Eyelash trichomegaly induced by erlotinib for metastatic lung cancer

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A 65-year-old Chinese woman was referred to the ophthalmology clinic complaining of grittiness in both eyes for 1 month. She had been diagnosed with stage IV metastatic pulmonary adenocarcinoma with positive mutation in epidermal growth factor receptor (EGFR) gene (L858R) and had been prescribed erlotinib 4 months previously as palliative treatment (Table).

Physical examination revealed bilateral long thick curly eyelashes (Figs 1 and 2) affecting all four eyelids. A papulopustular rash over the periocular region was also evident. The patient denied use of topical prostaglandin analogue for either medical or cosmetic use. A diagnosis was made of drug-induced trichomegaly. Corneal punctate epithelial erosion as a result of the misdirected lashes was treated symptomatically with regular epilation and topical lubricants.

Upon follow-up, gradual partial reversal of trichomegaly was evident at 6 weeks after erlotinib cessation. There was also improvement of the periorbital papulopustular rash. The reversal of trichomegaly after EGFR inhibitor cessation is not well documented in the literature. This case illustrates the presentation and partial resolution of drug-induced trichomegaly.

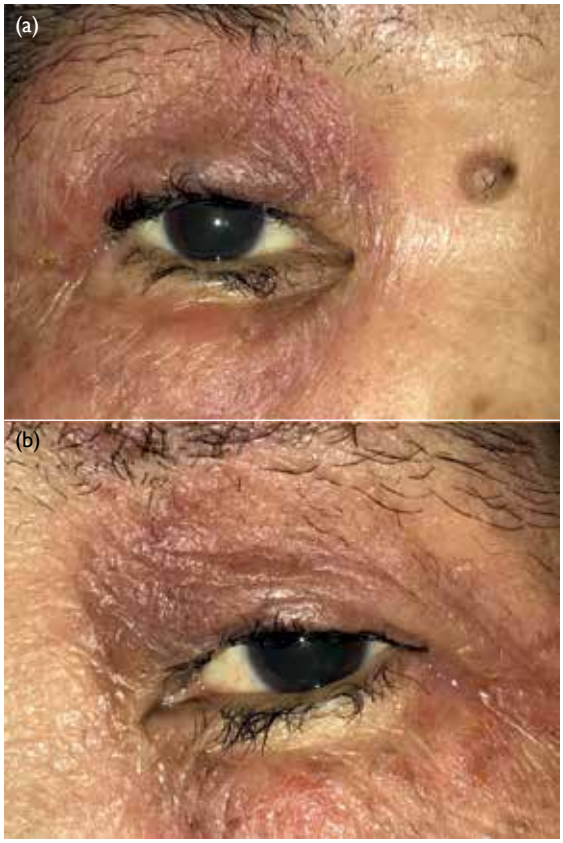

FIG 1. Clinical photographs of the (a) right and (b) left eyes of a 65-year-old woman who was taking palliative EGFR inhibitor erlotinib for 4 months. Trichomegaly with increased thickness, curling, pigmentation and length of the eyelashes affecting the right upper and lower lids is evident. The patient also has PRIDE syndrome with a papulopustular rash affecting the periocular skin (pharmacological mydriasis was induced as part of the complete ophthalmological examination)

TABLE. Timeline of the patient

Jun 2018	Gradual onset of poor balance and waddling gait
22 Aug 2018	Admitted to the medical ward MRI brain showed multiple cerebral and cerebellar masses
31 Aug 2018	Bronchoscopy with bronchoalveolar lavage, lung biopsy, fine needle aspiration cytology confirmed adenocarcinoma Polymerase chain reaction revealed L858R mutation in exon 21 of the EGFR gene
3 Oct 2018	Completed whole brain radiotherapy
4 Oct 2018	Started taking erlotinib 150 mg daily
12 Nov 2018	Noted severe skin reaction Gradual dose reduction of erlotinib to 100 mg on alternate days
21 Feb 2019	Presented to the ophthalmology clinic with trichomegaly and periorbital skin changes (Fig 1)
27 May 2019	Erlotinib stopped in view of significant adverse effect and minimal benefit on sequential imaging
12 Jul 2019	Partial reversal of trichomegaly noted during ophthalmology clinic follow-up (Fig 2). Patient was moribund and bedbound
12 Sep 2019	Deceased

Abbreviations: EGFR = epidermal growth factor receptor; MRI = magnetic resonance imaging

