National Journal of Physiology, Pharmacy and Pharmacology

CASE REPORT

Sorafenib-induced dermatologic Grade III toxicity: An important clinical manifestation

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Received: July 07, 2017; **Accepted:** July 25, 2017

ABSTRACT

Sorafenib is an oral multikinase inhibitor used as a palliative intent for advanced hepatocellular carcinoma (HCC). Dermatologic toxicity is the main adverse effect limiting its use in many patients. However, Grade III dermatologic toxicity is rarely seen with low-dose sorafenib administration. Here, we discuss the case of a 72-year-old male patient who was treated with sorafenib 400 mg for HCC. After 18 days of administration, the patient complained of intense pain with blisters and ulcerations. The drug was discontinued, and topical corticosteroids and analgesics were given for the management. Review of the patient's medication did not reveal the presence of any other possible drugs capable of producing dermatological toxicity.

KEY WORDS: Hepatocellular carcinoma; Sorafenib; Barcelona Clinic Liver Cancer Staging; Transarterial Chemoembolization

INTRODUCTION

Cirrhosis is the major cause for hepatocellular carcinoma (HCC), irrespective of its etiology. HCC is the fifth leading carcinoma in the world and third major cancer responsible for death.[1] In the past, HCC was diagnosed at an advanced stage. Now, patients diagnosed with cirrhosis are followed up every 6 months with ultrasonogram and serum alpha fetoprotein for the early detection and treatment of HCC. Patients diagnosed with HCC are then staged to understand the extent of tumor and assess the liver function.[2,3] There are various stagings available such as Okuda score, Barcelona Clinic Liver Cancer (BCLC) staging classification, Japan Integrated Staging, Chinese university prognostic index, and cancer of the liver Italian program score. However, BCLC staging is preferred for decision-making by many clinicians for treating complicated cancers using current data.[4]

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2018.8.0725025072017	

Sorafenib is an oral tyrosine kinase inhibitor approved by the Food and Drug Administration for its use in treating advanced renal cell carcinoma (resurgical treatment),[5,6] thyroid cancer,[7] and unresectable HCC.[8] Sorafenib acts by inhibiting growth of tumor and angiogenesis by inhibiting cell surface kinase receptors and intracellular Raf kinases (RAF/MEK/ERK, vascular endothelial growth factor receptor, and platelet-derived growth factor receptor).[9,10] Hand-foot skin reaction is the common adverse effect seen in patients who are on sorafenib. These reactions are toxic and dose-dependent reactions.[11]

CASE REPORT

A 72-year-old male who is a known case of chronic liver disease and type 2 diabetes mellitus was found to have space occupying lesions in the ultrasonogram. He underwent multiphase dynamic computed tomography abdomen multiphase with contrast was done which showed a segment 8 lesion consistent with HCC for which transarterial chemoembolization (TACE) was done multiple times over 3 years and the patient was on regular follow-up.

The patient's Child Pugh Score was A, and alpha fetoprotein AFP was 9.16 ng/ml. His BCLC staging was B for which he was on ursodeoxycholic acid tablet 300 mg BD, propranolol tablet 20 mg BD, Vitamin B complex tablet OD, rifaximin tablet 400 mg TID, and lactulose syrup at night for chronic liver disease and glimepiride tablet 2 mg BD for diabetes mellitus. He underwent TACE 3 years back and was on regular follow-up. During his follow-up, he was detected to have residual HCC on routine screening after a repeat CT showed multiple subcentimetric lesions in segment III, V, and VII. In view of child Pugh score B status of disease and multifocal HCC with BCLC stage C, TACE could not be done. Hence, the patient was started on oral sorafenib 200 mg BD with palliative intent. The patient took the medications for 18 days and developed painful multiple ulcers and blisters (Grade III: Dermatologic toxicity) on his leg, and sorafenib was stopped and no rechallenge was initiated. He was managed using topical corticosteroids and analgesics following which his symptoms subsided after 6 days.

DISCUSSION

Sorafenib is an oral multikinase inhibitor that limits tumor growth and angiogenesis by targeting two key pathways that are important for the progression of HCC.[8,9] According to BCLC staging treatment schedule, patients diagnosed with BCLC Stage A undergo hepatic resection/ablation can be the various treatment modalities of treatment; however, BCLC Stage B patients-TACE is the treatment option and advanced tumors with BCLC Stage C palliative therapy such as sorafenib or other oral tyrosine kinase inhibitors are the treatment options.[4]

A prospective single-center phase II study done on unresectable HCC found that sorafenib and DEB-TACE combination therapy modalities were well tolerated and safe among these patients.[12] Even though sorafenib is well tolerated in advanced HCC patients, our patient developed painful Grade III dermatologic toxicity over the feet and palm in spite of administering lower doses, and the occurrence of Grade III toxicity is comparatively low. The most commonly reported adverse drug reaction in these category of drugs is hand-foot skin reaction, diarrhea, nausea, elevated lipases, etc.[10] Therefore, physicians should educate patients regarding the possible adverse events associated with sorafenib use. There are evidence suggesting prophylactic use of pyridoxine for hand-foot skin reactions.[13] These skin reactions can be managed by the use of moisturizers, corticosteroids, and keratolytics (salicylic acid).[14]

CONCLUSION

Sorafenib is prescribed to patients who cannot be managed with conventional treatment modalities for HCC like TACE, RFA as a palliative treatment. Dermatologic toxicity due to sorafenib can be managed by lowering doses or by discontinuing the drug and by use of topical agents.

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How to cite this article: Kumar NM, Sreelatha P, Sadasivan S, Jain A, Anila KN. Sorafenib-induced dermatologic Grade III toxicity: An important clinical manifestation. Natl J Physiol Pharm Pharmacol 2018;8(1):144-145.

Source of Support: Nil, **Conflict of Interest:** None declared.