

Development of phimosis as an adverse drug reaction to capecitabine with irinotecan

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ABSTRACT

We present a case of a 32-year-old male who developed capecitabine-induced phimosis which resolved spontaneously without the need for circumcision within a few days of discontinuation of chemotherapy. The patient was on capecitabine with irinotecan chemotherapy for peritoneal metastasis from adenocarcinoma of the lower esophagus. A detailed literature review showed a few case reports with penile and scrotal erythema, ulceration, and swelling along with hand-foot syndrome, but none reported the occurrence of phimosis with spontaneous resolution.

CASE REPORT

A 32-year-old male was on capecitabine with irinotecan (CapeIRI) chemotherapy (palliative) for metastatic adenocarcinoma of the lower esophagus. During the third cycle, he developed painless erythema, followed by dry skin with marked discoloration over the soles, palms, and digits. The patient also noticed that skin over the soles, palms, and digits was getting peeled off exposing the underlying thick dermis (Figure 1a and 1b). All these features were consistent with the diagnosis of hand-foot syndrome (HFS) Grade I (National Cancer Institute). The patient also developed a fibrous ring over the prepuce and he had difficulty in retracting the prepuce at that time. After completion of the third cycle, he was not able to retract the prepuce and he was referred to the urology department (Figure 1c and 1d). The patient did not have any difficulty in voiding. On examination, we found tight phimosis with erythema over the foreskin. The patient was advised to discontinue chemotherapy until the resolution of HFS. One month after stopping the chemotherapy, the inflammation subsided and spontaneous resolution of HFS was noted (Figure 2a and 2b). There was also spontaneous resolution of phimosis, and the patient was able to retract

the preputial skin (Figure 2c and 2d). He was again started on the same chemotherapy regimen, and till last follow-up, he had completed seven cycles without developing phimosis or HFS again.

DISCUSSION

Capecitabine is an oral chemotherapeutic agent used in treating several malignancies. It metabolizes to 5-fluorouracil (5-FU), and this 5-FU metabolite is responsible for its side effects. Capecitabine is generally well tolerated. The most common adverse drug reaction is HFS or palmar-plantar erythrodysesthesia (PPE). HFS is characterized by redness, marked discomfort, swelling, and tingling in the palms of the hands or the soles of the feet. HFS is frequently seen with the use of many chemotherapeutic agents like capecitabine, 5FU, docetaxel, and liposomal doxorubicin.^[1] The exact mechanism behind capecitabine-induced HFS is unclear. As reported by Asgari *et al.*,^[2] capecitabine causes increased levels of thymidine phosphorylase in the keratocytes, leading to capecitabine metabolite accumulation, and affecting eccrine glands. Others postulated the theory that it occurs due to an inflammatory reaction caused by the rupture of tiny capillaries in the pressure areas due

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Received: 22.05.2022, **Revised:** 17.06.2022,

Accepted: 26.08.2022, **Published:** 01.10.2022

Financial support and sponsorship: Nil.

Conflicts of interest: There are no conflicts of interest.

Access this article online	
Quick Response Code:	Website:
	www.indianjurol.com
	DOI:
	10.4103/iju.iju_169_22



Figure 1: (a and b) Phimosis with thickened foreskin—not possible to retract. (c and d) Dry skin with marked discoloration and peeling off skin noted over palms, soles, and digits, features suggestive of Grade I hand-foot syndrome

to daily activity.^[3] Another hypothesis is related to the cyclooxygenase (COX-2)-mediated inflammatory reaction. One more hypothesis is related to dihydropyrimidine dehydrogenase (DPD) deficiency. DPD is an enzyme required for the rate-limiting step in the metabolism of 5-FU.^[4]

Usually, patients with HFS may experience dysesthesia, followed by painful, symmetrical swelling, and erythema of the palms, digits, and soles which may further result in blisters or erosions. The current grading system commonly used is given by the National Cancer Institute (NCI) [Table 1]. Very few cases of genital involvement are reported. Sapp. *et al.*^[5] reported erythema, painful ulceration, and swelling over the penis and scrotum in two cases associated with HFS due to capecitabine use. However, neither of the patients had phimosis.

There are various treatment options for the management of HFS including topical agents (steroids and retinoids) and systemic therapy, but their role is unclear. In our patient, no topical or systemic treatment was advised. The role of COX-2 inhibitors and pyridoxine (Vitamin B6) in preventing and managing manifestations of HFS is also doubtful. Other modalities include the use of systemic antibiotics to prevent infection, cold compression over extremities, and use of petroleum jelly over ulcerated/dry skin to trap moisture.

CONCLUSION

We report a very rare case of phimosis with HFS caused by capecitabine which resolved spontaneously. In such patients, a trial of spontaneous resolution of the phimosis may be recommended before circumcision.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his



Figure 2: (a and b) Easily retractable foreskin with complete resolution of phimosis after temporarily stopping capecitabine. (c and d) Resolution of hand-foot syndrome after temporarily stopping capecitabine

Table 1: Grading system for hand-foot syndrome by the National Cancer Institute

Grade	Clinical features
Grade 1	Minimal skin changes or dermatitis (e.g., erythema, edema, or hyperkeratosis) without pain
Grade 2	Skin changes (e.g., peeling, blisters, bleeding, edema, or hyperkeratosis) with pain, limiting instrumental ADL
Grade 3	Severe skin changes (e.g., peeling, blisters, bleeding, edema, or hyperkeratosis) with pain, limiting self-care ADL

ADL=Activities of daily living

consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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How to cite this article: Patel P, Mishra NN, Patel T. Development of phimosis as an adverse drug reaction to capecitabine with irinotecan. *Indian J Urol* 2022;38:307-8.