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Case Report/Review

Loss of Fingerprints as a Side Effect of Capecitabine Therapy: Case Report and Literature Review

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Hand–foot syndrome (HFS) is the main side effect of capecitabine and affects the compression zones of the body such as the palms and soles, causing numbness, paresthesias, skin swelling or erythema, scaling, chapping, hard nodule-like blisters, and severe pain. Loss of fingerprints is also observed in some cases. Severe cases of HFS are common in the review of clinical reports. However, loss of fingerprints has not received significant attention. Two reported cases of loss of fingerprints in *The New England Journal of Medicine* and *The BMJ* have drawn attention to this side effect of capecitabine. Loss of fingerprints has a serious impact on patients' daily life, especially on personal identification. This report describes a patient who lost her fingerprints during the early stage of chemotherapy. Our aim is to draw the medical profession's attention to this problem.

Key words: Hand–foot syndrome (HFS); Capecitabine; Loss of fingerprints; Breast cancer

CASE REPORT

Consent from the patient's family and approval by the ethics committee of our hospital have been obtained. A 73-year-old female patient visited our hospital on November 1990 due to "a mass found in the left breast half a year ago." The patient underwent radical left mastectomy with axillary lymph node dissection at another hospital after definitive diagnosis. Postoperative pathology indicated simple carcinoma. The size of the mass was 2.0 cm × 2.0 cm, and no metastatic lesion was found in the axillary lymph nodes (0/3). The postoperative diagnosis was stage IIA breast cancer (pT2N0M0). The patient underwent one cycle of postoperative CMF chemotherapy and then refused to continue chemotherapy. She subsequently underwent treatment with tamoxifen for 1 month as pathology demonstrated ER (+) and PR (+) tumor cells. The patient stopped taking tamoxifen without consultation with her doctor due to asthenia.

On June 2013, a mass was found in the left chest wall, and a biopsy was performed. Pathology showed metastatic carcinoma, which was considered to have originated from the breast, with ER (+), PR (+), HER-2 (1+), Ki-67 < 3% pathology. On August 2013, the patient received six cycles of TP chemotherapy with intravenous infusions of docetaxel 120 mg on day 1 and cisplatin 60 mg on days 1 and 2, every 21 days. The efficacy evaluation indicated stable disease. After chemotherapy, the patient received endocrine therapy with oral letrozole 2.5 mg daily until March 2015. Due to ulcerated cancerous nodules in the chest, the endocrine therapy regimen was changed to oral exemestane 25 mg daily.

On January 2017, the ulcer in the chest wall enlarged. On April 2017, a lung CT showed 1) multiple nodules in the right lung, with several newly found nodules and some enlarged nodules compared with the CT results of October 11, 2016, highly suspicious for metastasis; and 2) irregular soft tissue shadow in the left anterior chest

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wall found after the left mammectomy, with an enlarged area compared with the previous study, swelling of the right axillary fossa with enlarged lymph nodes, highly suspicious for malignant tumor. The disease had clearly progressed. The patient started to take combination chemotherapy with docetaxel and capecitabine (21-day cycles with intravenous infusion of docetaxel 120 mg on day 1 and oral capecitabine 1500 mg twice daily on days 1–14) in April 2017. On the 10th day of treatment, the skin of the hands and feet was found to be thinner. After the second cycle of medication, the patient experienced slight pain in the hands and feet, with thinner texture of the fingertips. The patient had difficulty opening the fingerprint lock of her front door when returning home. The skin of her interphalangeal joints became red and swollen.

At the end of the third cycle of medication, the patient's hand–foot syndrome (HFS) had worsened, with thinning and peeling of the skin of the fingers, toes, and interphalangeal joints, as well as a gradual loss of the texture of the palm and loss of fingerprints, resulting in inability to open her fingerprint lock. During the fourth cycle of medication, the peeling of the skin of the hands and feet gradually worsened, resulting in chapping and bleeding (Figs. 1 and 2). The patient was diagnosed with grade IV HFS, and Vaseline was applied to the affected area. The fifth cycle of chemotherapy was postponed for 2 weeks, and the HFS improved slightly. During the fifth and sixth cycles of chemotherapy, the dosage of capecitabine was reduced to 1,000 mg twice daily. The last dose of chemotherapy was administered on August 10, 2017. Due to severe HFS, the patient refused to continue chemotherapy and chose to be observed with follow-up. No disease progression had been observed at 17 months.

DISCUSSION

Chinese researchers have proposed a "full-course management strategy" for advanced breast cancer. Combination chemotherapy with capecitabine followed by maintenance capecitabine monotherapy is particularly suitable for the full-course management of advanced breast cancer[1]. As the clinical uses of capecitabine have expanded, its side effects have received more attention. More than 50% of patients who are treated with capecitabine develop HFS[2].

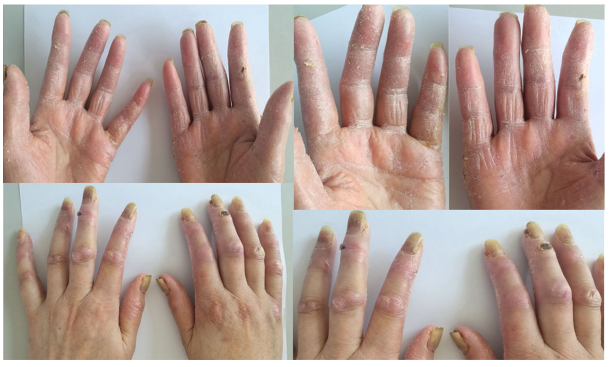

Figure 1. Severe hand–foot syndrome in the patient after the fourth cycle of chemotherapy, with loss of fingerprints, peeling of skin, blisters, chapping, and scabbing in some areas.

