Case Report

A case report on sorafenib induced adverse reaction

Irfan M. G. Khan¹, Sunil K. Nayak²*, Divyasri G.², Abhinay K.², Srideep D.²

¹Department of Oncology/Hematology, Chalmeda Anandrao Institute of Medical Sciences (CAIMS), Cancer Hospital and Research Institute, Karimnagar, Telangana, India
²Department of Clinical Pharmacy, Vaageswari College of Pharmacy, Karimnagar, Telangana, India

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*Correspondence:
Dr. Sunil K. Nayak,
E-mail: bsunilkumarnayak99@gmail.com

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ABSTRACT

Sorafenib is an oral multi-kinase inhibitor used primarily in the treatment of hepatic cellular carcinoma, renal cell carcinoma, and thyroid carcinoma. Hand-foot syndrome also is known as palmar-plantar erythrodysesthesia causes reddening, numbness, swelling of palms of hands and soles of feet. In this report, a known case of renal cell carcinoma, post right nephrectomy patient on treatment with tab sorafenib had developed the hand-foot syndrome.

Keywords: Sorafenib, Hand-foot syndrome, Renal cell carcinoma, Hepatic cell carcinoma, Multi kinase inhibitor

INTRODUCTION

Sorafenib is an oral multi-kinase inhibitor, that prevents the tumor growth by inhibiting tumor cell proliferation and angiogenesis. Sorafenib is used for the treatment of advanced renal cell carcinoma, hepatic cellular carcinoma, and differentiated thyroid carcinoma.¹-³ Sometimes it is also used in the treatment of gastrointestinal stromal tumor (advanced or metastatic disease) after failing the treatment with imitinib and sunitib.

Sorafenib blocks the enzyme Raf kinases (serine/threonine proteins) that activates Raf/MEK/ERK (CRAF, BRAF), PDGF, EGFR, VEGF-R 2/3, SCFR, cKIT, FLT-3 signaling pathways that mediate the cell proliferation, differentiation, and transformation.⁴ Adverse effects of sorafenib include hypertension, rash/desquamation, hand-foot syndrome, alopecia, gastrointestinal disturbances. Other effects include neutropenia, thrombocytopenia, dry skin, weight loss, and headache.¹

Hand-foot syndrome of grade III or IV was observed in 5% of patients with hepatic cell carcinoma and 13% of patients with renal cell carcinoma. A toxic dose of sorafenib had not clearly demonstrated. Sorafenib of 800 mg twice daily primary results in diarrhea, dermatological reactions and grade III hypertension.⁵ Hand-foot syndrome is characterized by reddening, swelling, numbness, and desquamation of soles and palms.⁶

CASE REPORT

A 46 years old moderately built gentleman, farmer by occupation with no comorbidities was diagnosed as renal cell carcinoma (RCC), underwent right radical nephrectomy at a private kidney center in December 2017. A post-operative histopathological report was s/o “clear cell renal cell carcinoma (Fuhrmen) nuclear grade-III, the tumor was 7 cm in greatest diameter limited to kidney and capsular invasions found with no lymphovascular extensions. Renal vascular and uterine resection margins are free from tumor”. A CECT of left renal mass was s/o 7.3*4.7*6 size with no peripheric...
infiltrations of renal vein & IVC-potent. CECT-chest with IV contrast was s/o multiple walls defined hyperdense nodular lesions in bilateral lung fields which suggests the METASTASIS. All other blood counts (RFTs, LFTs, CBP) were within normal limits. Based on the above findings patient was staged T2aN1M1 (stage-IV). He was started on palliative chemotherapy with Tyrosine Kinase Inhibitor, Tab Sorafenib 400 mg per oral daily on an empty stomach.

Figures 1 (A and B): The planter erythrodysesthesia.

After completing cycle 1, A complete blood picture, liver function tests were done where neutrophils count showed 32% (ANC-1984), Eosinophils-13%, mild raised bilirubin levels (TB-1.4, DB-0.5). Cycle 3 was delayed by a week as the patient had complaints of itching over the abdomen and generalized weakness. In view of these skin rashes, symptomatic treatment was given and the dose of Sorafenib was reduced to 200 mg. In spite of dose reduction patient developed grade III hand foot syndrome when he arrived for cycle 4 as seen in Figure 1.

He was prescribed moisturizing cream composed of urea, lactic acid, propylene glycol, and light liquid paraffin to apply locally 3-4 times a day, anti-histamine, Fexofenadine 180 mg, and an antidepressant, Zolpidem 10 mg orally was added as the patient was uncomfortable and depressed. Further medical oncologist consultation was sought, the reaction was non-fatal and was advised to continue Tab Sorafenib at a still lower dose of 200 mg alternate days for cycle 4 and if the symptoms subside, to continue with the same dose for cycle 5 or otherwise to stop and plan an alternative treatment.

For cycle 5, the patient felt better and same modified dose of Tab Sorafenib 200mg for alternate days was continued. During his visit for cycle 6, upon location examination (skin) - bilateral dry, scaly, plaques acne like mild lesions noted over both the lower limb extending from foot to lower third of leg (better compared to previous observations (Eosinophils-09%) and was advised to continue the same treatment. On subsequent cycles, patient was feeling better as lesions started disappearing, however, he had complaints of mild itching over lower limbs (Eosinophils-07%).

Causality assessment was done using Naranjo’s causality assessment scale. The algorithms showed that Sorafenib was the “definite” (score-11) cause of these adverse reactions. Severity assessment was done using Hartwig’s scale and was categorized as “moderately severe” (level-3).

DISCUSSION

Hand-foot syndrome (also known as palmar-plantar erythrodysesthesia) is the most common adverse effects manifested by Tab Sorafenib in most of the patients. Exposure of hands and feet to heat as well as friction increases the amount of drug in the capillaries. A small quantity of drug leak out of the capillaries into the palms of the hands and the soles of the feet, this leakage results in redness, swelling, tenderness, pain, blisters and possibly peeling of the palms and soles. Dose reduction and delays in the treatment are recommended if symptoms do not relieve. Vitamin-B6 (pyridoxine) which was used as the prophylaxis as treatment is no longer recommended now. HFS which is also seen as an adverse effect with other drugs such as IV 5-fluorouracil, oral Capecetibine etc. As an oncology Clinical pharmacist, prior information about the adverse reaction shall be informed to the patients so that they don't panic. Also, patient counseling regarding the non-pharmacological aspects of the treatment shall be discussed after the drug exposure and ADR. Limit daily activities to reduce friction and heat exposure to hands and feet for one week after IV 5FU or during the duration of oral exposure to capecitabine. Avoid long exposure to hot water, washing dishes, showers instead advised taking short showers in tepid water. To avoid the use of dishwashing gloves as the rubber will hold in the heat. Avoid jogging, aerobics, walking, jumping as it increases the pressure on the soles of feet. Not to use garden tools, screwdrivers, knives for chopping or performing other tasks that require squeezing hands on a hard surface as it increases the pressure on the palms of the hands.

Cooling procedures provide temporary relief of pain and tenderness. Using cold compresses like ice packs or frozen vegetables may reduce the severity of pain (alternate cold packs on & off for 15-20 minutes at a time). Emollients such as Petrolatum, Udderly smooth cream, and Bag Balm provide excellent moisturizing for hands and feet; lotions don't provide adequate protection. Corticosteroids and pain medications may be used to help alleviate inflammation and pain.

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