Case Letter

Keratosis pilaris-like rash with the tyrosine kinase inhibitor nilotinib: A side effect not to be ignored

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Sir,

Nilotinib is a second-generation tyrosine kinase inhibitor (TKI) generated from the BCR-ABL fusion protein, c-Kit, and platelet-derived growth factor receptor. It is approved for the management of chronic myelogenous leukemia in patients who have developed intolerance or resistance to imatinib [1,2].

A keratosis pilaris-like rash is identified as an adverse effect associated with TKIs, particularly, nilotinib [2]. Herein, we seek to enhance the existing literature by reporting a case of a keratosis pilaris-like eruption observed in a patient with chronic myeloid leukemia treated with nilotinib.

The patient was sixty years old and had been treated for seven years for chronic myeloid leukemia in the chronic phase, with a positive BCR-ABL transcript. She was initially treated with imatinib, yet due to the absence of a molecular response, second-line chemotherapy with nilotinib was started one month prior at a dose of 800 mg per day.

The patient presented with a mildly pruritic generalized rash that had been evolving since day 7 after the introduction of nilotinib. An examination identified diffuse erythematous, brownish hyperkeratotic follicular papules on the face, back, trunk, abdomen, and arms (Figs. 1a – 1c). Dermoscopic evaluation of the affected areas demonstrated peripilar erythema, keratotic plugs, and vellus hair (Fig. 2).

A biopsy showed orthokeratotic hyperkeratosis, follicular plug, and mild lymphocytic infiltrate.

We upheld the diagnosis of nilotinib-induced keratosis pilaris based on the temporal correlation between a drug intake and the onset of the lesions, along with the absence of any clinical or histological signs suggesting other differential diagnoses. The pharmacovigilance department was notified.

In our case, treatment substitution was not possible, so we prescribed an emollient containing 10% urea thrice daily and an antihistamine, which led to an improvement.

A keratosis pilaris-like rash was observed in association with second-generation multi-target TKIs like nilotinib and dasatinib [2-4]. The exact mechanism is not fully understood yet is believed to be caused by their increased ability to target a wider range of kinases associated with hair follicles [5].

Numerous cutaneous adverse effects associated with TKIs exist. The most commonly reported ones include alopecia, dry skin, maculopapular rashes, pruritus, hair and skin depigmentation, and superficial edema [5]. Keratosis pilaris is not a common adverse skin reaction to nilotinib; Chang et al. [6] reviewed a total of ten cases of nilotinib-induced keratosis pilaris. In the study, all patients exhibited a generalized distribution of lesions, involving the face, extremities, and trunk, which was consistent with the current case. A recent review by Ambrogio et al. reported fifteen cases of keratosis pilaris-like eruption related to TKIs [2].

The rash is commonly asymptomatic [5]; however, some publications have reported its pruritic nature [2-4].

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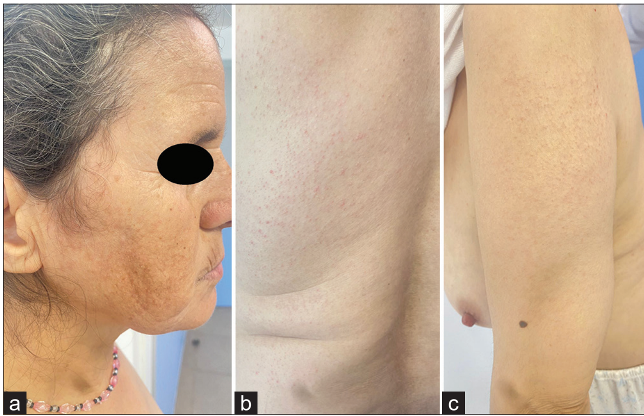

Figure 1: Multiple keratotic follicular papules on a) the face, b) back, and c) upper extremity.

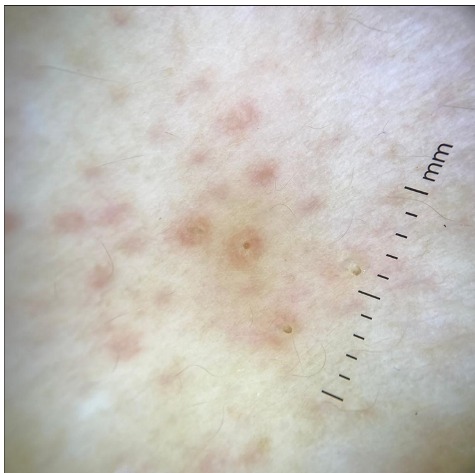

Figure 2: Dermoscopy of the affected area showing follicular hyperkeratosis with perifollicular erythema.

Associations with various conditions, including hair loss, perifollicular fibrosis, alopecia areata, non-scarring hair thinning, cicatricial alopecia, oral erosive lichen planus, and acne-like facial lesions, have been reported as case studies [4,7]. However, in our patient's case, the rash was not associated with any of these conditions.

There is no consensus regarding the management of these rashes [5]. Symptomatic treatment with emollients and keratolytic agents may be sufficient. Dermocorticoids were used with varying results [2]. In several reports, decreasing the dose of TKIs has shown significant improvements, while discontinuing them altogether has led to complete resolution [4]. However, some reports emphasize the importance of maintaining TKI therapy, as these cutaneous manifestations are frequently deemed mild and manageable, whereas the role of TKIs remains fundamental [7].

In general, the majority of cutaneous side effects with nilotinib are benign yet troublesome, specifically affecting the hair follicle. Nevertheless, care and caution should be exercised in the event of a cutaneous rash.

Consent

The patient examination was conducted according to the Declaration of Helsinki principles.

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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