Original Article

An After Effect Of Sorafenib Therapy- A Case Report

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Abstract

Sorafenib, a multikinase inhibitor, is FDA approved for the treatment of hepatocellular carcinoma (HCC), renal cell carcinoma (RCC) and thyroid carcinoma. Various adverse effects have been documented in patients taking standard sorafenib therapy. Out of which, hand-foot skin reaction (HFSR) is the most common cutaneous toxicity. Hand foot skin reaction presents with hyperkeratotic lesions with superficial blisters surrounded by peripheral erythema. It commonly affects the flexural surfaces of the digits and the pressure areas of palms and soles. The cutaneous side effects are dose dependent and are reported to occur in patients who are on a standard dose of 400 mg twice daily or more. But in our patient, it developed at a low dose (200 mg twice daily). Sorafenib-induced HFSR, though a dose dependent reversible reaction, has a significant impact on the quality of life. Hence prompt diagnosis and management at the earliest, can reduce the morbidity.

KEYWORDS: Adverse reactions, Carcinoma, Chemotherapy, Hand foot skin reaction

INTRODUCTION :

Sorafenib, a multikinase inhibitor, is widely used in the treatment of hepatocellular carcinoma (HCC), renal cell carcinoma (RCC) and thyroid carcinoma.[1][2][3] Various adverse effects have been documented in patients taking standard sorafenib therapy. Out of which, hand-foot skin reaction (HFSR) is the most common cutaneous toxicity. We report a case of HFSR in a patient with hepatocellular carcinoma taking sorafenib therapy at a lower dose of 200 mg twice daily.

CASE REPORT:

A 72-year-old male, who was a known case of diabetes mellitus, hypertension and recently diagnosed hepatocellular carcinoma was referred to the dermatology outpatient department with complaints of multiple painful lesions over both palms and soles for the past 4 days. It was associated with a burning sensation. History of inability to walk for the past 2 days. Initially, the patient experienced tingling and burning sensation over bilateral palms and soles, after which he developed multiple painful lesions which were interfering with his daily activities. He was on treatment with oral hypoglycemic agents and antihypertensive medications. There was no recent change in his routine medications. In view of hepatocellular carcinoma, he was prescribed Tab.Sorafenib 200 mg twice daily. After taking this medication for twenty days he developed painful lesions over both palms and soles.

On examination, there were hyperkeratotic tender plaques present over pressure bearing sites of bilateral soles, over right thumb, back of right index finger and ulnar border of left palm (Figure: 1). Palpable tender papular lesions over bilateral palms (Figure:1), lateral aspect of fingers and few vesicles scattered over bilateral soles were seen (Figure: 2). Hyperkeratotic tender plaque noted over the plantar aspect of great toe and over the base of ball of little toe (Figure: 2). Tender vesicles coalescing to form yellowish bullous lesions, surrounded by halo of erythema, present over bilateral soles on the medial aspect were present (Figure: 2). Other cutaneous examination was unremarkable. Routine blood investigations were within normal limits. Because of severe pain, patient was not willing for skin biopsy.

Based on the history and clinical findings, a diagnosis of hand foot Skin Reaction secondary to sorafenib was made. Our case was diagnosed as grade 3 hand foot skin reaction as per National Cancer Institute Common Terminology Criteria for Adverse Events v5.0 grading system.[4]

We advised the patient to stop Tab.Sorafenib 200mg. He was prescribed topical emollients and topical clobetasol propionate ointment 0.05% for palms and soles, twice a day for 10 days.

After 10 days, patient came for follow-up and the Patient was symptomatically better and the lesional sites showed desquamation and healing. (Figure: 3 & 4)

