

Inhabituel Toxicity of Sorafenib: Eryhema Multiform: A New Case Report and Review

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Abstract

Case Report

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.

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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



Figure 2: Favorable evolution of the eruption after three weeks of treatment by steroids and antihistaminic

DISCUSSION

Sorafenib is an oral small-molecule multikinase 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].

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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.

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