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Nilotinib Induced Hypotrichosis - Rare Phenomenon - Case Report

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1. Introduction

Tyrosine kinase inhibitors [TKI's] in chronic myeloid leukemia has made once incurable disease without stem cell transplant to become like chronic disease like diabetes and hypertension. These agents having some of distressing adverse events due to long term duration of treatment. The cutaneous adverse events make the patient non sociable, depressing and having impact on quality of life. The second generation BCR-ABL TKI nilotinib implicated in multiple dermatological issues [1]. Here we are reporting a case of Nilotinib Induced thinning and loss of eyebrow hair in a chronic phase chronic myeloid leukemia patient.

2. Case Report

A 56-years-old gentleman was diagnosed as Chronic myeloid leukemia -chronic phase Sokal high risk in august 2017, in view of high risk Sokal score initiated on Tab Nilotinib 400 mg twice a day orally, having good drug compliance. After 8 months he noticed to have loss of his eye brow hair in association with thinning of eye lashes in association with body hair loss, Since he was asymptomatic he was advised to continue on same dose but patient had complaint of social issues we reduced the dose to 300 mg twice a day regimen and he had appropriate response for RT-PCR for BCR-ABL (FIG. 1 & 2).

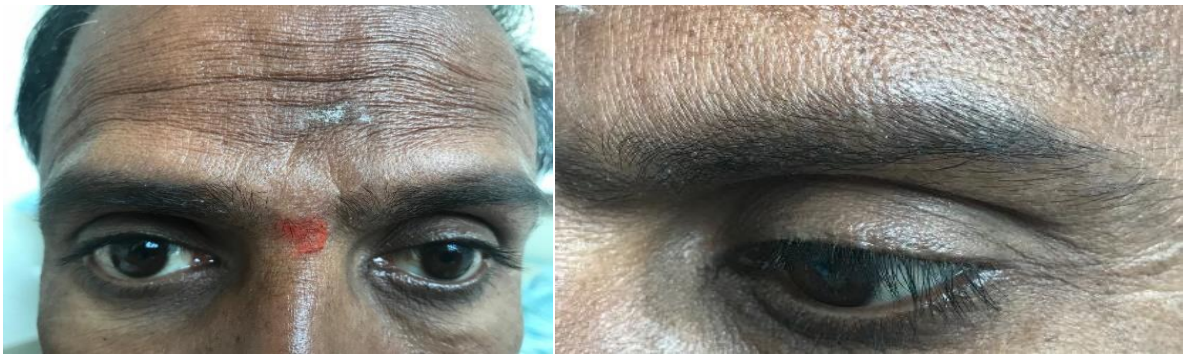

FIG. 1 **Before treatment.**

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FIG. 2. **While on treatment.**

3. Discussion

Newly developed tyrosine kinase inhibitors (TKIs) offer first-line alternatives to patients with chronic myeloid leukemia. However, these medications are generally well tolerated, cutaneous reactions occur frequently and can present a management challenge [2]. Cutaneous reactions to all three second generation TKI's [Nilotinib, Dasatinib and Ponatinib] were reported in 25%-34% of patients during treatment course [3].

Alopecia associated with EGFR TKIs has been well documented [4,5], but the clinical and histological characters of alopecia and hair thinning with multi-targeted TKIs are not well described in the literature [1].

A recent meta-analysis of the dermatological adverse effects seen with second generation TKI's highlighted specific pattern of eruptions, majority of dermatological events were mild grade, high grade were hardly 1.1%-2.6%, most commonly reported event was keratosis pilaris followed by lichen planus, among the hair related events thinning of hair was most commonly reported event [6].

A systematic review and meta-analysis shown that higher incidence of all grade rash in nilotinib (34.3%) compared to Dasatinib (23.4%), majority being low grade includes erythematous macules, papules and pruritus and alopecia not further characterized [6,7].

Timing of development of these dermatological events during time course was not documented clearly however most of case report mentioned in the literature it may develop in majority by 2 months after initiation [2], in our case eye brow hair thinning was started after 8 months.

In phase 1 clinical trials with nilotinib, alopecia was reported in about 6% of patients, however specific description of alopecia was not presented [8]. To best of our knowledge, this case report is first clinical description of nilotinib induced alopecia in India.

The literature on alopecia caused by multitargeted tyrosine kinase inhibitor is lacking, but similar binding sites [PDGFR and C-Kit] between Nilotinib, Sorafenib and Sunitinib suggest a similar mechanism responsible for alopecia [1]. Alopecia usually develop between weeks 3 and 15 of the treatment. Regrowth of hair was documented with continued treatment in some cases [9].

Nilotinib has been shown to interact with PDGFR as well as BCR-ABL, neither BCR-ABL gene activity nor inhibition has been linked to hair loss in literature. PDGFR shown to affect induction and maintenance of anagen phase in animal model [10]. Thus, PDGF inhibition significantly alters the hair follicle cycle toward shedding [1].

4. Conclusion

This case is the first detailed description of nilotinib induced alopecia from India, possibly implicated due to PDGFR inhibition. Alopecia causes cosmetic problems and social mobility restriction in these patients. Further investigations into the underlying mechanism of this event may produce more insight into the hair growth cycle and potential therapeutic targets.

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