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Cetuximab Related Eyelash Elongations for Patients with Metastatic Rectum Carcinoma: Metabolic Complete Response

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Dear Editor:

Colorectal cancer (CRC) is the second most common cause of cancer related death for developed countries. Over the past decades, significant improvements have been achieved on the pathogenesis of CRC and new therapeutic options are available today. However, it is not

Fig. 1. Eyelash elongation after cetuximab treatment (published with permission of patient).

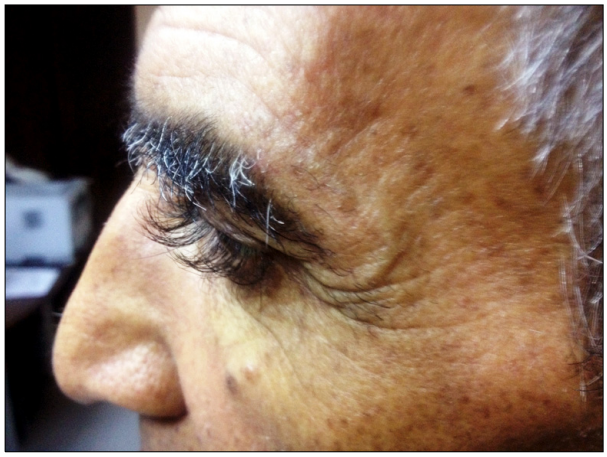

Fig. 2. Patient's second photograph after reintroduction of cetuximab (published with permission of patient).

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exactly known as some of the patients respond to treatments well while others have poor responses[1].

A 58-year-old man was diagnosed with stage IV rectum adenocarcinoma with multiple liver metastases. The whole body position emission tomography (PET) revealed that multiple liver metastases (SUV max between: 7.9 to 9.2). A KRAS test in the patient's primary tumor revealed no mutations in the KRAS gene. He received palliative chemotherapy with FOLFIRI plus cetuximab and showed a good tumor response after 6 months and discontinued further treatments. After the 6 cycles of treatment, the PET-computed tomography scan was taken and it revealed no pathological uptakes. However, after the 3 cycles of treatment, acneiform eruptions were observed and the patient noted changes in his eyelash (Fig. 1). Toxicities were induced by skin care, bath oils, emollient creams, sun protections and trimming eyelashes, and thus, cetuximab treatment was continued without dose reductions or interruptions. After the cetuximab was discontinued, the patient's eyelash and skin returned to pretreatment state. The patient exhibited progressive diseases after a relatively long period of tumor controls. His performance status was good and he was clearly a candidate for continuation of tumor-directed therapy. Treatment was continued with FOLFIRI plus cetuximab for another 6 months and good tumor responses were achieved again. Nonetheless, acneiform eruptions and eyelash elongation were observed after reintroductions of cetuximab (Fig. 2). The authors are indebted to the patient for his permission for publication.

Epidermal growth factor receptor (EGFR) is one of the new targets in the treatment of many tumor types. Cetuximab is a chimeric monoclonal antibody which binds the EGFR with high affinities and competitively inhibits ligand binding and inhibits activation of downstream signaling pathways. It has been reported that approximately 30% to 50% of metastatic CRC has K-ras mutations. K-ras wild type (WT) status is associated with survival benefits in cetuximab-treated metastatic colorectal cancers[2]. However, not all WT patients respond to cetuximab and some patients with mutant K-ras experience long-term disease controls, and thus, it is necessary for clinicians to predict clinical outcomes more accurately[1]. EGFR inhibitors (EGFRIs) are generally well-tolerated and do not have the severe systemic side effects. Nevertheless, EGFRIs frequently cause skin toxicity and may lead to discontinuation of treatment. Although papulopustular rash is the most observed toxicity, the xerosis, pruritis, paronychia, hyperpigmentation and hair changes can be noticed. Eyelash elongation is an uncommon drug-associated adverse effect of EGFRIs and it is most frequently associated with cetuximab[3-5]. The exact mechanisms of EGFRIs related skin toxicities are not fully understood but several mechanisms have been proposed. EGFR is highly expressed in the skin and hair follicles, and EGFR is important for normal skin development. For that reason, inhibiting the EGFR leads the toxicities, and it is frequently observed in patients. It was suggested in different studies that rash was associated with a better outcome and rash might be a surrogated clinical marker. However, management of EGFRIs related skin toxicities is important for maintaining both dose intensities for EGFRIs and quality of life. Although previous trials suggested that skin care, topical antibiotics and immunomodulatory agents, prophylactic uses of tetracycline and minocycline decrease the severity of rash, therefore, dose reductions, interruptions and cessations are required[3,4]. The long eyelashes are not a drug-limiting adverse effect, but trimming the lashes usually ameliorates local symptoms, and elongations of eyelashes might be associated with a better outcome and a surrogated clinical marker.

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