly. Drugs commonly in use such latanoprost, bimatoprost, travoprost, cyclosporine A, tacrolimus, cetuximab are also can result in trichomegaly.⁹ EGFR TKIs such as gefitinib also have been reported results in trichomegaly.⁵ These drugs inhibiting EGFR signals and cause changes in growth pattern thus induce abnormal hair growth.¹¹

There have been cases of trichomegaly after erlotinib. A similar condition was reported by Shan-Bing Wang et al in 2015, trichomegaly following treatment with erlotinib in non-small cell lung cancer patient¹². A woman with stage IV lung adenocarcinoma using erlotinib monotherapy reported to develop cutaneous toxicity³. In our case patient didn't develop any cutaneous toxicity. Judith E. et al in 2006 reported a case

trichomegaly after erlotinib whereby patient was complaining of visual disturbance and cornea irritation¹³. In our case patient did not have any ocular complains.

Conclusion

EGFR inhibitor are commonly cause skin toxicities and ocular side effects are rare. Trichomegaly of eyelashes has been reported sporadically. Eyelash trimmings with scissors or epilation can be a reasonable temporary solution for these patients.

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