Sorafenib (Nexavar®, BAY 43-9006)-induced Hand-foot Skin Reaction with Facial Erythema

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Sorafenib (Nexavar®, BAY 43-9006) is a novel, orally administered multi-kinase inhibitor that has recently been approved for the treatment of metastatic renal cell carcinoma. It is also used to delay disease progression in patients with advanced solid organ malignancies and metastatic melanoma. Sorafenib is associated with a relatively high incidence of dermatologic adverse events. The commonly occurring dermatologic adverse events associated with sorafenib include hand-foot skin reaction, facial erythema, splinter subungual hemorrhages, alopecia, pruritus and xerosis. We report here on a case of a 50-year-old man who was diagnosed with metastatic hepatocellular carcinoma. He developed both facial erythema and hand-foot skin reaction after the administration of sorafenib.

CASE REPORT

A 50-year-old male presented to our department for the evaluation of patches on his fingers and the soles of his feet. In addition, papules had been noted on his face one week earlier. The patient had HCC. Clinical examination revealed hyperkeratotic patches on the plantar pressure areas of his feet (Fig. 1A). There were erythematous patches with central yellow-colored blisters on the lateral sides and tips of his fingers (Fig. 1B). There were also small erythematous papules on his face (Fig. 2). The symptoms reported by the patient included paresthesias, tingling, burning and painful sensations on the palms and soles, as well as decreased tolerance for contacting hot objects. The skin lesions had developed 10 days after he began oral treatment with sorafenib, 800 mg/day. The histopathology of a skin biopsy taken from the hyperkeratotic patch of his sole showed parakeratosis, dyskeratosis and vacuolar degeneration of the keratinocytes in the epidermis (Fig. 3). As a result of the clinical and pathologic findings, the diagnosis was HFSR with facial erythema to sorafenib. The sorafenib was discontinued. Treatment with topical glucocorticoids and oral antihistamines was associated with a relatively high incidence of dermatologic adverse events. The commonly occurring dermatologic adverse events associated with sorafenib include hand-foot skin reaction (HFSR), facial erythema (rash and desquamation), splinter subungual hemorrhages, alopecia, pruritus and xerosis. The development of rash and hand-foot syndrome (HFS) has been reported in the majority of patients and appears to represent a toxic, dose-dependent reaction. We report here on a case of a 50-year-old man who was diagnosed with metastatic HCC. He developed both facial erythema and HFSR after the administration of sorafenib (800 mg/day for 10 days).
Fig. 1. (A) Yellow discoloration hyperkeratotic patches on the plantar pressure areas (B) Erythematous patches with central yellow-colored blisters on lateral sides and tips of fingers.

Fig. 2. Discrete erythematous tiny papules on the face. The lesions mostly involved the mediofacial area and spared the periorbital area.

Fig. 3. The histopathological findings of the hyperkeratotic patch showed parakeratosis, dyskeratosis and vacuolar degeneration of keratinocytes in the epidermis (H&E stain, ×100).

initiated, and the skin lesions cleared within two weeks.

**DISCUSSION**

Sorafenib (BAY43-9006) is a multi-kinase inhibitor that inhibits the molecular components of the Raf-MEK-ERK signaling pathway. The drug limits tumor growth and VEGFR-1, VEGFR-2, VEGFR-3 and PDGFR-β expressions, and so it inhibits neoangiogenesis. Sorafenib delays disease progression by targeting two key pathways that are known to be important in the pathogenesis of HCC. Sorafenib is generally safe and well-tolerated in patients who have advanced, progressive solid tumors, including RCC, melanoma, HCC and colorectal cancer. There is little evidence of any clinically relevant drug-drug interactions.

The most frequently reported toxicities attributed to sorafenib include rash, hypertension, fatigue, anorexia and diarrhea. Up to 93% of the patients who receive sorafenib as monotherapy experience cutaneous effects, including rash (18∼66%), HFS (25∼62%), alopecia (18∼53%), stomatitis (12∼35%), xerosis (11∼23%) and flushing (16%)³,⁴.

The rash on the patient’s face appeared as a homogeneous, slightly erythematous eruption that was associated with superficial desquamation. The lesions mostly involved the mediofacial area and they spared the periorbital area. The erythema was sometimes exacerbated by hot temperatures⁷. The facial eruptions related to sorafenib use are very similar to classic seborrheic dermatitis and