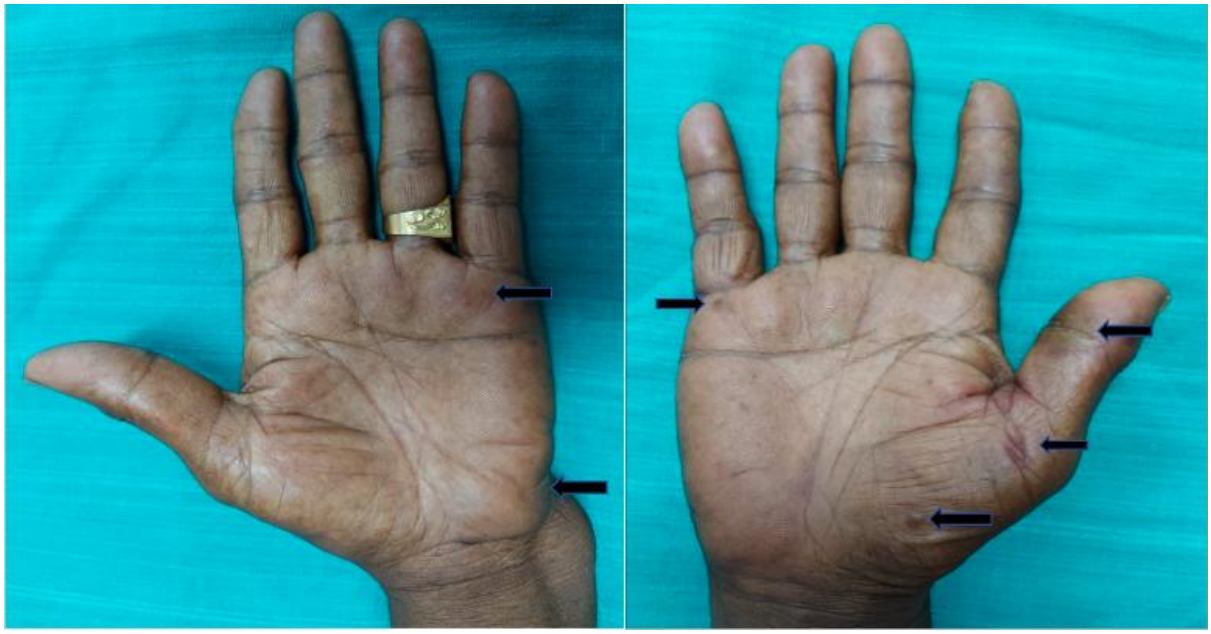

Figure: 1 - Hyperkeratotic tender plaques present over pressure bearing sites of bilateral soles, over right thumb, back of right index finger and ulnar border of left palm.
Palpable tender papular lesions over bilateral palms, lateral aspect of fingers.

