

taneous tissue. There is proliferation of fibroblasto-like spindle cells embedded in myxoid collagen stroma.

Tumor cells demonstrate immunoreactivity for CD34, CD99, vimentin, and the results of the epithelial membrane antigen are still inconsistent.<sup>4</sup> Radiological studies may reveal underlying bone erosions and fine needle cytology shows a cluster of loose spindle cells in the myxoid material. Malignant transformation, although rare, is possible.<sup>3,4</sup> Differential diagnosis of SAF should be made with nail/periungual fibroma, acquired digital fibrokeratoma, low-grade fibromyxoid sarcoma, dermatofibroma, superficial angiomyxoma, and myxoid neurofibroma. Treatment of choice is extensive surgical resection and periodic follow-up after excision is advisable, as recurrence rate may range from 10% to 24%. This recurrence has been associated with incomplete resection.<sup>2</sup> Mohs surgery has become a promising alternative due to greater control of the margins, reducing the possibility of recurrence and satisfactorily preserving tissues adjacent to the tumor.<sup>5</sup> SAF, although rare, should be included in the differential diagnosis of tumors involving chirodactyls and toes. □

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### Grade III hand-foot skin reaction induced by sorafenib\*

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#### Dear Editor:

Human cancer rates have increased in the last years. Although the effects of current treatment methods unfortunately include mutilation (surgery), radiation (radiotherapy), and poisoning of the body (chemotherapy), they remain the most effective weapons to fight the disease.

Sorafenib is a multikinase inhibitor that targets Raf, vascular endothelial growth factor family (VEGFR-2 and VEGFR-3), platelet-derived growth factor- $\beta$ , Flt-3, and c-Kit, inhibiting molecular pathogenesis, angiogenesis, and tumor cell proliferation. Although it represents the standardized treatment for advanced hepatocellular carcinoma nowadays, a number of case reports on its side effects have been published. Recent guidelines of the European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD) recommend sorafenib as the first-line therapy for patients with advanced hepatocellular carcinoma.<sup>1</sup>

Unfortunately, as with other cytostatic drugs, side effects are often associated with this drug. Hand-foot syndrome has been previously reported as an adverse event during sorafenib therapy. For example, in a recent Chinese study, 68.7% of 83 patients treated with sorafenib for metastatic renal cell carcinoma developed hand-foot syndrome. In a Japanese study, 45.0% of 241 patients diagnosed with advanced hepatocellular carcinoma developed this syndrome.<sup>2,3</sup>

We present the case of a 78-year-old female patient diagnosed with hepatocellular carcinoma who was referred to our dermatology unit due to intense redness and pain on both palms,

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discrete desquamation and more severe clinical complaints on the feet (Figure 1). The lesions were stationary and limited to the palms and feet. The patient reported no other drug intake or allergic background. No pruritus was reported.

Patient medication included Sorafenib at 400 mg twice daily, started 6 weeks prior to present consultation.

The patient refused biopsy for histopathological evaluation.

We tried topical steroids and urea 10% cream to improve the symptoms, but achieved no results after one month of continuous topical therapy. Despite the uncomfortable dermatological problems, the patient was advised to continue with sorafenib chemotherapy.

The list of sorafenib-related adverse reactions is long and gets even longer with new reports including hand-foot syndrome.<sup>4</sup> It has been classified into 3 grades based on clinical features:<sup>5</sup>

- **Grade I:** slight erythema and swelling with minimal dysesthesia;
- **Grade II:** pain is present along with other clinical changes and interferes with daily life;
- **Grade III:** blistering, desquamation and even ulceration accompanied by extremely severe pain.

Although the exact mechanism of these adverse reactions is still unclear, some possible explanations could be the pressure exerted on palms and feet and secondary increased blood flow to these areas. Therefore, the side effect is not an allergic reaction to a culprit drug.

The present case is a typical grade 3 hand-foot syndrome related to sorafenib treatment for advanced hepatocellular carcinoma.

Skin toxicity related to sorafenib has a great impact on the patients' quality of life and represents a challenge in oncology practice. Patient reassurance is crucial to avoid chemotherapy abandonment. □



**FIGURE 1:** Intense erythema on the right hand (a) and right foot (b) and desquamation on the right foot accompanied by invalidating pain

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## Biologic therapy-induced pemphigus\*

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Dear editor,

Pemphigus is an autoimmune bullous disease that can affect the skin and mucous membranes, mediated by autoantibodies against desmosomal desmogleins, the main adhesion structures

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