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Case Report

Two cases of palmar-plantar erythrodysesthesia induced by capecitabine

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ABSTRACT

Palmar-Plantar Erythrodysesthesia (PPE) (or) Burgdorf's Reaction (BR) (or) Hand-Foot Syndrome (HFS) is the most common and dose limiting reversible dermatologic adverse reaction induced by anticancer chemotherapy. We report two cases of palmar-plantar erythrodysesthesia (or) hand-foot syndrome of varying degree of severity induced by capecitabine.

Keywords: Burgdorf's reaction, Capecitabine, Hand foot syndrome, Palmar-Plantar erythrodysesthesia

INTRODUCTION

Capecitabine is registered for the treatment of several tumour entities, including colorectal-, gastric- and breast cancer. It is an orally administered 5-fluorouracil (5-FU) prodrug designed to mimic pharmacokinetics of infusional 5-FU.[1] Hand Foot Syndrome (HFS) was first reported in 1974 by Zuehlke in a patient who developed a syndrome of "erythematous eruption on the palms and soles" while receiving mitotane.[2] The clinical presentation of HFS is characterized by a prodorme of dysesthesia followed by development of painful, symmetrical edema and erythema of the palms, digits and soles that may evolve into blisters and erosions.[3,4] It is a common side effect of the anthracyclines (doxorubicin), taxanes (docetaxel), and pyrimidine analogues (cytarabine, 5-FU and capecitabine).[5] According to Common Terminology Criteria for Adverse Events (version 4.0), palmar-plantar erythrodysesthesia was defined as disorder characterized by redness, marked discomfort, swelling, and tingling in the palms of the hand or soles of the feet.

CASE REPORT

Case 1

A 62 year old male presented with chief complaints of pain in abdomen, loss of appetite, and bloody stools in April, 2015. On evaluation, biopsy revealed moderately differentiated adenocarcinoma and spiral CT scan of whole abdomen revealed carcinoma of stomach with liver

secondaries. He already received 3 cycles of epirubicin 70mg i.v, cisplatin 80mg i.v, and tab.capecitabine 500mg, 3 tablets after breakfast and 2 tablets after dinner for 14days. After 3rd cycle of chemotherapy he was admitted to another hospital and received 4 cycles of chemotherapy with epirubicin 70mg i.v, oxaliplatin 185mg i.v, and tab.capecitabine 500mg, 2 tablets after breakfast and 1 tablet after dinner for 21 days. After 4th cycle of chemotherapy he reported discoloration of palms and soles, peeling of skin on soles, uncomfortness while walking. Dermatological examination revealed hyperpigmentation, keratoderma of palms and soles, desquamation of soles. He was diagnosed as a case of HFS grade 3 and capecitabine was withheld. He was treated with salicyclic acid and urea ointment. The symptoms were resolved after 6 weeks.

Figure 1: Desquamation of skin of sole in patient 1.

Case 2

Figure 2: Keratinization and pigmentation of palms in patient 1.

A 45 year old woman suffered from carcinoma of the right breast in May, 2014. She was treated with adriamycin, cyclophosphamide and paclitaxel along with adjuvant radiotherapy. Again she was presented to the oncology ward in April, 2016. She was now diagnosed as a recurrent case of breast cancer with lung secondaries as new manifestation. Single agent tab. capecitabine 500mg, 3 tablets after breakfast and 2 tablets after dinner for 14 days was initiated. She successfully completed 3 chemotherapy cycles without any side effects. After the completion of the 3rd chemotherapy cycle, she reported discoloration of palms and soles, uncomfortable while walking due to pain. Dermatological examination revealed hyperpigmentation, keratinization like features of palms and soles. She was diagnosed as a case of HFS grade 2.

Figure 3: Figure 2: Keratinization and pigmentation of soles in patient 2.

DISCUSSION

HFS is a common, dose dependent and reversible adverse reaction often noticed with some chemotherapeutic agents as well as from tyrosine kinase inhibitors like sorafenib, sunitib etc. Information about pathogenesis and histopathological changes in HFS was remained unclear. Some recent studies suggest that cyclooxygenase 2 (COX-2) overexpression might be a potential mediator for development of HFS.[6] It would also appear that cytostatic pathway may mediate a toxic effect on basal keratinocytes, so that the high turnover rate of these cells could explain their particular susceptibility and also play a role on the preferential palmar and plantar presentation.[7]

Severe form of HFS is disabling and certainly impairs the quality of life of the patient. Although, life threatening complications rarely occur in HFS, a case report of death due to bacterial sepsis by pseudomonas super infection was reported.[8] Quality of life impairment among patients

with HFS can be determined by using HFS-14, a specific quality of life scale developed for patients suffering from HFS. This would allow early modification of cancer treatment and initiation of symptomatic therapy to avoid further treatment modification.[9]

Even after 30 years of reports related to this adverse event, scarce information points to an effective treatment or prevention. Furthermore, with the advent of new drugs such as multikinase inhibitors in this era of targeted therapy, the presence of HFS shall remain a limiting factor for more years to come.[10] Prevention of HFS would be imperative to avoid treatment delays and interruptions. Celecoxib appears to be the most promising agent for the prevention of HFS. A larger, multicenter, double blind trial is necessary; however, to confirm this hypothesis.[10] Topical adapalene when applied for 3 months significantly reduced the inflammation and pain following chemotherapy. Topical retinoids may have the potential to effectively treat capecitabine induced HFS.[11] Pyridoxine was not found to be effective to prevent HFS associated with capecitabine therapy.[12]

Topical emollients for soothening skin, antibiotics to prevent infections, steroids to prevent inflammation are other treatment strategies that can minimize the effects of HFS. Alteration of dose or discontinuation of treatment in case of severe form of HFS (grade 3) is strongly advised. Topical cream of salicyclic acid and urea ointment and discontinuation of treatment are the preventive measures used for case1, whereas dose reduction was the preventive measure used for case 2.

CONCLUSION

HFS-14 specific quality of life scale use would allow early modification of cancer treatment and initiation of symptomatic therapy to avoid further treatment modification. Prevention approaches would be imperative to avoid dose reduction and discontinuation of drug, possibly relating to improved disease outcomes and thus better care. Celecoxib was reported to be effective among other prevention measures and it should be used cautiously in patients having cardiovascular disease.

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