Original Research Paper Medical Science

Capecitabine Induced Hand-Foot Syndrome: A Case Report

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ABSTRACT

Hand - foot syndrome affects mainly palm plantar surfaces. Clinical presentation includes dysesthesia, erythematic lesions which become painful, callous & form thickening of Horney layer.

Capecitabine, indicated in metastatic breast cancer & colorectal cancer, produces adverse effects like hyperbilirubinemia, diarrhea & Hand-foot syndrome (HFS), also called as palmer-plantar erythrodysesthesia.

A 25 year old male patient diagnosed with transverse colon signet ring carcinoma stage II A (T3N0Mx), was treated with Inj. Oxaplatin 180mg in 5% dextrose 500ml IV slowly, with Tab. Capecitabine 2000 mg orally in two divided doses. Following which he developed hand-foot syndrome on completion of two cycles of chemotherapy.

There was peeling of skin over both palms and soles. On examination hyper pigmentation, eczematization and exfoliation of both palms & soles were observed.He was treated with Cosavate G cream &Vera lotion for local application twice daily. Symptoms were relieved after two months following reduction of Capecitabine dose.

KEYWORDS Capecitabine, hand-foot syndrome, palmer-plantar erythrodysesthesia

Introduction:

Capecitabine, is fluoropyrimidine a systemic prodrug of 5-fluorouracil (5-FU).

It can be administered orally and is indicated in metastatic breast cancer & colorectal cancer[1]. The dose dependent adverse effects caused by Capecitabine include hyperbilirubinemia, diarrhea & Hand-foot syndrome (HFS) which is also called as palmer-plantar erythrodysesthesia. Several other drugs like 5-FU, Capecitabine, Cytarabine, Doxorubicin, Epirubicin, Hydroxyurea, Mercaptopurine, and Cyclophosphamide & Docetaxel are also known to cause HFS.

Hand-foot syndrome is painful erythematous lesion affecting mainly palmoplantar surfaces. The symptoms of HFS, in less severe cases are numbness, dysaethesia, tingling, erythema, painless swelling. However, in more severe cases there occurs blister formation, ulceration, desquamation with severe pain on the palm & soles.[2, 3] It hampers the day today activities of the patient, negatively affecting quality of life. Hence, treatment interruption or dose reduction required to relieve patient of symptoms[4]

Case Report:

A 25 year old male patient presented with pain in abdomen & mass in abdomen (right iliac fossa) since one year in September 2015. Patient underwent colonoscopy & biopsy which revealed ileocecal carcinoma. Further, patient was subjected to right hemicolectomy & the specimen subjected to histopathological study.

The histopathological report confirmed transverse colon signet ring carcinoma stage II A ($T_3N_0M_x$). Further chemotherapy started with Inj.Oxaplatin 180mg in 5% dextrose 500ml IV slowly along with Tab. Capecitabine 2000mg orally in two divided doses in Oct 2015. After completion of two cycles of chemotherapy in Jan 2016 patient developed peeling of skin over both palms and soles.

On examination found hyper pigmentation, eczematization and exfoliation on both palms & soles. Patient did not have dysesthesia. He was diagnosed as a case of Hand-Foot syndrome (Fig. 1 & 2) Grade II(Table:1) due to Capecitabine & was treated with topical steroids, Cosavate G cream for local application twice daily, topical emollients, Vera lotion for local application twice daily, following which his symptoms were relieved after two months.

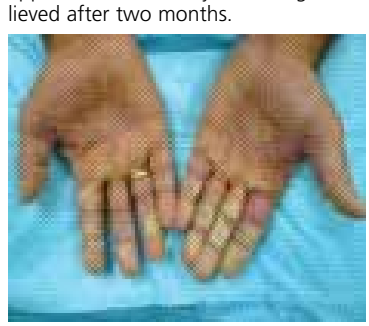

Fig-1 Exfoliative, eczematous, hyper pigmented lesions of palm

Fig-2 Exfoliative, eczematous, hyper pigmented lesions with blisters on sole.

Table: 1 Grades of severity for hand-foot syndrome.[5]

Grade	WHO	National Cancer Institute (NCI-CTCAE* Version 4.02)
I	(Decent) erythema, dysesthesia, normal activity possible	Minimal skin changes (e.g. erythema, swelling, or hyperkeratosis), no pain
II	Erythematous swelling, palmoplantar pain under mechanical stress	Skin lesions (e.g., blistering, bleeding, swelling, or hyperkeratosis) with pain and restricted daily activities
III	Painful erythematous swelling, fissures, restricted daily activity	Severe skin lesions (e.g., blistering, bleeding, swelling, or hyperkeratosis) with pain and limited autonomy
IV	Highly painful erythematous swelling, possible blistering and ulcers, impossible to perform usually daily activities	-

Discussion: -

Hand-foot syndrome which is also known as palmoplantar erythrodysesthesia was first described by Lokich & Moore in 1984[6]. Capecitabine is a prodrug which is converted to its active metabolite 5 fluorouracil by enzyme thymidine phosphorylase. As this enzyme is abundant in certain tumors, which will be targeted by active metabolite 5FU. Thus it is minimizing the side effects of active metabolite of 5 FU on host cells [7, 8, 9]

Hand-foot syndrome is a painful erythematous lesion which mainly affects palmoplantar surfaces. Clinical presentation includes initial dysesthesia & erythema which become painful & callous like thickening of Horney layer in the erythematous areas. In the thickened areas there may also be large tense blisters. HFS has been commonly reported as side effect of targeted cancer therapies with the incidence of 50-60 % [10, 11]. It causes damage to the skin is dose dependent manner after prolonged exposure.

It has been observed that there is an increase in frequency with development of HFS on combined use of Docetaxel & Capecitabine as compared to their individual usage. So also the severity of the HFS is more when they are used concurrently.[12]

Pathogenic mechanism:

The drug, 5 FU is excreted from sweat glands (eccrine sweat glands), that are abundant in palm and sole. Any micro trauma to the capillaries at the sites that are under mechanical stress causes the harmful agent to leak into the surrounding tissue showing its toxic effects.[13]

Also it is seen that there is high activity of relevant enzymes in the keratinocytes like thymidine phosphorylase which activates Capecitabine & dihydropyrimidine dehydrogenase which breaks down 5-FU & Capecitabine in palms & soles.[14, 15]

Conclusion:

Targeted chemotherapeutic agents are useful in preventing systemic side effects, though have high incidence of HFS which is rarely life threatening but hamper the quality of life. Therefore dose reduction recommended till HFS diminishes to Grade 0-I.

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