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**UNUSUAL SCROTAL AND PENILE ULCERATIONS TOGETHER WITH  
PALMAR-PLANTAR ERYTHRODYSESTHESIA SYNDROME IN A PATIENT  
WITH METASTATIC COLON CARCINOMA TREATED WITH CAPECITABINE**

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Unusual scrotal and penile ulcerations together with palmar-plantar erythrodysesthesia in a patient with metastatic colon carcinoma treated with capecitabine

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Capecitabine is an orally administered chemotherapeutic drug used in the treatment of colorectal and breast cancer, as well as of metastatic disease, either as a single agent or combined with other agents (1).

A 63 -year-old man presented with painful penile and scrotal ulcerations (Figure 1). Four years prior to admission, the patient underwent ileocecal resection for cecum cancer (pT3, N1, M0, Duke`s C) with metastases in the mesocolic lymph nodes. He received 6 cycles of Mayo Clinic adjuvant regimen consisting of 5-fluorouracil (5-FU) and leucovorin (folinic acid). Three years after resection, positron emission tomography - computed tomography (PET/CT) revealed metastases in the mediastinal and para-aortic lymph nodes and lungs. Following the surgical treatment, the pathohistological finding was consistent with metastatic adenocarcinoma of the colon. Two months after the second surgery the patient was started on XELIRI (irinotecan and capecitabine) + bevacizumab. At the end of the first cycle, the patient was complaining of tingling and burning sensation on the tips of his fingers and toes. During the second cycle, he was complaining of the painful redness of his feet and palms. On physical examination, a marked erythema of his palms and feet was noted and hand-foot syndrome (palmar-plantar erythrodysesthesia, PPE) was diagnosed (Figures 2a and 2b). A skin barrier cream and moisturized ointments together with a short course of potent topical corticosteroids were prescribed, but they did not relieve the symptoms. At the beginning of the fourth cycle of chemotherapy, erythema was followed by painful ulcerations of his penis and scrotum (Figure 1). Capecitabine was thus discontinued. The penile and scrotal ulcerations together with the hand and foot symptoms resolved within 3 weeks of discontinuing capecitabine. Three months after reintroducing capecitabine, the patient re-developed genital and scrotal redness and ulcerations, together with hand and foot redness.

The most common cutaneous side effect of capecitabine is hand-foot syndrome, also known as palmar–plantar erythrodysesthesia (PPE). Other cutaneous adverse reactions such as

alopecia, nail changes, skin discoloration, cutaneous hyperpigmentation, photosensitivity reaction, and radiation recall syndrome have also been reported.<sup>2-4</sup> Recently, a case report described a delayed-type hypersensitivity reaction,<sup>5</sup> while another report described scleroderma-like skin changes associated with PPE associated with capecitabine<sup>6</sup>. However, to our knowledge, the coexistence of both genital and scrotal ulcerations together with PPE has been described in three patients only.<sup>7, 8</sup> For that reason, there is no consistent grading system to describe scrotal and penile involvement associated with capecitabine. Sapp et al<sup>7</sup> suggest that the manifestations of PPE are similar to the symptoms experienced with scrotal and penile involvement, and that this variant should be incorporated into the grading system describing PPE. Grade 1 PPE is characterized by the following symptoms: numbness, dysesthesia and tingling in the hands and feet.<sup>9</sup> In Grade 1, chemotherapy is usually continued and a skin barrier cream and moisturized ointment are prescribed.<sup>10</sup> In Grade 2 PPE, patients experience painful erythema with swelling of palms and soles, while Grade 3 is characterized by desquamation, ulceration, blistering and severe pain.<sup>9</sup> In this grade, the dose of chemotherapy is either maintained or reduced by 25%.<sup>9</sup> Managing Grade 3 PPE includes interrupting one cycle of chemotherapy, followed by the dose adjustment alongside moist ointment and supportive care.<sup>10</sup> Genital and scrotal ulcerations fall into Grade 3 severity.

The burning sensation of the skin, together with painful ulcerations, especially in the genital region, have negative influence on the quality of life, belief in recovery, and often result with the need of permanent or temporary interruption of the oncological treatment, which may endanger the completion of the therapy.

This case represents a rare side-effect of capecitabine. Based on the significant pain and discomfort that our patient suffered, it is important for practitioners to recognize this entity as a side effect of capecitabine, in order to minimize discomfort and complications.

## Disclosure

The authors have stated that they have no conflicts of interest.

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Figure 1

Ulceration of the penis and scrotum in patient with metastatic colon carcinoma treated with capecitabine



Figure 2a and 2b

Palmar-plantar erythrodysesthesia in patient with metastatic colon carcinoma treated with capecitabine



