Sorafenib-Associated Psoriasiform Eruption in a Patient With Hepatocellular Carcinoma

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As the use of new chemotherapeutic agents becomes more common, the associated side effects increase. Sorafenib tosylate (Nexavar® tablets, Bayer Healthcare Pharmaceuticals Inc.) is approved for use in the treatment of unresectable hepatocellular carcinoma (HCC), advanced renal cell carcinoma, and locally recurrent or metastatic, progressive, differentiated thyroid carcinoma refractory to radioactive iodine treatment. It inhibits tyrosine kinase receptors such as vascular endothelial growth factor, platelet-derived growth factor, cKit, and Raf kinases. Although some cutaneous side effects of sorafenib are well described, a possible association of psoriasiform eruption and sorafenib has been reported more recently.[1-6] We present herein another patient who developed cutaneous psoriatic lesions following sorafenib therapy.

A 69-year-old man with a history of HCC presented to our dermatology clinic with a complaint of scaly erythematous lesions on the trunk and extremities. He had a 40-year history of stable mild-to-moderate localized plaque-type psoriasis that was in remission for at least 10 years. After surgical resection of HCC, sorafenib (400 mg twice daily orally) was initiated due to the lung metastases. Ten days after the drug was started, scaly erythematous papules developed on his elbows. A skin biopsy showed confluent parakeratosis, hypogranulosis, suprapapiller thinning, psoriasiform hyperplasia, and proliferating congested capillaries in elevated papilla. These changes are all consistent with classical psoriasis. Then, discontinuation of sorafenib for one month was recommended by the Department of Oncology. When drug was taken again, multiple guttate erythematous papules and plaques scattered gradually over his trunk, knees, and arms (Figure 1). Biopsy taken from a femoral papule showed confluent parakeratosis, hypogranulosis, Munro microabscesses, intraspinous neutrophils, suprapapiller thinning of epidermis, and psoriasiform epidermal hyperplasia, a few necrotic keratinocytes, as well as superficial perivascular lymphocytes and many eosinophils in the dermis (Figure 2). His lesions improved significantly two weeks after treatment with clobetasol 17-propionate ointment and narrow-band UVB phototherapy, while sorafenib was discontinued.

FIGURE 1. Multiple psoriasiform papules and plaques, mainly of the guttate type, on the arms.

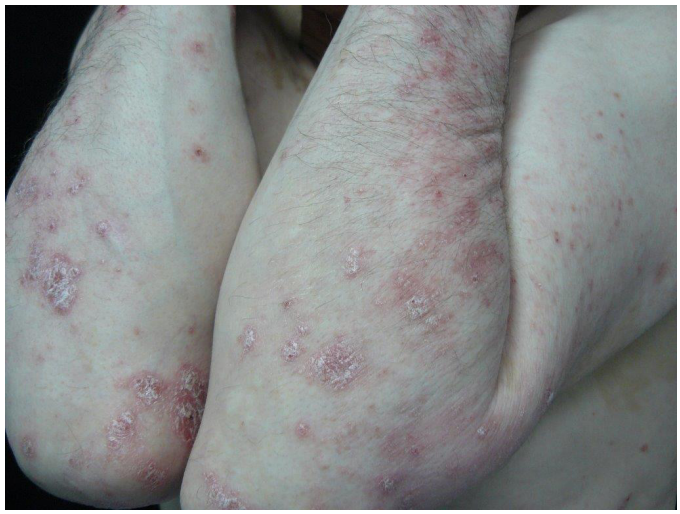
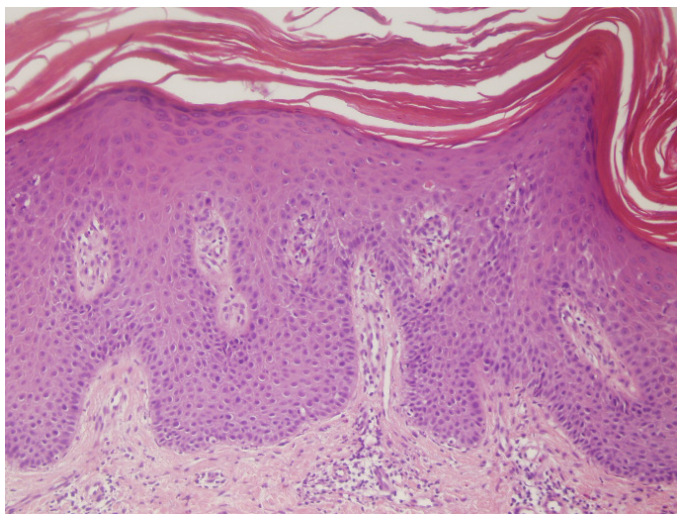


FIGURE 2. Irregular epidermal psoriasiform hyperplasia, confluent parakeratosis, a few necrotic keratinocytes, and dermal perivascular eosinophil leucocytes (original magnification X20 HE).



Sorafenib is usually well tolerated, however, various cutaneous side effects including hand-foot skin reaction, facial erythema, acral erythema, alopecia, xerosis, a non-specific exanthem, stomatitis, and subungual splinter hemorrhages have been frequently reported. Less commonly, multiple squamous cell carcinoma, keratoacanthoma, eruptive melanocytic lesions, and epidermoid cysts have also been described. Even though cutaneous toxicities are not usually life threatening, they may lead to dose modification or discontinuation of critical antineoplastic therapy. On the other hand, a recent study indicated that patients with sorafenib-related cutaneous reactions might be associated with a good survival prognosis in HCC, and therefore early identification and management of these reactions might be critical for continuing sorafenib therapy.[7]

To our knowledge, there have been only a few reported cases of psoriasiform eruption associated with sorafenib therapy.[1-6] Although drug-induced psoriasiform eruptions are indistinguishable from idiopathic psoriasis, they may be differentiated histologically by the absence of tortuous capillaries in the dermal papillae associated with suprapapillary thinning, and presence of eosinophils around the blood vessels of the superficial plexus.[8] While the second biopsy taken from our case was consistent with psoriasiform drug eruption, we cannot definitively determine if the patient's elbow lesions were due to a sorefanib-induced psoriasis exacerbation or psoriasiform drug eruption. However, he reported a direct correlation between starting sorefanib and appearence of elbow lesions.

The pathogenesis of sorefanib induced psoriasis remains obscure, but the presence of dysfunctional CD4+CD25+ immunosuppressive regulatory T cells leading to an imbalance between regulatory and effector T-cell functions in patients with psoriasis has been hypothesized to play an important role. It has been suspected that tyrosine kinase inhibitors including sorafenib may block the signal transduction pathways in both regulatory and effector T cells.[4] It has been also suggested that sorafenib might alter the keratinocyte proliferation and differentiation by a yet unknown mechanism.[3]

Actually, the occurrence of psoriasiform eruptions in patients associated with sorafenib seems paradoxical. In recent trials, the spectrum of diseases in which kinase inhibitors are used has increasingly expanded to include immune-mediated diseases. It was proposed that blocking kinases may be an effective way to inhibit immune cell activation and abnormal epidermal angiogenesis, involved in the pathogenesis of psoriasis. To this respect, a patient with metastatic hypernephroma and concomitant recalcitrant psoriasis who responded well to sorafenib has been reported.[9] More recently, novel protein kinase inhibitors are also under clinical investigation based on this hypothesis for treatment of psoriasis.[10]

Consequently, the pathogenesis of sorafenib-induced psoriasiform eruptions is difficult to explain. Further molecular investigations exploring the connection between sorafenib and psoriasis may increase our understanding of this issue.

Disclosure

None of the authors have declared any relevant conflicts.

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