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Melanonychia and Blue lunulae with the Multikinase Inhibitor Sorafenib

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Introduction

Molecular targeted therapy with monoclonal antibodies and low molecular weight inhibitors have gained increasing importance particularly in the treatment of malignant tumors. Sorafenib (Nexavar®) is an oral multikinase inhibitor that blocks tumor cell proliferation and angiogenesis and is used for the treatment of advanced renal cell carcinoma, hepatocellular carcinoma, and other solid tumors including metastatic differentiated thyroid cancer, at a starting dose of 400 mg twice daily [1-4]. The most common adverse effects are fatigue, diarrhea, and various other dermatologic side effects [1]. Recently, a meta-analysis of dermatological toxicities associated with sorafenib has been published, [5] and a hand-foot-skin reactions (HFSR) was most often found, but also rash/desquamation, alopecia, pruritus and dry skin. Nail involvement has been reported, in particular sub-ungual splinter hemorrhages [6]. We describe a patient with longitudinal melanonychia and blue lunulae that developed during sorafenib therapy of metastatic thyroid carcinoma.

Keywords: Melanonychia; Sorafenib

Case Report

A 51-year-old woman had a diagnosis of well differentiated papillar thyroid carcinoma, stage IV, with multiple gross bone metastases. She had undergone total thyroidectomy subsequently to several courses of radioiodine (I^{131}). Four years later, the disease progressed with new bone lesions and pulmonary metastasis. The disease was classified as resistant to radioiodine treatment. Orthopedic surgery of the spine was performed twice (D10-D11 and L-L4). Other therapeutic options were evaluated and the patient began a treatment with sorafenib, 400 mg twice daily.

After four weeks of continuous treatment, she developed diffuse pruritus and facial erythema with dysesthesia and noticed intensive hair loss. On physical examination, we found longitudinal melanonychia of the left great toe nail (Figure 1) and a bluish discoloration of the lunulae was evident in both great toenails (Figure 2). The patient denied to have had similar nail alterations before and any recent medication changes.

Discussion

Several cutaneous side effects have been reported with sorafenib [1,5-10]. A meta-analysis to determine the type, incidence and risks of dermatological toxicities associated with sorafenib treatment of advanced solid tumors, usually at a starting dose of 400 mg twice daily, showed that the most frequent dermatological adverse effects were hand-foot-skin reactions (HFSR) (39.0%), rash/desquamation (35.4%), alopecia (25.5%), pruritus (14%) and dry skin (14,1%). The HFSR is clinically distinct from the well-known chemotherapy-induced hand-foot syndrome, because it presents as painful symmetrical erythematous and edematous areas on the palms and/or soles commonly associated with paresthesias, but the erythema turns thick with desquamation and sometimes callus-like hyperkeratosis, particularly but not exclusively on pressure areas [7]. No significant correlation between HFSR severity and response to treatment was seen [7].

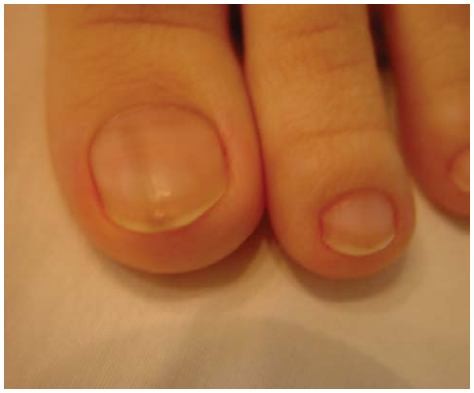

Figure 1: Longitudinal melanonychia.

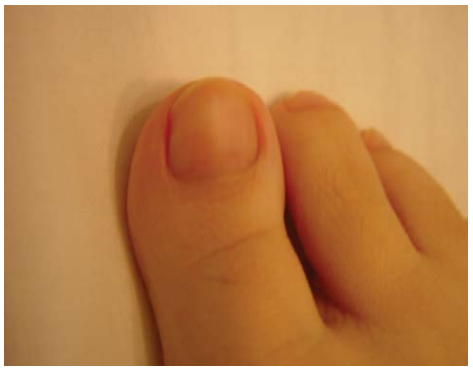

Figure 2: Blue discoloration of the lunula.

Other cutaneous adverse effects include facial/scalp erythema/dysesthesias, a keratosis pilaris-like eruption and more rarely eruptive keratoacanthomas, nevi, cysts, inflamed actinic and seborrheic keratoses.

Nail involvement has been reported [1,2,5-10], mainly multiple, painless subungual splinter hemorrhages. These hemorrhages usually developed 2 to 4 weeks after the onset of therapy and are probably

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related to inhibition of vascular endothelial growth factor receptor [6]. Our patient presented with diffuse pruritus, facial erythema with dysesthesia, pronounced effluvium and peculiar nail involvement. Besides a longitudinal melanonychia on the left great toenail, a bluish discoloration of the lunulae was present in both great toenails. To our knowledge, the appearance of blue lunulae has not been reported before with sorafenib.

Skin toxicities of sorafenib are mainly mild or moderate as they usually do not require drug withdrawal [5-10]. Sometimes they require dose modifications and/or treatment interruptions [11]. Increased awareness by dermatologists who work with oncologists, of the diversity, frequency, and treatment of sorafenib-induced cutaneous adverse reactions will be helpful for patients who require long-term therapy with this medication for their cancers.

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