Capecitabine-Induced Muco-Cutaneous Manifestations – A Descriptive Cross-Sectional Study from a Tertiary Care Center

Dear Editor,

Capecitabine is an oral chemotherapeutic agent which is a prodrug of 5-fluorouracil and a selective inhibitor of the enzyme thymidylate synthase, commonly used for solid organ cancers. It is usually used for gastrointestinal cancers, hepatobiliary, pancreatic, and breast cancers. Capecitabine is known to cause several muco-cutaneous manifestations like hand foot syndrome (HFS), stomatitis, skin pigmentation, nail pigmentation, and rash.[1]

This is a descriptive cross-sectional study done in a tertiary care center after ethical considerations in a cohort of patients who were given capecitabine from the oncology department. The inclusion criteria included all cancer patients who were started on capecitabine monotherapy as first-line chemotherapy, while exclusion criteria were patients receiving combination chemotherapy with capecitabine and concurrent radiation therapy.

The data collected were analyzed in terms of descriptive statistics.

There were 60 cases in this study (n = 60), 39 males (65%) and 21 females (35%) with a male/female ratio of 1.86:1. Majority of the patients belonged to the age group 60–69 (21 cases, 35%). Colo-rectal cancer was the commonest indication for capecitabine therapy, given for 44 cases (73.3%). Muco-cutaneous adverse effects were observed in 58 patients (96.7%). The various muco-cutaneous manifestations are given in Figure 1. HFS was the commonest muco-cutaneous adverse effect observed in 40 patients (66.7%) [Figure 2]. HFS was seen more in males, 30 patients (30/40, 76.9%), and this was statistically significant (P = 0.043). HFS was most seen in colorectal cancer, accounting for 31 patients (31/44, 70.46%). The commonest combination was HFS with hyperpigmentation off palms and soles, seen in 20 patients (33.3%). The various muco-cutaneous manifestations in relation to organ-specific malignancy are given in Table 1. Nail pigmentation was the commonest nail change (8/12, 66.7%). Stomatitis was most seen in colo-rectal cancer, and this was statistically significant (P = 0.008) [Figure 3].

Majority of the patients (35%) in this study who developed reactions were in the seventh decade of life. This is consistent with other studies. Hence, it can be surmised that the incidence of mucocutaneous adverse effects increases with age.[2] There was a male predominance (65%) in our study. This is because the commonest malignancy in this cohort was colo-rectal, which was seen more in males, and the muco-cutaneous adverse reactions were most common in this group. The overwhelming majority of the patients in this study (96.7%) developed cutaneous adverse reactions. Similar studies show a prevalence of 17% to 60% in capecitabine-induced cutaneous adverse reactions.[3,4] The increased incidence of cutaneous adverse reactions in this study could be due to racial factors. HFS was the commonest cutaneous adverse effect noted in this study (66.7%).