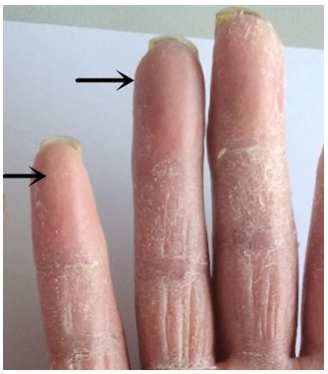

Figure 2. Location of lost fingerprints indicated by the arrows.

Capecitabine-related loss of fingerprints was initially reported by Chavarri-Guerra and Soto-Perez-de-Celis[3]. The patient in that report experienced loss of fingerprints after oral treatment with Xeloda, which made it impossible for the patient to conduct routine banking activities through fingerprint identification. She had grade 1 PPE when she was treated with capecitabine in combination with bevacizumab in the first cycle, and this improved after topical treatment. In the third cycle of chemotherapy, the patient developed limited use of her hands and feet. The dosage of capecitabine was subsequently reduced. No acute toxicity occurred, but the patient's fingerprints disappeared. The authors believed that the loss of fingerprints in this patient was closely related to the HFS caused by Xeloda.

Al-Ahwal reported that a patient who received capecitabine chemotherapy had a grade 1 HFS after the second and third cycles of chemotherapy, and a grade 3 HFS and disappearance of fingerprints after the fifth and sixth cycles of chemotherapy[4]. The patient delayed chemotherapy and reduced capecitabine while receiving paracetamol, tramadol, and a local moisturizer. He lost the ability to process required government documents because of his fingerprint loss. This unbearable phenomenon seriously affected the quality of life. When the patient began second-line Bev-Xeliri 18 weeks after completing the first-line treatment, he developed a grade 3 HFS, although the capecitabine dose was not high in the second-line regimen[4].

Lightowlers and Soomal also reported a case of fingerprint loss after chemotherapy[5]. The patient was unable to turn on his cell phone using the fingerprint recognition

technology, as he had previously done, after he experienced skin dryness and palmar erythema during chemotherapy with oxaliplatin and capecitabine. His cell phone could not recognize his fingerprints due to his skin peeling and loss of the surface texture. The authors also believed that the loss of fingerprints was related to HFS.

However, a prospective study by the Erasmus Medical Center Cancer Institute offers a different perspective. Mathijssen and colleagues suggested that the loss of fingerprints induced by capecitabine might not be associated with the severe skin reactions caused by HFS[6]. Their study collected fingerprint information from 66 patients who were treated with capecitabine. After 8 weeks of treatment, 9 patients had loss of fingerprints, while 46 patients had severe HFS. Although some patients were afflicted with severe HFS, they did not experience loss of fingerprints, and vice versa. This finding suggested that there is no definite correlation between the severity of HFS and loss of fingerprints. Most of the damaged fingerprints improved within 2 to 4 weeks after the treatment was stopped. No study to date has offered a plausible explanation for the mechanism underlying loss of fingerprints secondary to HFS.

The patient in our report experienced gradually worsening HFS immediately after the first cycle of treatment, with thinning and partial peeling of the skin of both hands, as well as fading of fingerprints on the fingertips. After the fourth cycle, the skin of the entire palm of both hands started to peel off, and she also experienced chapping, loss of fingerprints, and gradual fading of palm texture. Hard nodule-like blisters were observed in some areas of the fingers, along with nail discoloration. She also experienced swollen joints and restricted flexion of the fingers, which caused her significant discomfort. The patient was unable to open the door to her home due to loss of fingerprints. The patient reported that "she could not return to her home," which caused her psychological harm. The reported median time to onset of HFS is 79 days (ranging from 11 to 360 days)[7]. Most of the symptoms are grade 1. The patient in our report developed HFS on the 10th day after the start of treatment, and her fingerprints disappeared during the fourth cycle of treatment, possibly because the patient was overly sensitive to the drug.

Because capecitabine-induced HFS may be related to the overexpression of the COX-2 enzyme in the hands and feet, metabolism of capecitabine in small sweat glands, or mechanical compression[8–10], it can be speculated that COX-2 inhibitors can treat or prevent capecitabine-induced HFS, such as celecoxib. Most experts suggest that reducing capecitabine doses and delaying chemotherapy can be a key way to relieve symptoms in the absence of evidence[11]. The therapeutic methods of HFS include oral celecoxib, cod liver oil, vitamin B6, etc., as well as topical antiperspirants, urea ointment, antioxidants, or regional cooling[12,13]. There are also many traditional Chinese medicine decoction used for the treatment of HFS[14]. These studies suggest that oral celecoxib has a preventive effect on ≥2 grade HFS, while regional use of urea ointment and antiperspirant has no preventive effect on HFS[12,13]. Oral cod liver oil, oral vitamin B6, and local cooling or use of local antioxidants may be effective, but they are not as effective as celecoxib. However, these treatments cannot completely prevent or cure the effects of HFS, especially loss of fingerprints[10,15–17]. Loss of fingerprints is a low-risk adverse reaction. However, as a type of unique personal information, fingerprints are increasingly used for personal identification for electronic devices such as smart phones, laptops, and door locks. Loss of fingerprints brings great inconvenience to patients. Clinicians should inform the patient of the loss of fingerprints as a common adverse reaction and should encourage patients to save relevant fingerprint information before chemotherapy so that they can provide such information when needed. We hope that this case report calls clinicians' attention to this adverse reaction.

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