CASE REPORT

Psoriasis flare-ups following sorafenib therapy: A rare case

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Introduction

As the use of targeted therapies has expanded dramatically, the associated cutaneous side effects have also increased and they negatively impact patients' quality of life. While various dermatologic side effects of sorafenib have been reported, sorafenib-induced psoriasiform eruption, however, is extremely rare. Here, we describe a case of psoriasis flare-ups following sorafenib therapy.

Case Report

A 68-year-old Taiwanese male with a history of chronic hepatitis type B, liver cirrhosis, and hepatocellular carcinoma (HCC) presented to our dermatology clinic with a complaint of painful skin eruption on the trunk, buttocks, and lower limbs. He also had a previous 4-year history of mild, localized plaque-type psoriasis that had been in remission for at least 40 years. After palliative treatment with transarterial chemoembolization, sorafenib (200 mg once daily) was initiated for HCC with pulmonary metastasis. Two months later, numerous sharply demarcated, scaly erythematous papules and plaques with painful sensation developed on the trunk, buttocks, and extremities (Figure 1). On admission, the patient was afebrile with normal vitals and declared no other simultaneous medication that was likely to exacerbate the psoriasis.

Skin biopsy revealed focal parakeratosis, Munro microabscesses, hypogranulosis, neutrophilic spongiform pustules of Kogoj, acanthosis, and dilated blood vessels with perivascular infiltration of lymphocytes and neutrophils in the papillary dermis (Figure 2). Gram and periodic acid–Schiff stains in addition to culture taken from pustules were negative. All these findings were consistent with the diagnosis of pustular psoriasis.

After discontinuation of sorafenib, his skin lesions improved significantly under the treatment of a potent topical steroid with occlusive dressing therapy, topical vitamin D3, and narrow-band UV-B phototherapy. After discharge, the patient was administered sorafenib at a substantially lower frequency (200 mg every 2–3 days) by his gastrointestinal doctor. Multiple scaly erythematous papules and plaques reappeared gradually over his trunk, buttocks, and extremities, but to a lesser extent. There was no pustule formation as well. The chronological data revealing an unusual subsequent clinical pattern of lesions when compared with its past history, along with the reappearance of skin lesions after rechallenge of sorafenib, implied a possible causal relationship between sorafenib and psoriatic flare-ups.

Discussion

Sorafenib as an oral multikinase inhibitor that blocks tumor cell proliferation and angiogenesis is used for treatment of advanced renal cell carcinoma, unresectable HCC, and other solid tumors. It inhibits numerous tyrosine kinases, including the family of vascular
endothelial growth factor receptors (VEGFR-2 and VEGFR-3), platelet-derived growth factor receptor, stem cell growth factor receptor (c-KIT), Fms-like tyrosine-kinase 3, and RET and RAF kinases (RAF-1 and B-RAF). About 90% of the patients treated with sorafenib may suffer from its cutaneous side effects including hand-foot skin reaction, erythematous rash on the face and scalp, subungual splinter hemorrhages, scalp dysesthesia, alopecia, pruritus, xerosis, spiny follicular hyperkeratosis, and skin neoplasmas. Less commonly described are areolar hyperkeratosis or pain, eruptive nevi, eruptive facial cyst, and psoriasiform rash. To our knowledge, only seven cases of sorafenib-associated psoriasiform eruption have been reported, but pathogenesis remained undetermined. Dysfunctional CD4⁺CD25⁺ immuno-suppressive regulatory T cells leading to an imbalance between regulatory and effector T-cell functions may play a crucial role. It has also been suggested that tyrosine kinase inhibitors, such as sorafenib, may block the signal transduction pathways in both regulatory and effector T cells. However, the occurrence of psoriasiform eruptions in patients following sorafenib treatment seems paradoxical, as it blocks the angiogenesis that has been reported as an overexpression of vascular endothelial growth factor by keratinocytes in psoriatic lesions. In addition, remission of recalcitrant psoriatic lesions in a patient with metastatic renal cell carcinoma has been reported after treatment with sorafenib.

While cutaneous toxicities associated with sorafenib are usually manageable and not life-threatening, they may affect critical anti-neoplastic therapy by causing dose modification or discontinuation of sorafenib. Therefore, early detection and proper management of these adverse reactions are crucial to continuing treatment with sorafenib, seeing that skin toxicities in patients treated with sorafenib are correlated with a good prognosis in HCC.

The differential diagnosis of pustular psoriasis includes acute general exanthematous pustulosis and subcorneal pustular dermatosis. Acute general exanthematous pustulosis usually affects a large and flexural area of the body, and is associated with a limited range of drugs such as antibiotics. In the present case having the known drug culprit (sorafenib), a diagnosis of subcorneal pustular dermatosis is less likely. Although the mechanism that induces psoriasiform and pustular eruption needs to be clarified, the induction of pustules in our case may be referred to as an exacerbation of psoriasis accordingly.

Our patient presents a rare case of sorafenib-associated psoriatic flare-up, which responded dramatically to topical treatment and narrow-band UV-B phototherapy after discontinuation of sorafenib. It is of vital importance that dermatologists and other physicians are confident in prompt identification and management of sorafenib-induced psoriasiform dermatitis to prevent further deterioration of patient’s quality of life. Further investigations are also warranted to elucidate the correlation between sorafenib and psoriasis, and to improve our understanding of this issue so that more strategies for effective management can be worked out.

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References