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Sorafenib inducingerythema multiforme: a new case report and review

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ABSTRACT

Sorafenib, an oral small-molecule multikinase inhibitor used in the treatment of some solid tumors is associated with a various adverse skin reactions. Erythema multiforme is a very rare cutaneous side effect induced by this drug. We present this new interesting case to show and discuss cutaneous side effects of sorafenib,
especially erythema multiforme in a women who presented a metastatic medullary carcinoma of thyroid after 8days of treatment initiation.

Keywords: Sorafenib, side effect, skin, erythema multiforme

I. INTRODUCTION

Sorafenib is an oral small-moleculemultikinase inhibitor that used forthe treatment of advanced renal cell carcinoma, unresectablehepatocellular carcinoma,andradioactive iodine–resistant, advanced,differentiated thyroid carcinoma**(1).**The use ofsorafenib in the treatment of metastatic medullary thyroid cancer was limited to a few phase 2 studies**(2).**Cutaneous adverse events of this drug were observed frequently and it affect up to 90%of patients**.**Commonlyreported eruptions include nonspecific rash andhand-foot skin reactions.Erythemamultiforme (EM)is a rare and severe skin reaction which been described**(3)**

II. CASE REPORT

A 73-year-old female without past medical history especially without drug allergics, presented to our institution with lymphatic and liver metastases of medullary thyroid carcinoma. The patient receivedtreatment by sorafenib.She takes two tablets of 200 mg twice daily equivalent to 800 mg a total daily dose two hours after the meal .At day 8 after initiation therapy with this drug, the patient developed erythematous papules and plaques in the back, and bilateral upper and lower limbs.**(Figure 1)**. Erythema spread over his whole body. The patient was clinically diagnosed witherythema multiforme andsorafenib treatment was withheld.

Eruption decreased within 3 weeks after discontinuation of sorafenib and topicaltreatment with steroid and antihistaminic. **(Figure 2)**

III. DISCUSSION :

Sorafenib is an oral small-moleculemultikinase inhibitor that targets vascular endothelial growth factor receptors (VEGFR) 2 and 3, platelet-derivedgrowth factor receptor (PDGFR), rearranged during transfection (RET), FMS-like tyrosine kinase 3 (FLT3), c-KIT, and C- andB-RAF**(3).**It is currently approved for the treatmentof solid tumors such as advanced renal cell cancer, hepatocellular carcinoma, melanoma and thyroid cancers**(4,5).**

As with other antineoplastic agents, sorafenib is associated with various toxicities, including hypertension, diarrhea, anorexia, fatigue and skin toxicities**(6).**

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 **(1,7).**MacGregorand al. reported the first case of EM induced by sorafenib in the literature in 2007 **(8)** . He described EM in a women patientwith metastatic melanoma on sorafenibas generalized tender erythematous papules and plaques with dusky or pseudovesiculararcenters over her face, trunk, extremities, palms, and soles**(8).** The second case

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report was published in 2009 in a 59 year- old men treated with sorafenib for renal cell carcinoma **(7).**Other clinical cases have been reported in the literature.

Histological examination of the skin specimens found liquefaction degeneration in the epidermis, infiltrate of lymphocytes and eosinophils and edema in the upper dermis**. (9)**

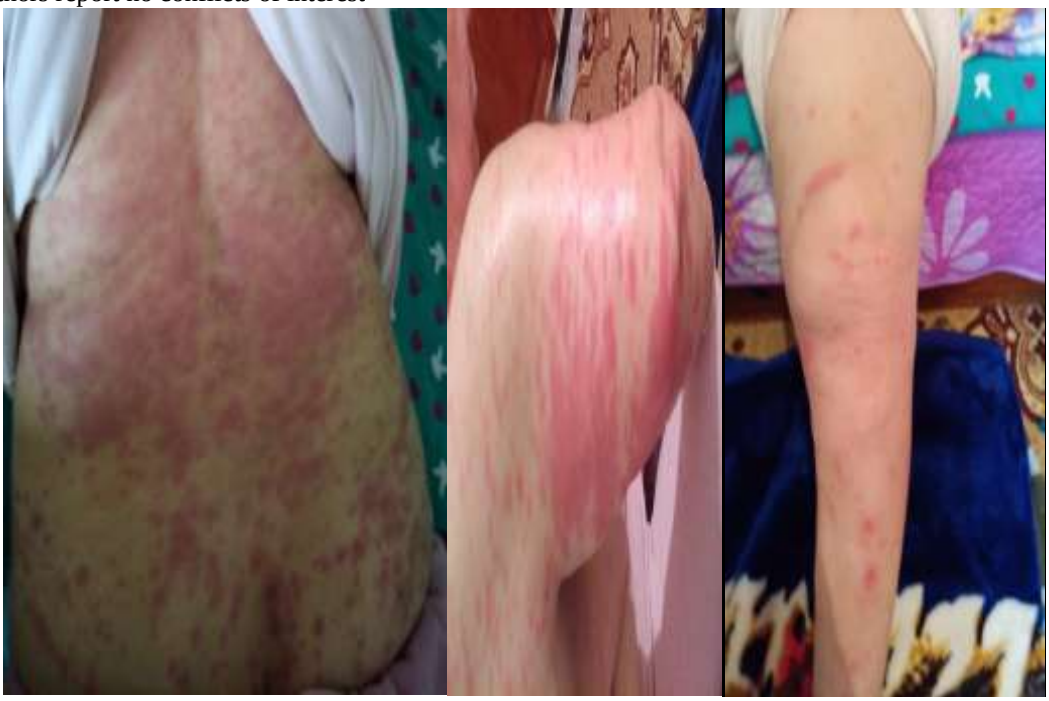
Erythema multiform secondary tosorafenib can be caused by the dose-dependent pharmacological action, like the hand-and-foot syndrome because reduction of the dose did not lead to eruption in some cases.In other cases, reduces doses also induced this skin reaction suggestingthat the underlying mechanism is allergy which needs sensitization. In many cases, however, it is difficult to define which mechanism plays a major role in sorafenibinduced

