

Trichomegaly of the eyelashes induced by the epidermal growth factor receptor inhibitor cetuximab in the treatment of metastatic colorectal cancer

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DESCRIPTION

Cetuximab is a chimeric monoclonal antibody (MoAb) that competitively binds and inhibits the epidermal growth factor receptor (EGFR). EGFR is constitutively expressed in normal tissues such as the epidermis and hair follicle epithelium but also in some tumours, including colon and rectum.¹ Cetuximab proved to be effective in the treatment of metastatic colorectal cancer when tumours are RAS wild type for mutation in exons 2, 3 and 4 of the KRAS and NRAS genes. Skin toxicity is the most important side effect of this agent, with up to 80% incidence, 15% of which are reported as severe.² The mechanism appears to be related to modulation of the EGFR signalling pathway in keratinocytes. Additionally, serum levels of CXCL8 appear to be important for individual EGFR inhibitor-induced toxicity. The release of cytokines and other mediators of inflammation leads to altered cell growth and differentiation.³ It presents most commonly as an acneiform rash in the face and trunk and appears to be a sign of response. Other skin and hair toxicities can occur, although less reported, especially in clinical trials. Trichomegaly is one of these adverse events, usually occurring after 2–5 months of treatment, not always preceded by rash. Although apparently harmless, it can lead to eyelid infections and corneal ulceration due to abnormal eyelash growth. Therefore, oncologists should be aware of this side effect to assure prevention of complications. Prior to initiating treatment, patients should be elucidated about toxicities. If trichomegaly arises, patient counselling regarding lid hygiene, with avoidance of eye rubbing, should be performed. Management consists of eyelash clipping every 2–4 weeks and referral to an ophthalmologist for correct advise and complications.

We report the case of a 45-year-old woman, diagnosed in November 2017 with adenocarcinoma of left colon. Complete staging revealed multiple pulmonary and liver metastasis, not feasible for resection. Baseline carcinoembryonic antigen was 311 ng/mL. Genetic analysis of the tumour did not show mutations of KRAS and NRAS genes, predicting response to anti-EGFR agents. Furthermore, no mutations on exon 15 of the BRAF gene were documented. Based on patient's excellent performance status, stage IV disease at diagnosis and after agreement, she initiated in December 2017 first-line palliative chemotherapy with C-FOLFIRI (cetuximab 450 mg/m² intravenous loading dose, followed by 250 mg/m²

subsequent cycles; irinotecan 180 mg/m² intravenous, leucovorin 50 mg intravenous, fluorouracil 400 mg/m² intravenous, followed by 2400 mg/m² infusion pump for 46 hours). The patient reported good tolerance to treatment, being of underline the appearance of eczematous rash in the face after five cycles, G1 (CTCAE-v4.0). She maintained C-FOLFIRI, with documented response. After 14 cycles, she went to the oncology clinics with an acute infection of the eyelids that was clinically diagnosed as a hordeolum. Concomitantly, she complained of abnormal growth of her eyelashes, which became lengthened and curly (figures 1 and 2) and described this issue as extremely troublesome and unpleasant. She reported that this change had arisen 3 weeks earlier and worsening. Since our patient was not receiving other trichomegaly-inducing



Figure 1 Trichomegaly of the eyelashes after treatment with cetuximab, 32 mm length.



Figure 2 Trichomegaly of the eyelashes after treatment with cetuximab, profile.



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drugs, we have assigned this adverse event to the MoAb. After

Patient's perspective

People often come to me and say 'where have you made your eyelashes, they look so real'. This is the fun part. The not so fun part is the discomfort and itching that the long eyelids cause, and when you scratch with your hands, the more likely it is to make infections. And this is terrible. I totally agree that I should keep treatment, because it is helping me, but I just wish there was a more easy way to manage my 'beauty problem'.

Learning points

- ▶ Cetuximab is an antiepidermal growth factor receptor, with skin toxicity being the most frequent and remarkable one.
- ▶ Trichomegaly of the eyelashes is a rare and thus underreported side effect of cetuximab, appearing usually within 2–5 months of treatment.
- ▶ Understanding cutaneous side effects of epidermal growth factor receptor inhibitors, with correct management of complications and patient education and counselling, is important in order to improve quality of life.

elucidating the patient about this effect and its cause, we've decided, with patient's agreement, to maintain treatment due to the excellent tumour response and good tolerability. After shortening of the eyelashes with the help of a beautician and advise on cleaning and management to avoid infections, the patient reported a marked improvement in her quality of life.

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