Onycholysis Associated With Capecitabine in Combination With Irinotecan in Two Patients With Colorectal Cancer

Onycholysis, or the separation of the nail from its bed, is a non–life-threatening toxicity, but one that may impair function and be visibly unpleasant. Anthracyclines and taxanes, alone or in combination, are the cytotoxic drugs most frequently associated with onycholysis (1,2). During the last year, we have treated 36 patients with metastatic colorectal cancer with an irinotecan–capecitabine combination and have noted that two patients developed chemotherapy-induced onycholysis. To our knowledge, there is only one report of capecitabine-induced onycholysis (3), which occurred in a woman with breast cancer, and no reports of irinotecan-induced onycholysis.

The first patient, a 58-year-old Caucasian man with lung and liver metastases from colorectal cancer, was being treated with irinotecan at 225 mg/m² on day 1 and capecitabine at 1000 mg/m² twice daily on days 2–15 every 3 weeks. He had reached a sustained partial response after six and nine cycles with mild toxicity, with the exception of a grade 1 hand–foot syndrome after nearly every course. After the ninth course, he developed a grade 2 foot skin reaction and separation of the left fifth toenail (Fig. 1). He subsequently lost the nail. No other toenails or fingernails were involved. The patient was advised to wear closed sandals, and the onycholysis resolved, despite continued irinotecan–capecitabine therapy.

The second patient, a 62-year-old Caucasian man, was found to have multiple liver metastases from colorectal cancer. Irinotecan–capecitabine therapy with the same administration schedule as that of the first patient was initiated, and within the first three cycles, he achieved a partial response. After the sixth course of chemotherapy, he experienced a grade 3 foot skin reaction, concurrently with some bleeding from the hyponychia of both fifth toenails and left fourth toenail. Capecitabine therapy was stopped on day 11, and 1 week later, the patient experienced a painless loss of his fifth toenails. As with the first patient, fingernails were not involved. The second patient received two more cycles with a 25% reduction in the dose of capecitabine and had no evidence of a recurrent foot skin reaction and onycholysis.

In our two patients, onycholysis occurred simultaneously with a moderate hand–foot skin reaction and, in both patients, skin and nail toxicities were limited to the feet. One patient experienced evident inflammation and bleeding from the hyponychia that was associated with onycholysis. No other nail changes such as leukonychia or hyponychium hyperpigmentation were observed in theremainder nails, and there were no signs
of onychomycosis. We think that inflammatory phenomena of the skin of the digital tip are a consequence of a capecitabine-induced foot skin reaction and are associated with direct hyponychium toxicity, which resulted in onycholysis in our patients. By contrast with another report (1), we believe that sunlight exposure has no etiologic role for our patients because they developed onycholysis during the winter and toxicity was limited to covered toenails.

We want to call attention to this infrequent toxicity because of the expanding role of capecitabine-based regimens for the adjuvant and palliative treatment of colorectal cancer (4,5). Although the explanation for onycholysis in our patients may be hyponychial inflammation associated with hand–foot syndrome, further evaluation of capecitabine-induced onycholysis is warranted if more reports are described.

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