

## CAPECITABINE-INDUCED HAND-FOOT SYNDROME: A CASE REPORT

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**ABSTRACT:** Capecitabine is a chemotherapeutic agent indicated, among other things, as monotherapy for metastatic breast cancer. Hand-foot syndrome is one of the adverse effects associated with its use and is characterized by painful erythema, edema, dysesthesia, desquamation, blistering and ulcers in the palms and soles. This study presents a case report on a patient with left-sided breast cancer metastasized to the liver, who suffered from capecitabine-induced hand-foot syndrome. The patient was being treated at a university hospital in a state in the Northeast of Brazil in 2016. Her antineoplastic protocol had to be suspended. After the use of *Aloe vera* gel to treat the affected areas, there was a partial remission of symptoms. It is important to expand knowledge about this adverse reaction, facilitating its identification and management, in order to improve quality of life in cancer patients.

**DESCRIPTORS:** Hand-foot Syndrome; Antineoplastic Agents; Breast Neoplasms.

### SÍNDROME MÃO-PÉ INDUZIDA POR CAPECITABINA: RELATO DE CASO

**RESUMO:** A capecitabina é um agente quimioterápico indicado, dentre outros casos, como monoterapia no câncer de mama metastático. A síndrome mão-pé consiste numa das reações adversas associadas ao seu uso e caracteriza-se por eritema doloroso, edema, disestesia, descamação, bolhas e úlceras nas regiões palmar e plantar. Objetivou-se descrever o caso de uma paciente portadora de carcinoma de mama esquerda com metástase hepática que apresentou síndrome mão-pé decorrente do tratamento com capecitabina. Trata-se de um relato de caso ocorrido num hospital universitário de um estado do nordeste do Brasil em 2016. Foi necessária a suspensão do protocolo antineoplásico utilizado. Observou-se remissão parcial dos sintomas após o uso do gel de *Aloe vera* para o tratamento das áreas afetadas. Ressalta-se a importância do relato para conhecimento dessa reação adversa, facilitando sua identificação e manejo, para promover melhora da qualidade de vida do paciente oncológico.

**DESCRIPTORIOS:** Síndrome mão-pé; Antineoplásicos; Neoplasias da mama.

### SÍNDROME MANO-PIE INDUCIDO POR CAPECITABINA: RELATO DE CASO

**RESUMEN:** La capecitabina es un agente quimioterápico indicado, entre otros casos, como monoterapia en cáncer de mama metastático. El síndrome mano-pie consiste en una de las reacciones adversas asociadas a su uso, caracterizada por eritema doloroso, edema, parestesia, descamación, ampollas y úlceras en regiones palmar y plantar. Se objetivó describir el caso de una paciente con carcinoma en mama izquierda, con metástasis hepática presentando síndrome de mano-pie derivado del tratamiento con capecitabina. Relato de caso ocurrido en hospital universitario de estado del Noreste brasileño en 2016. Fue necesaria la suspensión del protocolo antineoplásico utilizado. Se observó remisión parcial de los síntomas luego de uso de gel de *Aloe Vera* para tratamiento de las áreas afectadas. Se destaca la importancia del relato para conocimiento de esta reacción adversa, permitiendo su identificación y manejo, promoviendo mejora de calidad de vida del paciente oncológico.

**DESCRIPTORIOS:** Síndrome Mano-Pie; Antineoplásicos; Neoplasias de la Mama.

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## ● INTRODUCTION

Capecitabine is a fluoropyrimidine, a systemic prodrug of 5-fluorouracil (5-FU), with the advantage of oral administration. It is used as adjuvant therapy for colorectal cancer, first-line therapy for metastatic colorectal cancer and as mono- or combination-therapy with docetaxel to treat metastatic breast cancer. The most common forms of dose-dependent toxicity related to capecitabine are hyperbilirubinemia, diarrhea and hand-foot syndrome (HFS)<sup>(1)</sup>.

In addition to capecitabine, the most common chemotherapeutic agents that trigger this syndrome are: pegylated liposomal doxorubicin, 5-fluorouracil, citarabine, and docetaxel. New multikinase inhibitors such as sorafenib, sunitinib, axitinib, pazopanib, regorafenib, and vemurafenib can also cause HFS<sup>(2)</sup>.

Also known as palmar-plantar erythrodysesthesia or acral erythema, HFS is an adverse effect of chemotherapeutic and biological agents<sup>(3)</sup> first described in association with mitotane by Zuehlke in 1974<sup>(2)</sup>. Mild to moderate cases result in painful erythema and edema, and different levels of dysesthesia, which can be followed by moist or dry desquamation of palms and soles. More severe cases include: cracked and peeled skin, blistering, ulcers, and intense pain that can interfere in activities of daily living<sup>(3)</sup>.

