Case Report

Nilotinib-induced Perforating Folliculitis: Two Cases

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ABSTRACT

Cutaneous adverse effects of chemotherapy are widely known but underreported. A significant advancement is made in the field of oncology with the advent of new classes of drug being added to the existing classes at a fast pace. Most of these cutaneous adverse effects are self-limiting and subsides on suspending the drug either temporarily or permanently. Some of these effects are merely overlooked by the patients and the treating physician hence goes un-noticed. Nilotinib is a newer second-generation tyrosine-kinase inhibitor approved for the management of chronic myeloid leukemia. This drug is rapidly establishing itself as a first-line therapy for chronic myeloid leukemia. Like other chemotherapeutic agents, a wide array of cutaneous adverse effects is noted with this drug. We report two cases of perforating folliculitis induced by nilotinib.

Key words: Collagen, nilotinib, perforating folliculitis

INTRODUCTION

Addition of tyrosine-kinase inhibitors in the armamentarium of chemotherapeutic agents has revolutionized the management of chronic myeloid leukemia (CML). Over last few decades, Imatinib has made a disease-free life, a possibility for many CML patients. Even with a promising and excellent profile of imatinib, issues such as resistance have surfaced, leading to active search of newer molecules in the same class, which culminated in the discovery of second-generation molecules such as nilotinib and dasatinib.

Nilotinib is an orally active, second-generation tyrosine-kinase inhibitor, approved as first-line therapy in the management of CML. It competitively and selectively binds to the specific amino acid residue in BCR-ABL protein which is 30 times more potent than imatinib.1,2

It is approved for treatment of newly diagnosed cases of Philadelphia chromosome-positive CML in both its chronic and accelerated phase. Over the years, nilotinib has established itself as a safe, well-tolerated, and effective therapy in patients resistant or intolerable to imatinib. However, like other chemotherapeutic agents, this drug is not devoid of its cutaneous adverse effects.

CASE REPORTS

Case 1

A 36-year-old male, a diagnosed case of CML in 2016, reported to our dermatology outpatient department (OPD) with complaints of multiple dark, raised, itchy lesions on body of 6-week duration. He gave a history of being treated with tablet nilotinib 300 mg twice a day 3 weeks before the onset of the lesions. There was no history of intake of any other medication, fever, any other underlying disorder, or photosensitivity. He was prescribed some topical antibiotics by a private practitioner for local application, to which he had minimal response.

His routine investigations were normal. Dermatological examination revealed multiple, polysized, folliculocentric, discrete erythematous to hyperpigmented papules and nodules distributed over both lower and upper body. He was treated with oral steroids and topical antibiotics, which gave minimal response.

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extremities and back, predominantly involving the extensor aspects [Figure 1]. Skin biopsy from a lesion on leg revealed a crater in the center of the lesion filled with parakeratotic keratin and neutrophil debris. The base of the crater showed break in the continuity of epidermis. Adjacent epidermis was thickened with compact hyperkeratosis. Strands of collagen were seen to project in the crater [Figures 2]. There was a degeneration of dermal connective tissue adjacent to the involved follicle.

**Case 2**

A 30-year-old male reported to our OPD with complaints of dark, raised lesions on both legs of 5 weeks’ duration. He gave a history of being treated for CML which was diagnosed 2 years back. Initially, he was managed with imatinib, to which he developed resistance, and hence he was switched over to tablet nilotinib 300 mg twice a day for the past 7 weeks. Two weeks after the intake of nilotinib, he noticed few dark, raised lesions on both the legs. He had no history of any drug allergy, fever, photosensitivity, or weight loss.

His systemic examination and routine investigations were unremarkable. Dermatological examination revealed multiple, folliculocentric, hyperpigmented papules and nodules on extensor aspect of both legs [Figure 3]. Biopsy from the lesion revealed shallow extrafollicular cup-shaped epidermal invagination filled with compact orthokeratosis, and dermis showed dense inflammatory infiltrate [Figure 4].

**DISCUSSION**

In 1968, Mehregan and Coskey described perforating folliculitis as a form of transepidermal elimination of dermal content. Transepidermal elimination is the term used for the phenomenon leading to extrusion of connective tissue or any foreign body to the external environment through epidermis. This entity is seen in conditions such as Kyrle’s disease, elastosis perforans serpiginosa, reactive perforating collagenosis, granuloma annulare, pseudoxanthoma elasticum, and necrobiosis lipoidica diabeticorum.[3,4]

Perforating folliculitis is usually associated with underlying conditions such as chronic renal failure, diabetes mellitus, Vitamin A deficiency, and human immunodeficiency virus. The association of drugs with perforating folliculitis is a rarely reported entity.

However, in terms of drugs causing perforating disorders and in particular perforating folliculitis, only a few drugs
have been reported so far, and hence, it is known to be a rare phenomenon. Drugs which are reported to be associated with perforating folliculitis include tumor necrosis factor-alpha inhibitors such as infliximab and etanercept,[5] sorafenib,[6] and bendamustine.[7] Nilotinib is a second-generation BCR-ABL tyrosine-kinase inhibitor which selectively and competitively binds to specific amino acid residue in BCR-ABL protein. The drug is approved for treatment of CML. Like other chemotherapeutic agents, nilotinib is also associated with a variety of adverse cutaneous adverse effects such as rashes, eczematous lesions, erythema nodosum, ecchymosis, and urticaria.

Nilotinib acts through inhibiting platelet-derived growth factor receptor, a kinase which has a role in the development of normal hair follicle. Perforating folliculitis can result as an effect of this inhibition.

We encountered these two patients, who were diagnosed cases of CML, on nilotinib 300 mg twice daily, who developed perforating folliculitis 2 weeks and 3 weeks of the therapy. Similar findings were observed by Llamas-Velasco et al. in their case.[8]

**CONCLUSION**

A wide variety of diseases are known to be associated with perforating folliculitis. Very few documented reports of perforating folliculitis have been published so far. Our finding is consistent with the observation of other authors. With the report, we want to highlight that nilotinib is also associated with perforating folliculitis.

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**Conflicts of interest**

There are no conflicts of interest.

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