Dermatological Toxicity of Ixabepilone

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Abstract. Ixabepilone is a new class of non-taxane microtubule-stabilizing agents. These agents bind tubulin, stabilize microtubules and, thus, block mitosis and result in cell death (1-8). In phase I studies, neutropenia was the only grade 4 toxicity while fatigue, anorexia and mucositis occurred as grade 3 toxicities. Neuropathy, myalgia, arthralgia, alopecia and gastro-intestinal toxicities also occurred at grades 1 and 2. No dermatological effects have been documented to date. Here, a case is reported of a 62-year-old woman with stage 4 breast cancer being treated with Ixabepilone (40 mg/m²) who developed a dermatological reaction not previously described as a toxicity from Ixabepilone therapy.

Case Report

Ixabepilone is a new class of non-taxane microtubule-stabilizing agents. These agents bind tubulin, stabilize microtubules and, thus, block mitosis and result in cell death (1-8). The patient was a 62-year-old woman who had been diagnosed 4 years earlier with locally advanced (stage 3), invasive ductal carcinoma of the breast. She had received neoadjuvant doxorubicin (60 mg/m²) and cyclophosphamide (600 mg/m²) i.v. once every 3 weeks for four treatments, achieving a partial response. She had then undergone a modified radical mastectomy followed by paclitaxel (175 mg/m²) chemotherapy i.v. once every 3 weeks for four treatments, achieving a partial response. She had then undergone a modified radical mastectomy followed by paclitaxel (175 mg/m²) chemotherapy i.v. once every 3 weeks for three treatments, before entry into a clinical trial of a high-dose alkylator chemotherapy with stem cell support. The conditioning regimen was cyclophosphamide/thiotepa/carboplatin (STAMP V). Other than transient total body hyperpigmentation associated with thiotepa, no dermatological side-effects presented.

The patient had progressed well until 4 years later, when she relapsed with disease in her lung and bones. After biopsy confirmation of the relapse, the patient was enrolled in a phase II trial of Ixabepilone (40 mg/m²) given i.v. over 3 hours every 3 weeks. After two cycles, partial response was noted on CT scan. She initially tolerated the Ixabepilone well, with only mild myalgias and peripheral neuropathy emerging after the second dose. On physical examination prior to her third dose, however, the dorsums of both her feet were noted to be dry, cracked and erythematous. She was advised to use a strong emollient, bringing significant relief. The erythema remained the same up to the fourth dose, however, after this dose, she noted swelling of her feet that began the day after infusion and self-resolved within a few days. After her fifth dose, she developed very pronounced erythematous, hyperpigmentation of her feet, ankles, lower calves, hands and wrists, bilaterally in a stocking/glove distribution (Figures 1-4). At the same time, she complained of severe peripheral neuropathic symptoms in her fingers and the dorsum of her feet, which interfered with her daily activities. Ixabepilone was discontinued because of this peripheral neuropathy. However, the rash on the patient’s hands and feet required no further treatment, resolving over the following 4 weeks.

Discussion

The rash caused by Ixabepilone was reminiscent of the dermatological toxicity of Docetaxel with the emergence of small patches of hyperpigmentation and erythema, which may be painful, associated with swelling and eventual superficial desquamation of these areas (8). It appears to be cumulative and no treatment is needed. Our patient was removed from the study when the rash became clinically significant, however, if patients are to continue with Ixabepilone treatment, topical steroids might be useful.

References


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Figures 1-4. Swelling, erythema and superficial desquamation of the hands and feet in a patient treated with Isabepilone.