Inhabituel Toxicity of Sorafenib: Eryhema Multiform: A New Case Report and Review
Lamia Aalaoui1*, Anouar Mokhlis1, Mohamed Reda Khmamouche1, RachidTanz1, Hassan Errihani2, Mohamed Ichou1

1Medical Oncology Department, Military Hospital Mohammed V, Rabat, Morocco
2Medical Oncology Department, National Institute of Oncology Sidi Mohamed Ben Abdellah, Rabat, Morocco

DOI: 10.36347/sjmc.2021.20.02.10 | Received: 29.12.2021 | Accepted: 08.02.2022 | Published: 13.02.2022

*Corresponding author: Lamia Aalaoui
Medical Oncology Department, Military Hospital Mohammed V, Rabat, Morocco

Abstract
Sorafenib, an oral small molecule multikinase inhibitor indicated for the treatment of some solid tumors, has been associated with a variety of cutaneous adverse events. Erythema multiforme is one of the extremely rare skin toxicities reported. We present this interesting case to show and discuss the cutaneous side effects of sorafenib, in particular the erythema multiforme that occurred in a woman treated for metastatic hepatocellular cancer after only five days of treatment.

Keywords: Sorafenib, skin side effect, erythema multiforme.

Copyright © 2022 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION
Sorafenib is the first multi-kinase inhibitor (TKI) approved for the treatment of advanced hepatocellular cancer (HCC) and metastatic renal cell cancer (RCC). It also has a place in well-differentiated, iodine-resistant thyroid cancer (DTC) [1]. Sorafenib continues to be used as a first-line treatment for hepatocellular carcinoma despite the advent of immunotherapy [2].

Dermatological side effects are quite common and non-specific such as hand-foot syndrome, skin xerosis, facial and scalp erythema. Erythema multiforme (EM) is a rare and severe skin reaction that has been described [3].

CASE REPORT
Our patient is 60-year-old woman, with no medical history and no drug allergies, she is followed in our training for non-operable hepatocellular carcinoma Child A. The patient was put on first-line sorafenib chemotherapy at the optimal daily dose of 800 mg, two hours after the meal. On the fifth day after the start of treatment, the patient developed extensive erythematous papules, plaques on the back (Figure 1) and bilateral lower extremities. The patient was diagnosed with erythema multiforme by the dermatologist and treatment with sorafenib was discontinued.

The rash resolved within 3 weeks after discontinuation of sorafenib and administration of topical treatment with steroids and antihistamines (Figure 2).

Figure 1: Skin eruptions in the back at day 5 of sorafenib treatment
DISCUSSION

Sorafenib is an oral small-molecule multi-kinase inhibitor that targets vascular endothelial growth factor receptors (VEGFR) 2 and 3, platelet-derived growth factor receptor (PDGFR), rearranged during transfection (RET), FMS-like tyrosine kinase 3 (FLT3), c-KIT, and C- and B-RAF [3].

It is the first multi-kinase inhibitor (TKI) approved for the treatment of advanced hepatocellular cancer (HCC) and metastatic renal cell cancer (RCC). It also indicated in well-differentiated, iodine-resistant thyroid cancer (DTC) [1].

Although sorafenib has demonstrated many benefits in patients, adverse effects cannot be ignored. The most common side effects of this drug are diarrhea, fatigue, hand-foot skin reaction, and hypertension [4]. Most of these toxicities are considered mild to moderate and manageable to varying degrees; however, skin reactions may lead to dose reduction or outright discontinuation of treatment despite its effectiveness.

The most cutaneous side effects of sorafenib are: Rash, Hand and foot syndrome reaction (HFSR), exfoliative dermatitis, acne, edema, subungual splinter hemorrhages, facial and scalp eruptions, and flushing.

Folliculitis, eczema, and erythema multiforme (EM) are rarely seen cutaneous reactions [1, 5].

The first case of sorafenib-induced EM was reported by MacGregor and et al., in 2007, in a patient with metastatic melanoma on sorafenib who presented with generalized tender erythematous papules and plaques with dark or pseudo vesicular centers on the trunk, extremities, palms and soles, and even on the face [6].

The second case report was published two years later in a 59-year-old man treated with sorafenib for renal cell carcinoma [5]. Subsequently, other clinical cases have been reported in the literature.

Histologically, it corresponds to liquefaction degeneration in the epidermis and edema in the upper dermis with an infiltrate of lymphocytes and eosinophils [7].

In many cases, however, it is difficult to define which mechanism plays a major role in sorafenib induced EM [8]. The most skin side effects induced by sorafenib are dose dependent and disappear with discontinuation of the treatment [7].

CONCLUSION

Erythema multiforme induced by Sorafenib is a rarely occurring cutaneous adverse event. Patients should be educated to avoid cutaneous adverse events after the treatment’s initiation by this small molecule. This side effect is dose dependent and disappear with discontinuation of the treatment and corticosteroids topics.

Declaration of Interest: The authors report no conflicts of interest.

BIBLIOGRAPHY

1. Autier, J., Escudier, B., Wechslcr, J., Spatz, A., & Robert, C. (2008). Prospective study of the cutaneous adverse effects of sorafenib, a novel multi-kinase inhibitor. Archives of dermatology, 144(7), 886-892.
2. Tang, W., Chen, Z., Zhang, W., Cheng, Y., Zhang, B., Wu, F., ... & Wang, X. (2020). The mechanisms of sorafenib resistance in hepatocellular carcinoma: theoretical basis and therapeutic aspects. Signal transduction and targeted therapy, 5(1), 1-15.
3. Pichard, D. C., Cardones, A. R., Chu, E. Y., Dahut, W. L., & Kong, H. H. (2016). Sorafenib-induced eruption mimicking erythema multiforme. JAMA dermatology, 152(2), 227-228.
4. Ikeda, M., Fujita, T., Mii, S., Tanabe, K. I., Tabata, K. I., Matsumoto, K., ... & Iwamura, M. (2012). Erythema multiforme induced by sorafenib for metastatic renal cell carcinoma. Japanese Journal of Clinical Oncology, 42(9), 820-824.
5. Bilaç, C., Muezzinoglu, T., Ermentcan, A. T., Kayhan, T. C., Temeltaş, G., Öztürkcan, S., & Temiz, P. (2009). Sorafenib-induced erythema multiforme in metastatic renal cell carcinoma. Cutaneous and ocular toxicology, 28(2), 90-92.
6. MacGregor, J. L., Silvers, D. N., Grossman, M. E., & Sherman, W. H. (2007). Sorafenib-induced erythema multiforme. Journal of the American Academy of Dermatology, 56(3), 527-528.
7. Namba, M., Tsunemi, Y., & Kawashima, M. (2012). Sorafenib-induced erythema multiforme: three cases. European Journal of Dermatology, 21(6), 1015-1016.
8. Kodaira, M., Takahashi, S., Takeuchi, K., Yuasa, T., Saotome, T., Yonese, J., ... & Hatake, K. (2010). Sorafenib-induced erythema multiforme for metastatic renal cell carcinoma. Annals of oncology, 21(7), 1563-1565.