Considering that HFS has a considerable impact on quality of life in cancer patients, it is necessary to document cases of this adverse reaction to expand existing knowledge and facilitate its identification and management. Thus, the objective was to report a case of HFS occurrence in a patient at a university hospital in a state in northeast Brazil.

## ● CASE REPORT

This case report was about patient D.S.S., female, 39 years old, dark-skinned, teacher, diagnosed with left-sided breast cancer metastasized to the liver. Initial treatment consisted of neoadjuvant chemotherapy with doxorubicin and cyclophosphamide, followed by docetaxel (AC-T) for one cycle, which was substituted by weekly paclitaxel and trastuzumab.

Paclitaxel was suspended due to the development of grade 2 limiting neurotoxicity, with 3.5g/day dose of capecitabine for 14 days, in 21-day cycles. During the 3rd cycle, the patient reported pain, erythema, swelling, tingling and desquamation of the palmar and plantar regions, especially the latter, indicative of capecitabine-induced hand-foot syndrome. Medical conduct included suspending capecitabine and starting treatment with docetaxel.

After the 15<sup>th</sup> day, the patient returned to the hospital presenting pain, swelling, desquamation, blistering, and problems walking and conducting activities of daily living. She was diagnosed with grade 2 HFS, according to the classification proposed by the National Cancer Institute<sup>(4)</sup>.

After nursing evaluation, the patient began to apply *Aloe vera* gel on the affected areas, three times per day. There was partial remission of symptoms after two weeks of use, as observed by the clinical pharmacist during visitation. This case was monitored for approximately two months. After the identification of HFS and successful therapeutic management, the patient's quality of life improved significantly.

## ● DISCUSSION

HFS diagnosis is based on its clinical characteristics<sup>(5)</sup> and, in this case report, the patient was diagnosed with grade 2 syndrome. Grade 1 HFS involves slight changes to skin or dermatitis (such as erythema, edema or hyperkeratosis) but no pain, whereas grade 3 HFS is characterized by severe symptoms (such as desquamation, blistering, bleeding, edema or hyperkeratosis) with pain and limited ability for self-care<sup>(4)</sup>.

Among the drugs used during the patient's antineoplastic therapy, in addition to capecitabine,

trastuzumab<sup>(6)</sup> and paclitaxel<sup>(7)</sup> can also be related to HFS. However, the emergence of this syndrome only occurred after the administration of capecitabine, and symptoms remitted after capecitabine treatment suspension.

In general, HFS emerges during the first weeks of therapy with the triggering agent; however, for some drugs such as capecitabine, it can take several months after treatment begins<sup>(8)</sup>, consistent with the situation described here. Key clinical trials on the use of different doses of capecitabine in breast cancer treatment indicate a 32-62% incidence for all grades of HFS<sup>(9)</sup>.

Risk factors of HFS include dose of the chemotherapeutic agent and being a woman<sup>(2)</sup>. The presence of hyperkeratosis, eczema, fungal infection and misalignment resulting in unequal distribution of pressure are also predisposing factors that must be evaluated before starting therapy and, when necessary, treated<sup>(8)</sup>.

Topical *Aloe vera* was chosen to treat the patient's skin injuries. This gel has moisturizing, emollient, anti-inflammatory, healing and tissue healing properties<sup>(10)</sup>.

Partial remission of the patient's symptoms was observed, similar to another case report<sup>(10)</sup> that also showed a significant improvement in chemotherapy-induced HSE, using aqueous gel *Aloe vera*, based on its properties and references of use for radiotherapy-induced dermatitis. These authors indicated that there were no other studies on the use of this herbal remedy for HFS<sup>(10)</sup>. Another study showed the use of *Aloe vera* skin products to treat symptoms of HFS<sup>(11)</sup>.

Effective management of HFS consists in increasing the interval between capecitabine administration, reducing doses or interrupting treatment<sup>(12)</sup>, in accordance with medical conduct. Other measures to treat HFS include topical emollients, antibiotics to prevent secondary infections, corticosteroid creams, pyridoxine, and cyclooxygenase 2 inhibitors<sup>(1)</sup>.

## ● CONCLUSION

Considering that capecitabine is one of the most commonly used chemotherapeutic agents and its relationship with HFS, it is essential to know more about the syndrome and its clinical diagnosis. Multidisciplinary teams must be knowledgeable to take preventive measures and follow-up on treatment to improve quality of life in cancer patients. Given the positive results obtained with *Aloe vera* gel in treating HFS symptoms, further studies should be conducted to shed light on the repercussion not only of its therapeutic use, but also as a prophylactic measure for this condition.

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