Article

Hand-foot syndrome and nail changes caused by capecitabine chemotherapy.

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Abstract: The effects of targeted therapy are not limited with cancer cells and, unfortunately, are associated with many and numerous side effects. Dermatological manifestations are one of the most frequently observed, and in severe and/or prolonged they inevitably affect the quality of life of patients. The management of these various side effects is empirical and largely based on expert advice and consensus. Many cytotoxic and biological drugs are the cause of severe dermatological side effects, such as hand-foot syndrome (HFS). An oncological patient with HFS presents relevant symptoms that interfere with daily activities and with adherence to anticancer treatment. Control and treatment of HFRS are the most important goals of improving the quality of life of cancer patients.
Below we present the case of a 62-year-old woman undergoing treatment with capecitabine and paclitaxel for breast cancer.

Keywords: hand and foot syndrome, capecitabine, oncologists, chemotherapy, drug's reaction.

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1. Introduction

Capecitabine (Xeloda; Hoffmann-La Roche Inc, Nutley, NJ, USA), a fluoropyrimidine carbamate derivative that is a prodrug of 5-fluorouracil, is an orally administered tumor selective cytotoxic agent [1], [2]. It is used in combination with docetaxel or with paclitaxel for the treatment of locally advanced or metastatic breast cancer [3]. It is also used as a first-line treatment for metastatic colorectal carcinoma. Hand-and-foot syndrome (HFS) is listed as a well-known adverse effect on the patient information brochure. HFS is also seen with other chemotherapeutic agents and found that 92.9% of HFS developed within the first two cycles of treatment. HFS is usually self-limiting and rarely leads to hospitalization or life-threatening manifestations. However, it has an on treatment schedule and quality of life [4], and the cumulative nature of HFS difficult to ascertain [5].

A 62-year-old woman was seen in the outpatient Department one and a half years after undergoing a modified Mastectomy carcinoma of the left breast. She underwent chemotherapy with two cycles of injection of cyclofosfamide (750 mg), 5-fluorouracil (750 mg) and methotrexate (75 mg) before surgery and three more cycles after surgery. Then she began six cycles of radiation therapy. In the end, she was started on paclitaxel (240 mg in one pint of normal saline infused over 3 hours) and capecitabine (500 mg) three tablets twice a day for 14 days, followed by 7-day pill-free phase.

After the second cycle of paclitaxel and capecitabine, the patient complained on tingling in hands and feet associated with progressive burning. During the week, she also noted discomfort, tightness, soreness, and stiffness when holding objects. During the examination, swelling and hyperemia of the palms and soles were noted [Fig. 1]. It was thickening of the skin accompanied it, more on the pads of the toes and heels [Fig. 2 A,B]. Besides there was a pronounced peeling on the legs. The nail plates of the hands and feet significantly thickened and changed color. Some of the plates were flaking off.

The patient was the clinical diagnosis HFS Grade III intensity levels induced by capecitabine. She refused a skin biopsy on her hands. She was assigned a softening agent containing allantoin and thermal water, 2% salicylic ointment on areas of hyperkeratosis. She also started taking oral pyridoxine (40 mg) once a day. Third capecitabine cycle was delayed.

During the observation one week later there was a significant decrease in pain, stiffness, tingling and burning. Thickening, peeling and flaking decreased [Fig. 3 A,B]. However, there was only a slight decrease in hyperemia of the hands and feet. At this stage, treatment was resumed with a reduced dose of capecitabine, 1g twice a day, for 14 days. Fifteen days later, there was no recurrence of symptoms or there. The patient continued to receive chemotherapy.

Hand-foot syndrome, acral erythema, palmar-plantar erythrodysesthesia syndrome were first reported by Zuehlke in 1974 [6]. Since then syndrome is ofter reported such an adverse event in many chemotherapy regimens. 5-Fluorouracil, cytarabine, doxorubicin, methotrexate, etoposide and commonly used agents are associated with HFS [7]. Of the new agents, there have been many reports that capecitabine causes HFS [1], [2], [5].

HFS appears to be a drug-addicted dose. It is assumed that the reaction is spused by the accumulation of a large amount of the drug in the stratum corneum of the palms and soles that have sebaceous glands but do have a large number of eccrine glands. All this contributes to the local toxic accumulation of the drug. However, this fact has not been proven yet. HFS manifests itself initially as dysesthesia, paresthesia and increasing discomfort on the hands and feet. Patients complain of burning, pain, tenderness when holding objects that may be accompanied by difficulties in standing or walking. In the future there might be swelling, progressive erythema along with, we can witness the development of hyperkeratosis and calluses and corns on hands and feet. In very severe cases, blisters may be seen. The condition improves within a few weeks with the peeling on the hands and feet. HFS manifests initially as dysesthesia, paresthesia and an increasing discomfort in the hands and feet [8].

Some cases may be accompanied by nail changes such as onycholysis and nail discoloration. Acral skin lesion for the disorder was registered in less than 5% of the patients, who received capecitabine only and in about 15% of the patients who received during either capecitabine and docetaxel or docetaxel alone metastatic breast cancer treatment [9]. The colors and thickening of our patient's nail plates may be seen as part of the HFS. HFS has three grades of severity Grade1 shows erythema of lateral aspects of fingers, progressing to thenar and hypothenar eminences, with swelling, numbness, dysesthesia/paresthesia, and tingling, especially over the pads of distal phalanges. A similar picture may be seen on the feet. However, it does not interfere with the patient's normal daily activity. Grade2 shows a progression of manifestations of grade 1, along with the pain, tenderness and discomfort affecting daily activities. In grade 3, along with severe pain, there is also development of blisters, moist desquamation and ulcer formation. The histopathological findings are nonspecific, with mild focal spongiosis in the epidermis, mild epidermal atypia, and mononuclear cell infiltration of the upper dermis. Immunofluorescence studies did not reveal any particular criteria in diagnosis [10].

