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Palmoplantar Keratoderma Like Drug Eruption Due to Sorafenib

Sorafenibe Bağlı Palmoplantar Keratoderma Benzeri İlaç Reaksiyonu

Dear Editor,

A 69 year-old female patient was admitted to our outpatient clinic for the tenderness of palms and soles and the thickening of the skin under the feet. These complaints lasted for three months and the pain of her feet started to cause difficulty when walking. Medical history revealed that she was on follow-up for a hepatic tumor of unknown origin for three years at oncology department. A malignant transformation was suspected and she was diagnosed hepatocellular adenocarcinoma after a liver needle biopsy 9 months ago. She was given adriamycin chemotherapy for three months. After finishing this treatment, sorafenib therapy was commenced for the last three months. Soon after the initiation of sorafenib therapy, tenderness of palms and soles started. On dermatologic examination, mild palmar erythema and hyperkeratosis along with superficial fissuring on palmar sides of the fingers were noted. Severe hyperkeratotic plaques and nodosities were found especially on lateral plantar surfaces of bilateral feet and on plantar surfaces and pulpas of the third, fourth and fifth toes (Figure 1 and 2). The epidermal changes and sudden onset of painful keratoderma was related to sorafenib use as the complaints correlated with the commence of this treatment. A biopsy was suggested but not accepted by the patient. She was prescribed topical keratolytics and put on follow-up with a slight symptomatic relief after this therapy. Sorafenib is a multi-target tyrosine kinase inhibitor used for unresectable hepatocellular carcinoma and advanced renal carcinoma which decreases cell proliferation by inhibiting intracellular (c-RAF, b-RAF; V600E mutant BRAF) and cell surface kinases [KIT, FMS-like tyrosine kinase-3, RET, vascular endothelial growth factor receptor (VEGFR)-1, VEGFR-2, VEGFR-3, and platelet-derived growth factor receptor-ß] that are involved in

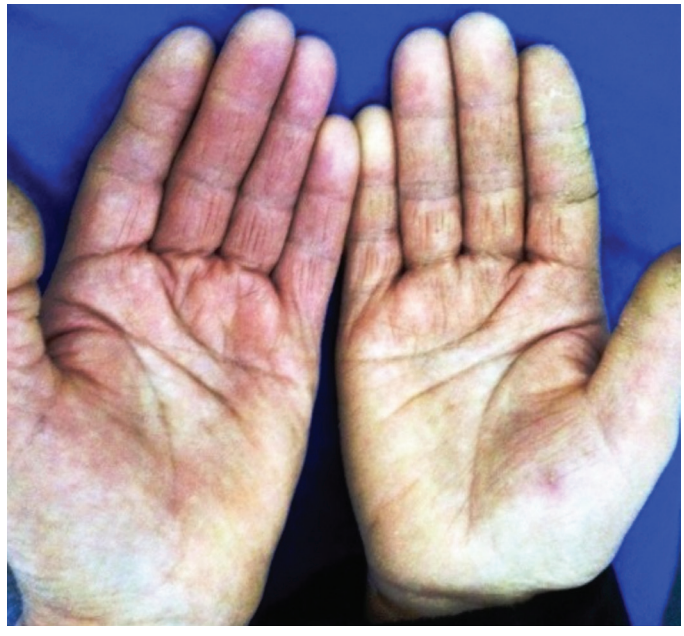

Figure 1. Hyperkeratosis and fissuration on the palms

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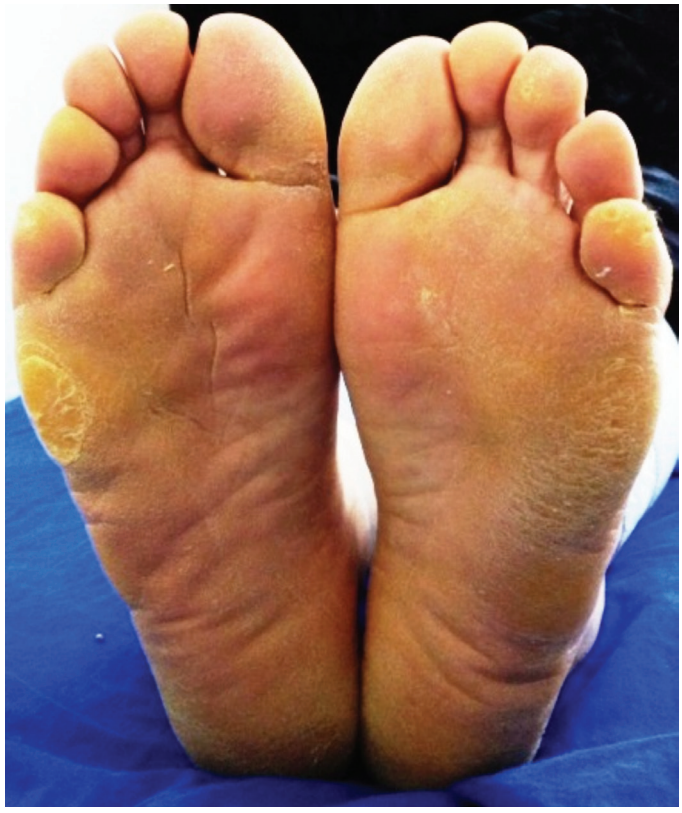

Figure 2. Severe hyperkeratotic nodules and plaques on lateral aspects of the feet and toes, hyperkeratosis of the soles

cell signaling, angiogenesis and apoptosis (1-3). It is known to cause a variety of toxic skin reactions including painless swelling, erythema, moist desquamation, ulceration and blistering (2,4). Painful hand-foot skin reaction and rash is the most common adverse reaction of sorafenib which usually appear during the first six weeks of treatment (2,4,5). Topical symptomatic relieving therapies for pain, dose modification and treatment interruption in more severe reactions are general approaches for the patients (2,5). Erythema multiforme and keratoacanthomas/squamous cell cancer of the skin induced after sorafenib was also recently reported in the literature (6-8). Lately, RAF inhibitors are proved to cause proliferative interaction for latent RAS mutant keratinocytes but the exact pathway of hyperkeratinization induction and inflammation of keratinizing tissues has not been defined yet (9). To our knowledge painful nodular keratoderma induced after sorafenib use was reported in our patient for the first time. We believe that the reporting of various cutaneous side effects of new antineoplastic agents increase knowledge about their unknown pharmacological side effects and is necessary.

Ethics

Peer-review: Internally peer-reviewed.

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