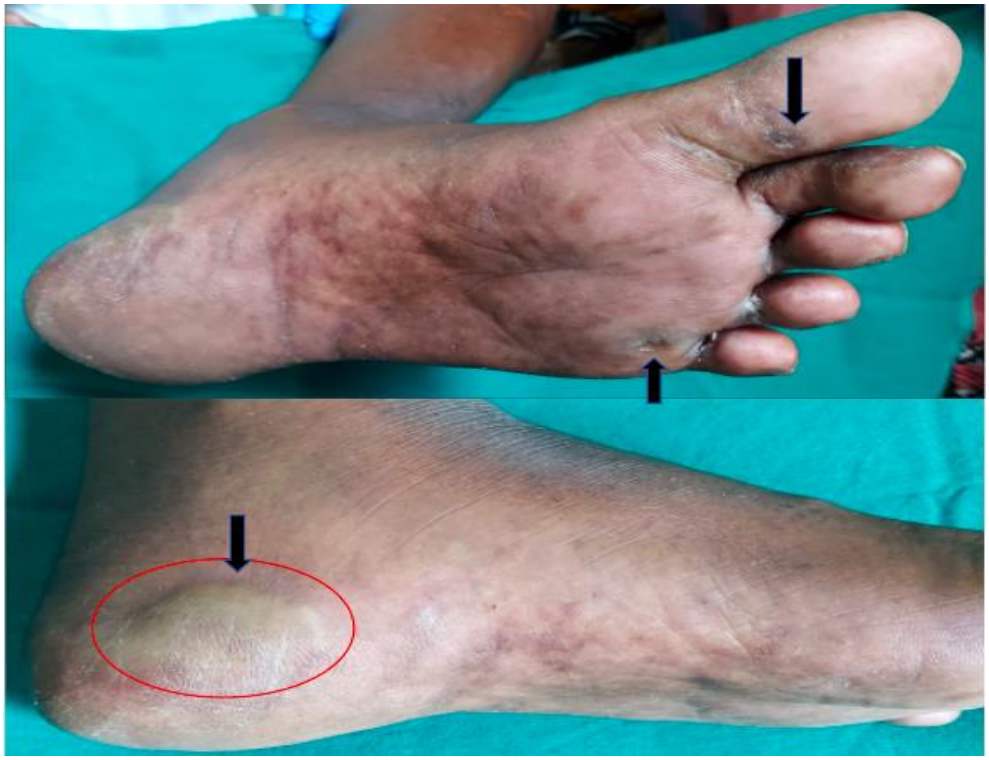

Figure : 2 - Palpable tender papular lesions and few vesicles scattered over bilateral soles were seen.

Hyperkeratotic tender plaque noted over the plantar aspect of great toe and over the base of ball of little toe.
Tender vesicles coalescing to form yellowish bullous lesions, surrounded by halo of erythema, present over bilateral soles on the medial aspect were present.