3. Discussion

The drugs that provoke HFS most often are part of the basic schemes of chemotherapy, which are widely used in the treatment of cancer pathology. HFS is caused by cupecitabine in 74% of patients, 5-fluorouracil (34%), idarubicin (48%) as well as by methotrexate, etoposide and a combination of agents [5]. Less frequently HFS occurs with continuous infusion of doxorubicin, treatment with high doses of interleukin-2, liposomal doxorubicin, cytarabine, idarubicin, cyclophosphamide, hydroxyurea, docetaxel, mercaptopurine, mitozatronom, paclitaxel, vinorelbine, floxuridine, tegafur. Targeted therapy with sorafenib, sunitinib and lapatinib also provokes the development of this syndrome.

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Simple topical care with wet dressings, topical steroids, and emollients is enough to improve the condition of some patients, without interrupting therapy [7]. In some patients, moderate reduction of the dose of the offending agent, along with an intensive local care regimen, may be required. In a third subset of patients, the offending agent needs to be stopped completely to avoid recurrences or worsening of the condition. Patients are also recommended to avoid excessive exposure to sunlight and heat.

Knowing the symptoms and methods of aid will help to avoid the HFS syndrome. This will allow to resume treatment without reducing the drugs dosage or withdrawing it.

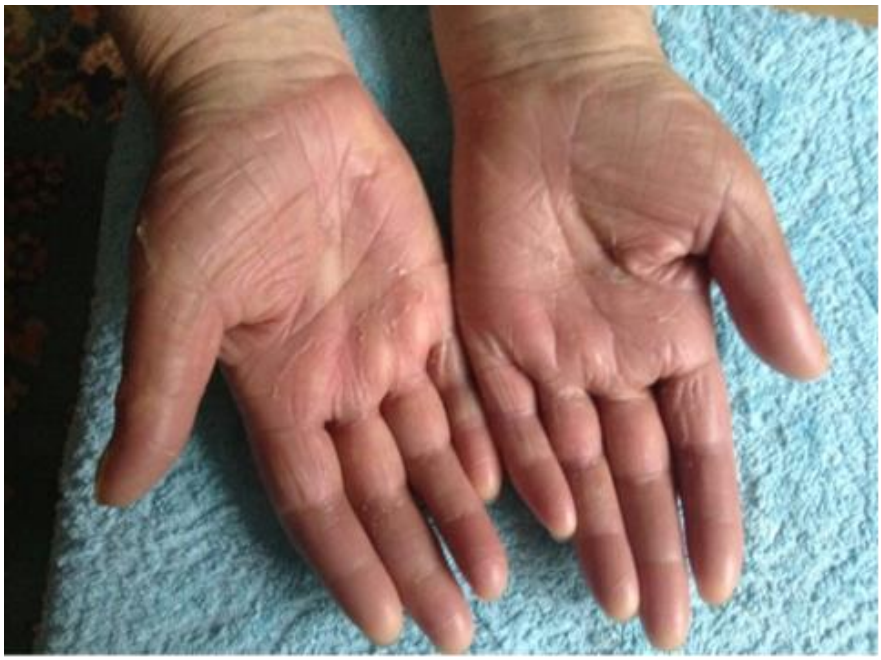

Figure 1. Fig.1 Skin changes, specifically swelling and hyperemia of the palms.

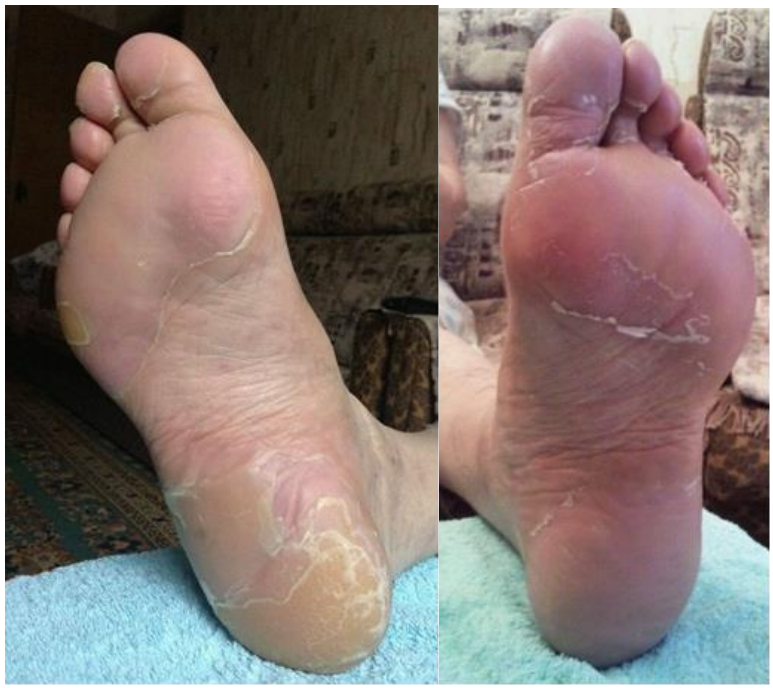

Figure 2 (A, B). Skin lesions, in particular, thickening of the skin more pronounced on the fingertips and in the heel area.

Figure 3 (A, B). In the process of therapy one week later there was a significant decrease in pain, stiffness, thickening peeling and flaking decreased.

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