Cetuximab-induced Facial Hypertrichosis in a Female Patient Treated for Metastatic Colon Adenocarcinoma

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Abstract

Anti-epidermal growth factor receptor (EGFR) antibodies are standard of care in the management of metastatic colorectal and head and neck cancers as a targeted therapy inhibiting tumor proliferation. The inhibition of EGFR pathway in the skin results in several cutaneous complications such as skin rash, hypertrichosis, and male pattern alopecia. We report a case of a 55-year-old female patient who developed hypertrichosis following six cycles of Cetuximab with a normal hirsutism-related hormone profile.

Keywords: Cetuximab; Acne Rash; Hypertrichosis.

Introduction

Cetuximab is a monoclonal antibody directed selectively against EGFR receptors that blocks ligand binding preventing the conformational change of receptor need for dimerization. Moreover, EGFR receptors are widely expressed in epithelial, mesenchymal, and neuronal tissues and play a major role in normal cellular processes. Therefore, some form of skin toxicity occurs in 80–95% of patients treated with cetuximab.[1] Cutaneous toxicity is commonly acne-like papulopustular rash mainly involving the face and upper trunk with dry itchy skin. Less common skin toxicities include seborrheic dermatitis-like eruptions, paronychia, desquamation, pruritus, male pattern alopecia, hypertrichosis, and trichomegaly.[1] The mechanism of action in Cetuximab-induced skin toxicity is not clear but, because the EGFR expression level is high, especially in the skin epithelial tissue, cutaneous toxicities are common due to EGFR inhibitors.[2]

Case Report

A 55 years old female patient with co-morbidity of Type II Diabetes mellitus controlled by diet was diagnosed with stage III sigmoid adenocarcinoma post Laparoscopic high anterior resection pT_3N_2(7/14) Mx (left para-aortic lymphadenopathy 17 mm in maximum short axis) in 2018. She received 12 cycles of mFOLFOX6 [5-fluorouracil, leucovorin, oxaliplatin] chemotherapy. She tolerated chemotherapy well apart from grade I peripheral neuropathy. She was under follow up until a PET CT [Positron Emission Tomography and Computed Tomography scan] in October 2019 showed increased uptake in left para-aortic lymph nodes (increase in size from 1.9 to 2.4 cm and increase SUV from 7 to 10) with new left supraclavicular LN (size 1.5 cm & SUV 6.3). A CT-guided Biopsy of the Para-aortic lymph node, showed Metastatic adenocarcinoma consistent with metastasis from the colorectal primary. The tumor molecular profile showed MMRp [mismatch repair proteins were proficient], Her-2 Negative by IHC [immunohistochemistry], N and K RAS oncogene wild type, and RAF oncogene wild type.

She wanted to avoid multi-agent chemotherapy, however, she agreed to have Capecitabine with bevacizumab. There was an initial response to this regimen, however a PET CT scan after nine cycles showed progression of disease

in left supraclavicular lymph nodes, mediastinal, Paraaortic lymphadenopathy with CEA [carcinoembryonic antigen] =10 [N= Less 5], After counseled, she started on CAPOX [Capecitabine, Oxaliplatin] with Cetuximab.

After Six cycles of CAPOX with Cetuximab, she noted gradual abnormal excessive facial hair growth requiring hair removal [Figure 1]. She was investigated for hirsutism. Her hormone profile included normal levels of Thyroid-stimulating hormone 1.8 UI/mL [N = 0.35 to 5.5 UI/ML], Testosterone 0.396 nmol/L[N Female = 0 to 2.6 nmol/L], Prolactin 163 mlU/L[Nonpregnant females102 to 496 mIU/L], cortisol random 175 nmol/L[N= 140 to 690 nmol/L], Dehydroepiandrosterone 2.63[N=0.96 to 6.95 µmol/]. Her follicle-stimulating hormone is 56.32 UI/L[Peri-menopausal above 30 UI/L], and her luteinizing hormone is 33.04 UI/L [Before menopause: 5 to 25 IU/L after menopause: 14.2 to 52.3 IU/L] were consistent with peri-menopausal status. Upper abdominal imaging to rule out any adrenal lesions were normal.

The patient was distressed by the cosmetic appearance and cetuximab was withheld for 6 weeks and with close monitoring with regression of facial hair [Figure 2]. She had an excellent response to treatment, a PET scan done after cycle four, and a regimen amounting to the almost complete disappearance of metastatic disease.