EM **(9).**Further investigations are necessary to disclose themechanism and establish the effective therapy for sorafenib induced EM, which might not be a rare adverse event particularly inJapanese patients**. (10)**.The most cutaneous side effects induced by sorafenib are dose dependent and disappear with discontinuation of the treatment. In most cases,restart with the same dose is possible and the symptoms may resolve without dose modification**(10)**

In conclusion, sorafenib may be use safety and carefully in clinical practice of oncologists, and patients should be educated on the possibility of skin drug reactions upon initiation of sorafenib treatment.

Declaration of interest:

The authors report no conflicts of interest



A **B** **C**

Figure 1:Skin eruptions in the back (A) in upper limb (B) and lower limb (C) ,at day 8 of sorafenib treatment

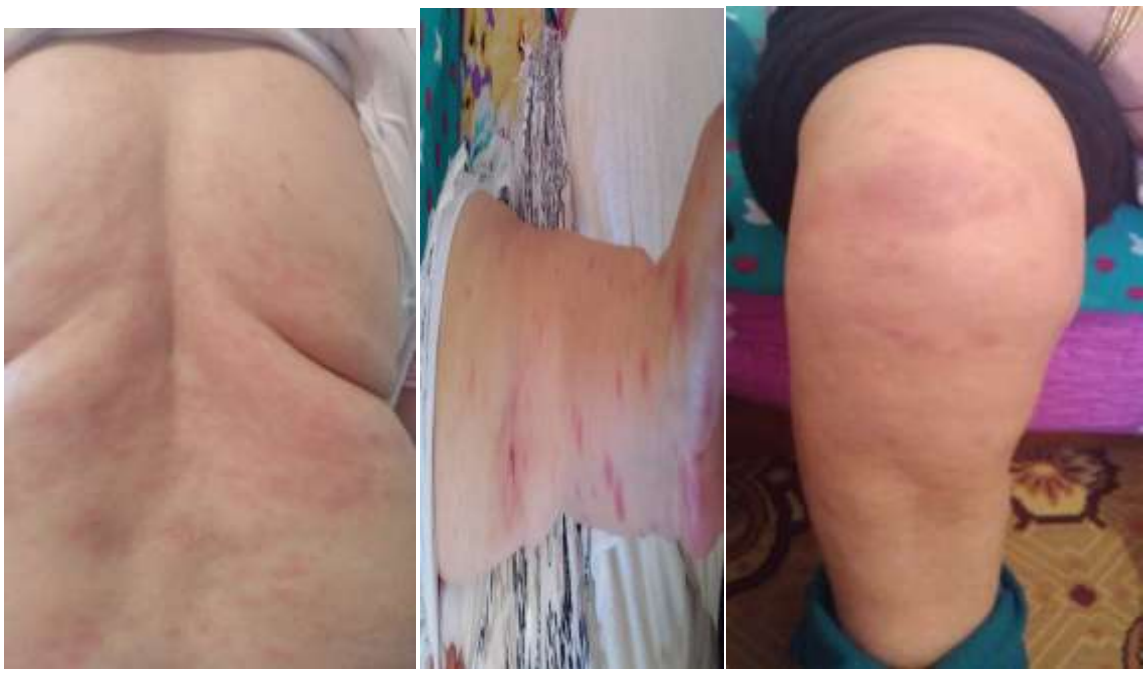


Figure2: favorable evolution of the eruption after three weeks of treatment by streoids and antihistaminic

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