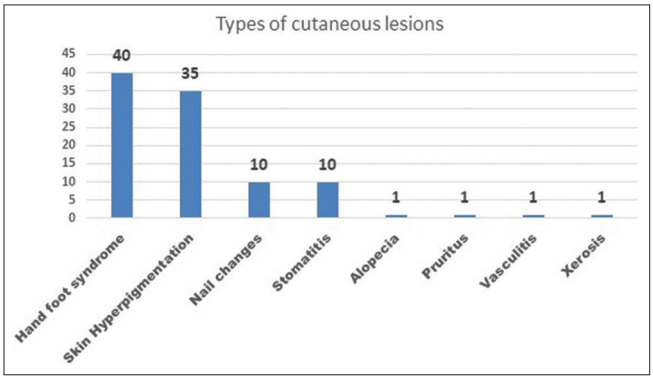

Figure 1: Graph showing muco-cutaneous manifestations of capecitabine

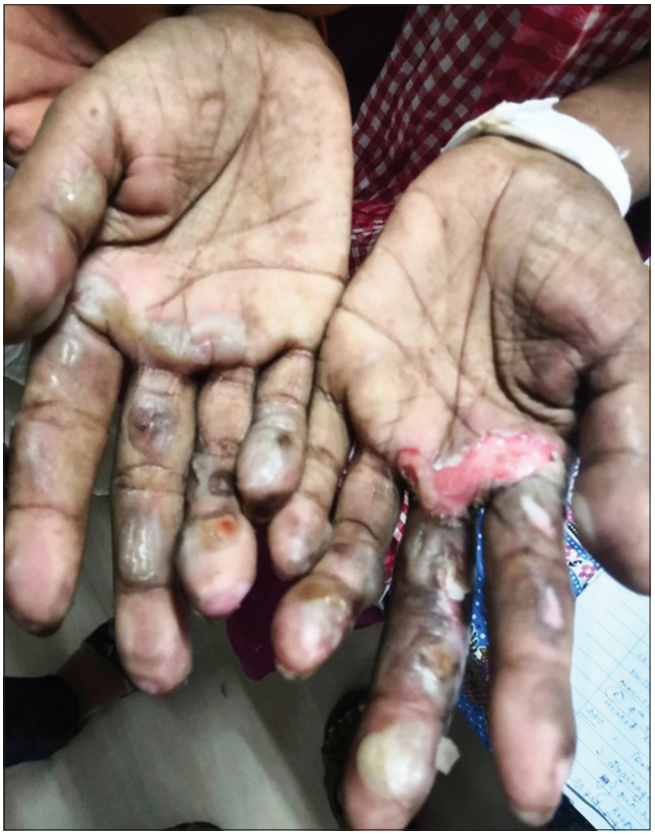

Figure 2: Erythema, edema, blisters, and erosions of hand foot syndrome

Table 1: Muco-cutaneous manifestations in relation to organ malignancy

Muco-cutaneous adverse effects	Malignancy (No. and %)				
	Colorectal	Breast	Pancreas	Hepato-biliary	Gastroesophageal
Hand foot syndrome	31 (70.5%)	6 (60%)	3 (100%)	0 (0)	0 (0)
Hyperpigmentation	27 (61.4%)	7 (70%)	1 (33.3%)	0 (0)	0 (0)
Nail changes	8 (18.2%)	2 (20%)	1 (33.3%)	1 (50%)	0 (0)
Stomatitis	7 (15.9%)	0 (0)	3 (100%)	0 (0)	0 (0)
Alopecia	1 (2.5%)	0 (0)	0 (0)	0 (0)	0 (0)
Pruritus	1 (2.5%)	0 (0)	0 (0)	0 (0)	0 (0)
Xerosis	1 (2.5%)	0 (0)	0 (0)	0 (0)	0 (0)
Vasculitis	1 (2.5%)	0 (0)	0 (0)	0 (0)	0 (0)

Figure 3: Capecitabine-induced stomatitis

Majority were of grade 1 (75%), and 62.5% developed after a latency of three cycles of therapy. Most studies have shown HFS to be the commonest cutaneous adverse reaction to capecitabine with prevalence rates ranging from 57 to 60%.[5] Our study and the aforementioned studies also showed that the adverse reactions are more common after multiple cycles of therapy (three or more). In the present study, HFS was more common in males, and this was significant (P = 0.043). This could be that since HFS most occurred in colo-rectal cancers, and this was seen more in male patients. HFS clinically starts as a prodrome of dysesthesia on palms and soles, followed by a well-defined, symmetric, painful erythema and edema, later progressing to blisters, erosions, and ulcerations. The exact mechanism of HFS is not known. The mechanism suggested is that the metabolites of capecitabine are excreted through eccrine sweat glands, which are abundant in palms and soles which causes the lesions. The lesions are self-limited and respond to emollients and topical steroids.

Hyperpigmentation of the palms and soles was the next common cutaneous adverse reaction in this study seen in 58% of the subjects. In 20 cases, this was also associated with HFS. The incidence of hyperpigmentation in this study is much higher than in similar studies, but this could be attributed to the fact that the present study was conducted in subjects with Fitzpatrick skin types 3 and 4.[4,5]

Stomatitis was seen in 16.7% of patients presenting as cheilitis, glossitis, and ulcers on the buccal mucosa. This was consistent with other studies.[3-5]

Nail changes were seen in 20%, characterized by pigmentation, nail loss, and paronychia. Nail changes were most seen in colo-rectal cancers and in association with HFS, similar to other studies.

Early recognition and treatment of capecitabine-induced adverse reactions facilitates a satisfactory control and cure of the manifestations, decreasing morbidity and allowing further continuation and maintenance of the chemotherapy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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