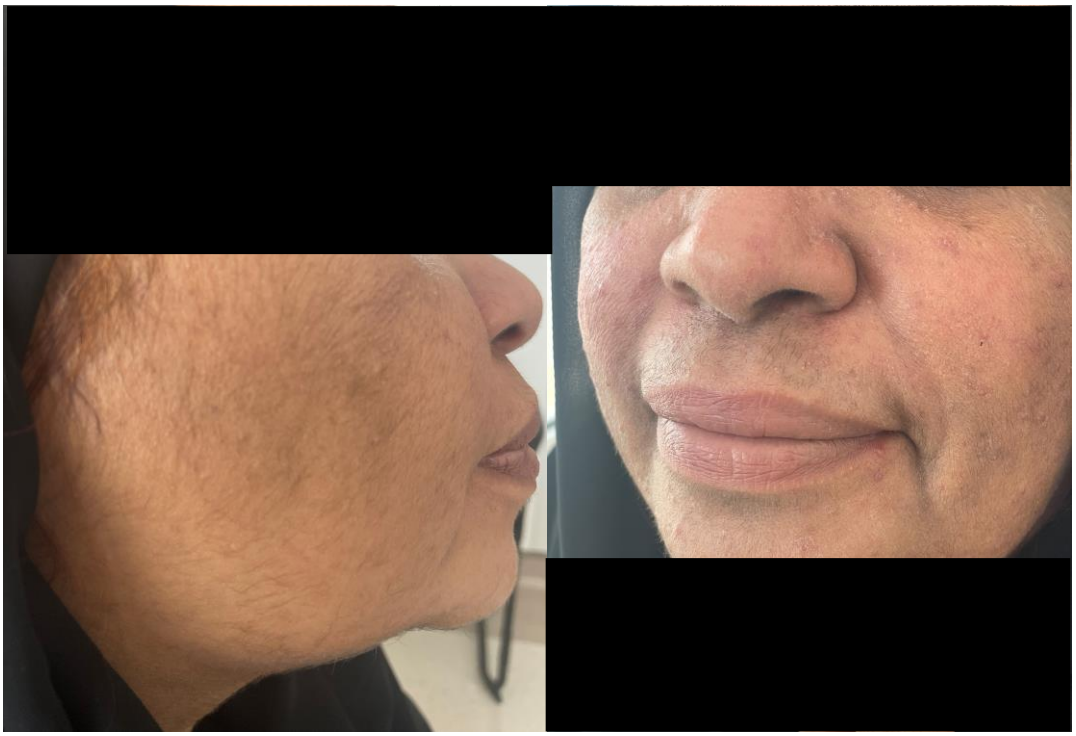

Figure 1: Abnormal excessive facial hair growth.

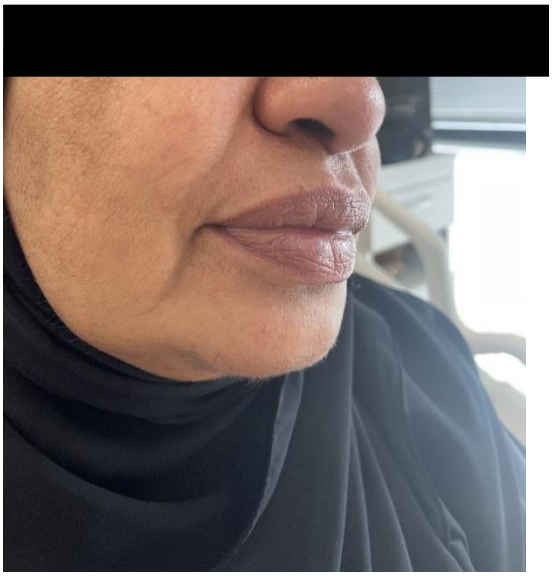

Figure 2: Facial hair regression.

Discussion

Hypertrichosis is a very rare side effect in patients treated with cetuximab, and a significant cosmetic implication, especially in female patients. The incidence of hypertrichosis with cetuximab is not well defined, but it is thought to occur in a small percentage of patients who receive the drug. The hair growth typically appears on the face, scalp, and upper back, and it can be permanent or temporary. Turker et al[3] reported hypertrichosis, trichomegaly, and androgenic alopecia in patients treated with cetuximab and chemotherapy for RAS-wild-type metastatic colon cancer. Moreover, *Montagut et.al reported* abnormal hair growth and acneiform follicular eruption *in a 66-year-old male patient treated by cetuximab and carboplatin in a second-line setting for supraglottic* squamous cell carcinoma with resolution of skin toxicity upon cetuximab discontinuation.[4] Similarly, Vano-Galvan et al, reported scalp and eyelashes hair growth in a bald male patient 100 years old with good performance status treated in the third line by cetuximab for squamous cell carcinoma of the scalp.[5] The EGFRs are widely distributed in skin tissue, and therefore the disruption of signaling is involved in the initiation of the anagen phase of the hair cycle resulting in dysregulation of hair growth.

The impact of hypertrichosis on the prognosis of patients with colon cancer is not well understood. However, it is a relatively uncommon and mild side effect of cetuximab, and it is not known to affect the effectiveness of the drug in treating cancer. Therefore, the presence of hypertrichosis in a patient receiving cetuximab for colon cancer is not likely to have a significant impact on their prognosis,

FIRE-3 (AIO KRK0306) trial spoke about skin toxicity, Acneiform rash, Nail changes, Desquamation, and Dry skin which showed clinical predictors of good response, but it never reported any case in all 199 patients with hypertrichosis because it is a rare condition.[6]

On the other hand, Jaka et al in an observation study of 116 patients with metastatic colon adenocarcinoma who received anti-EGFR, noted papulopustular rash and xerosis may be clinical predictors of good response.[7]

Conclusion

Cetuximab-induced hypertrichosis is a rare side effect, and it is considered a critical side effect, especially in women. Hypertrichosis is not reported as a prognosis factor for response and it has self-recovery by hold treatment.

Disclosure

Written informed consent for publication of their clinical details and clinical images was obtained from the patient

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