Eyelash trichomegaly is a rare condition characterised by increase in length, thickness, pigmentation, and curling of the eyelashes. The eyelash follicle, just as the scalp hair follicle, undergoes the cycle of anagen, catagen, and telogen phase. The anagen phase of eyelashes (ie, the growth phase) typically spans 8 weeks in Asian patients and occurs in 18% of eyelashes at any given time.[1]

Drug-induced trichomegaly is the most common form of trichomegaly to present in a general ophthalmology setting. Prostaglandin analogues

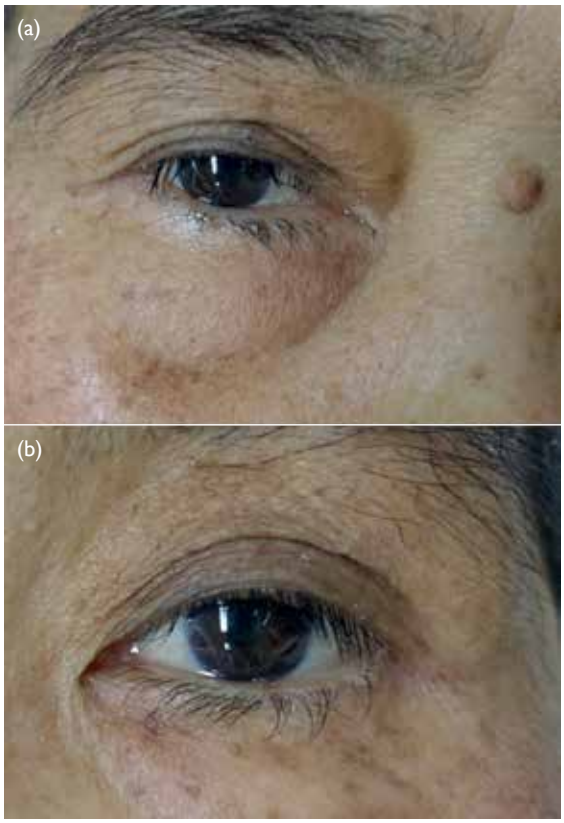

FIG 2. Clinical photographs of the (a) right and (b) left eyes of the same patient 6 weeks after cessation of erlotinib treatment. Partial reversal of trichomegaly of the right eye is demonstrated. The curling and pigmentation of eyelashes had resolved although increased thickness and length of eyelashes persisted. Periocular skin inflammation had completely subsided

such as latanoprost and bimatoprost, although commonly used as antiglaucomatous drugs, are well known for their side-effect of eyelash trichomegaly. The effect is due to up-regulation of prostaglandin E2, D2 receptor expressed in hair follicles.[2]

The occurrence of EGFR inhibitor–induced trichomegaly is seen less often but is not uncommon in the ophthalmology setting. It has been postulated that EGFR inhibitors inactivate the nuclear factor of activated T-cells. This leads to activation of stem cell bulge and suprabulbar region of the eyelash hair follicles.[3] In a typical course, trichomegaly develops between the second and fifth month of EGFR inhibitor treatment.[4] An Asian study reported that 2% of patients prescribed EGFR inhibitor treatment had trichomegaly.[5] The EGFR inhibitor is also well known to cause a series of cutaneous adverse effects known as the PRIDE syndrome (papulopustules and/or paronychia, regulatory abnormalities of hair growth, itching, and dryness).[6] In this case, the patient exhibited PRIDE syndrome affecting the periocular skin as demonstrated in Figures 1 and 2.

Trichomegaly is a benign condition, but long misdirected lashes may lead to corneal punctate epithelial erosion and corneal abrasion. Frequent trimming, epilation, and topical lubricants serve as first-line treatment. Electro-epilation or cryoablation directed at the affected hair follicles may be considered in instances of recurrent misdirected lashes with corneal complications such as infective corneal ulcer.

This case highlights the clinical course of EGFR inhibitor–induced trichomegaly upon cessation of drug therapy, which is not well documented in the literature. Partial reversal of trichomegaly was achieved after stopping erlotinib for 6 weeks. It is evident that the time required for trichomegaly resolution follows the typical eyelash follicle cycle.

Author contributions

All authors contributed to the design, acquisition of data, analysis of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

As an adviser of the journal, HKL Yuen was not involved in the peer review process. Other authors have disclosed no conflicts of interest.

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Ethics approval

The patient was treated in accordance with the Declaration of Helsinki. The patient provided written informed consent for the treatment/procedures, and consent for publication.

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