CASE REPORT

Trichomegaly of the Eyelashes During Therapy With Epidermal Growth Factor Receptor Inhibitors: Report of 3 Cases

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A wide spectrum of skin toxicities has been described in patients receiving epidermal growth factor receptor (EGFR), inhibitors, including papulopustular rash, xerosis and fissures, pruritus, mucositis, paronychia, and hair changes.Trichomegaly of the eyelashes is a rare adverse effect of EGFR inhibitor therapy and is characterized by a paradoxical overgrowth of eyelashes. We present 3 cases of trichomegaly occurred during EGFR inhibitor therapy.

THE OVEREXPRESSION of the epidermal growth factor receptor (EGFR) is strongly associated with cancer development. It is known that EGFR can be inhibited by monoclonal antibodies such as cetuximab and panitumumab or by small-molecule tyrosine kinase inhibitors such as erlotinib and gefitinib.[1]

The higher specific pharmacological target of these drugs can lower hematologic toxicity, but the risk of dermatological reactions is quite higher related to these drugs.[2] The EGFR, in fact, is expressed in basal and suprabasal layers of the epidermis, in sebaceous glands, and in the outer root sheath of the hair follicles.[3]

A wide spectrum of skin toxicities has been described in patients receiving EGFR inhibitors, including papulopustular rash, xerosis and fissures, pruritus, mucositis, paronychia, and hair changes. All these adverse effects can have significant physical and emotional discomfort.[4]

Hypertrichosis refers to excessive hair growth in normally hairy, non–androgen-dependent regions. Trichomegaly of the eyelashes is a rare adverse effect of EGFR inhibitor therapy and is characterized by a paradoxical overgrowth of eyelashes. It usually occurs in 2 to 5 months after the start of treatment and may resolve in several weeks or months after discontinuation of treatment.[5]

We present 3 cases of trichomegaly that occurred during EGFR inhibitor therapy.

CASE REPORT

All 3 patients were females and referred to our outpatient department from February through September 2011.

The first patient, aged 45 years, had a metastatic gastric cancer and was put on therapy with panitumumab + FOLFOX protocol (5-FU + folinic acid + oxaliplatinum) for 3 months. Six weeks after starting panitumumab, she developed an abnormal growth of her eyelashes (Fig. 1).

The second patient, aged 54 years, had a metastatic gastric cancer too. She had been on therapy with panitumumab for 4 months in the last year, and she had suspended therapy 6 months before our observation. Three months after administration of panitumumab, she noticed the development of long, curly eyelashes. This clinical sign was maintained during the whole duration of the therapy and persisted for 6 months after its discontinuation (Fig. 2).

The third patient had metastatic lung cancer and has been under treatment with erlotinib for 3 months. She had been previously treated with 4 cycles of cisplatinum + vinorelbine and 2 cycles of pemetrexed. Eight weeks after starting erlotinib, she developed trichomegaly (Fig. 3).

All the 3 patients had long and curly eyelashes, without associated symptoms such as pain or itching. They showed also other signs of EGFR inhibitor skin toxicity.

The first patient showed a papulopustular rash (G2 grading according to the Common Toxicity Criteria version 4.03) involving the trunk and face; furthermore, she had hypertrichosis of the face.

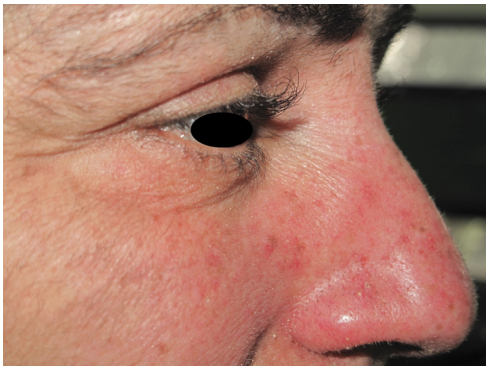

Figure 1A. Trichomegaly during treatment with panitunumab.

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Even if the second patient had already interrupted panitumumab when she came to our observation, she still showed paronychia and dry skin as delayed adverse effects of this therapy. Moreover, she referred that she had had a papulopustular rash during the treatment with panitumumab; this rash disappeared after the suspension of the therapy.

The third patient showed a papulopustular rash that started after the first 2 weeks of treatment with erlotinib. Lesions involved less than 50% of the body surface and were associated with moderate pruritus (G2 grading according to the Common Toxicity Criteria version 4.03). In the last month, the patient had also noted changes in the quality of her hair, which at our observation were curly and brittle.

The pathogenesis of trichomegaly related to the assumption of EGFR inhibitors is not completely understood. Epidermal growth factor receptor is expressed in the keratinocytes of the outer sheath of the hair follicle, and it acts such as an on/off switch at the beginning and at the end of the anagen phase. The inhibition of the EGFR signaling disrupts the progression of the anagen to the telogen phase, leading to an aberrant anagen phase and subsequently to abnormal hair growth. This can stimulate the formation of a disorganized hair follicle.[6]

Anyway, it is not well understood how these drugs can be responsible for frailer scalp hair and stronger and longer lashes.

Although this kind of disorder is rarely related to pain, pruritus, or any kind of discomfort, it can represent an important cause of aesthetic damage, especially for female patients. Periodical trimming is an appropriate therapeutic modality. This adverse effect tends to persist for the duration of the treatment with EGFR inhibitors, and it could last for a long period after drug discontinuation, as in our second patient.

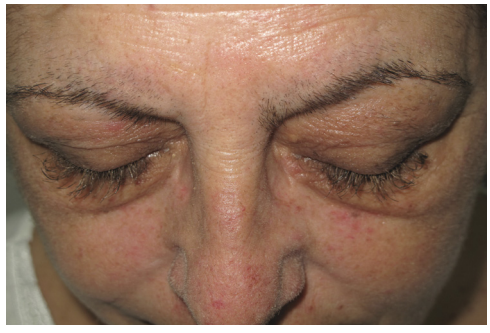

Figure 1B. Trichomegaly during treatment with panitunumab.

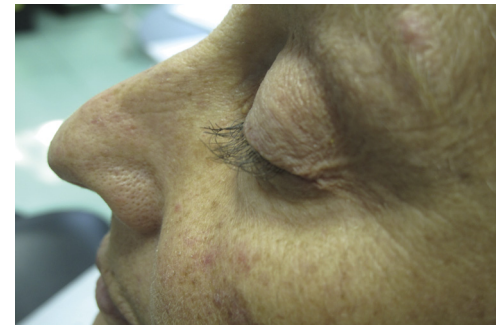

Figure 2. Trichomegaly during treatment with erlotinib.

Sometimes, the elongation of eyelashes can be complicated by trichiasis and secondary corneal ulceration. For this reason, patients affected by trichomegaly should have ophthalmologic consultation.

With the increasing use of this new class of drugs, dermatologists and oncologists should be aware of this effect. An early identification of trichomegaly can protect patients from ocular damages and can improve their quality of life.

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