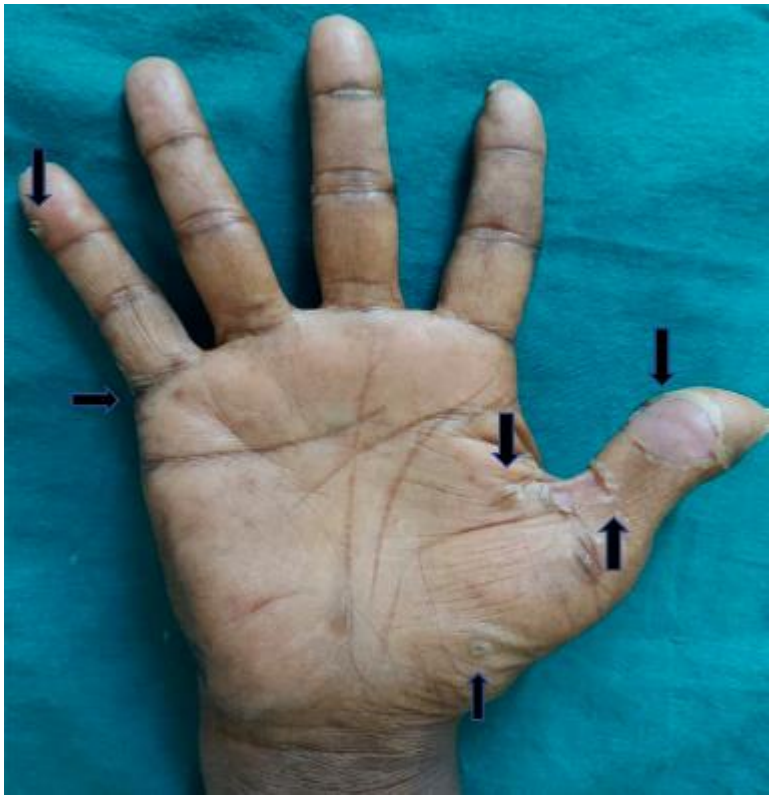

Figure : 3

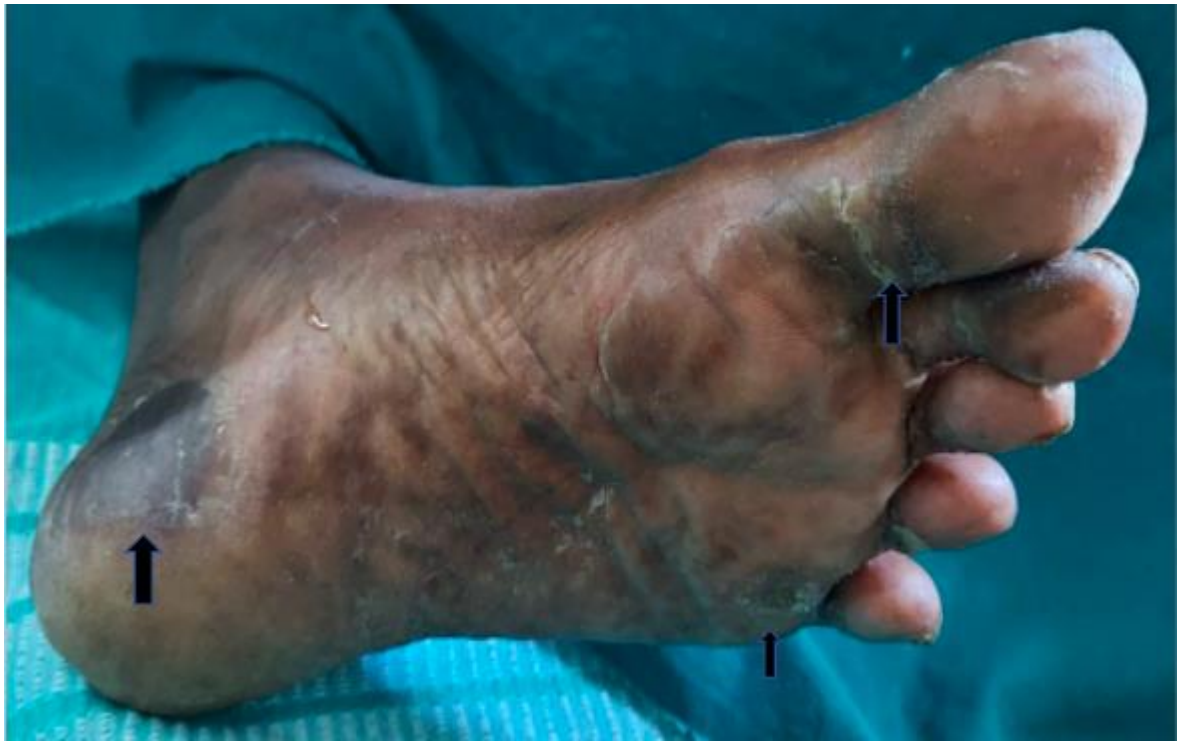

Figure : 4

Figure: 3 & 4 -After 10 days, patient came for follow-up and the Patient was symptomatically better and the lesional sites showed desquamation and healing.

DISCUSSION:

Sorafenib, a multikinase inhibitor with potent antiangiogenic, antiproliferative, and antineoplastic effects. It is used in the treatment of hepatocellular carcinoma, renal cell carcinoma, and thyroid carcinoma.[1][2][3] The most common side effects of sorafenib are fatigue, loss of appetite, weight loss, hand foot skin reaction and hypertension.[1] Hand foot skin reaction presents with hyperkeratotic lesions with superficial yellowish blisters surrounded by a peripheral halo of erythema.[1][2] It commonly affects the flexural surfaces of the digits and the pressure areas of palms and soles. It usually appears in the first 2-4 weeks of treatment.[2] The cutaneous side effects are dose dependent and is reported to occur in patients who are on a standard dose of 400 mg twice daily or more.[3] But in our patient, it developed at a low dose (200 mg twice daily). The most widely accepted theory for the causation of HFSR is inhibition of platelet-derived growth factor receptor (PDGFR) and c-KIT receptors on human keratinocytes. Being a tyrosine kinase inhibitor, it also affects vascular endothelial growth factor (VEGF), VEGF receptor (VEGFR), thus affecting the endothelium of the capillary vessels in the peripheral areas.[1] This leads to reactions in areas that undergo repeated high-pressure insult, such as palms and soles. The other dermatological side effects are rash/desquamation, alopecia, acne, flushing, xerosis, facial erythema, splinter subungual hemorrhages, keratoacanthomas and pruritus.[2] In case of first occurrence of hand foot skin reaction in a patient taking sorafenib, reduction in the dosage can be considered. Since our patient was already on a low dose, we advised the patient to stop the drug until he improves. In a case of grade 3 hand foot skin reaction, rechallenge of drug can be tried up to 3 times, beyond which recurrence of reactions mandates discontinuation of the drug.[1] This patient was also educated about the option of rechallenge of drug, but he was not willing at present. Trials have shown that ingestion of dried bonito broth one week prior to rechallenge can prevent hand foot skin reaction by maintaining blood flow.

CONCLUSION:

We report this case due to the occurrence of HFSR at a low dose (200 mg twice daily). Sorafenib-induced HFSR, though a dose dependent reversible reaction, has a significant impact on the quality of life. Hence prompt diagnosis and management at the earliest, can reduce the morbidity.

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