



CASE REPORT

# Case Report: Non-infectious causes of palmoplantar rashes, what to consider [version 1; referees: 2 approved, 1 approved with reservations]

Rashmi Advani , Danit Arad

Department of Internal Medicine, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, NY, 10467, USA

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**Abstract**

**Background:** Palm and sole skin eruptions have a broad differential diagnosis. It is particularly important to recognize common causes as well as their association with certain chemotherapy regimens such as Capecitabine.  
**Case report:** A 79-year-old woman presented with a painful rash on her hands and feet for 1 week. She had metastatic colon cancer and was in her third week of treatment with capecitabine. Her diagnosis was a medication side-effect from chemotherapy. Capecitabine was stopped and she had some clinical improvement over the next two days. She was discharged with oncology follow up for resumption of Capecitabine at a lower dose with improvement in her rash 3 weeks later.  
**Discussion:** Skin rashes are a commonly encountered complaint in patients in the inpatient and outpatient setting. It is important to maintain a broad differential diagnosis in those with rashes of the palmoplantar surfaces of the hands and feet. Recognizing skin changes as a possible manifestation of underlying malignancy or a medication side-effect is key in appropriate diagnosis and treatment.

**Open Peer Review**

Referee Status: 

	Invited Referees		
	1	2	3
<b>version 1</b> published 11 Jan 2018	 report	 report	 report

- Sidharth Sonthalia** , Skinnocence: The Skin Clinic & Research Center, India
- Mohamed Badawy Abdel-Naser**, Ain Shams University Hospital, Egypt
- Regina Fölster-Holst**, Universität Kiel, Germany

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**Corresponding author:** Danit Arad ([darad@montefiore.org](mailto:darad@montefiore.org))

**Author roles:** Advani R: Conceptualization, Data Curation, Investigation, Writing – Original Draft Preparation, Writing – Review & Editing; Arad D: Resources, Supervision, Validation, Visualization

**Competing interests:** No competing interests were disclosed.

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## Introduction

Palmoplantar skin eruption is a commonly encountered diagnosis in the inpatient and outpatient setting. Most likely causes include Type IV hypersensitivity reactions (i.e. contact dermatitis), tinea pedis/manuum, psoriasis, and dyshidrotic dermatitis. These rashes may also be associated with underlying malignancies, especially gastrointestinal malignancies or can be associated with a medication side-effect<sup>1</sup>. Palmoplantar erythrodysesthesia (PPE), also known as hand-foot syndrome is a toxic, cutaneous side effect of well-associated chemotherapeutic agents, especially capecitabine<sup>2-4</sup>. The pathophysiology of this condition is not well understood and is an active area of investigation. It is important to recognize this side effect early in patients treated with oral capecitabine chemotherapy and to differentiate it from similar presentations in other disease entities. We present a case of a woman on chemotherapy for metastatic colon cancer with a palmoplantar rash.

## Case report

A 79- year-old Hispanic woman presented with a one-week history of painful rash on her palms and soles. She reported no recent viral illness, travel, previous rashes, joint pains, new lotion, soap or fabric use. She had metastatic colon cancer previously treated with radiation and hemicolectomy three years prior. She currently completed her second week of Capecitabine therapy (1,250mg/m<sup>2</sup> twice a day). She had no other contributory medical history or family history and was on no other medications. She describes never having a similar rash in the past.

On physical exam, she was afebrile, normotensive and appeared chronically ill. Her palms and soles were tender to touch, erythematous, and diffusely edematous with desquamation over the fingertips and toes (Figure 1 and Figure 2). Biochemical



**Figure 1.** Erythema, swelling, and desquamation of the palmar surfaces.



**Figure 2.** Erythema, swelling, and desquamation of the plantar surfaces.

testing including complete metabolic panel and complete blood count were normal. Given her recently administered chemotherapy, it was suspected that the patients' palmoplantar rash was a result of a medication side-effect from Capecitabine. Other less likely diagnoses were contact dermatitis, tinea pedis/manuum, or dyshidrotic dermatitis.

After Capecitabine was stopped, she had mild clinical improvement over the next two days. She was discharged with resumption of Capecitabine at a lower dose (565 mg/m<sup>2</sup> twice daily) and had complete clinical resolution of her rash 3 week later.

## Discussion

Palmoplantar skin eruption carries a varied differential diagnosis. Common causes include contact dermatitis, tinea pedis/manuum, psoriasis, dyshidrotic dermatitis and palmoplantar pustulosis. Other palmoplantar rashes such as palmoplantar keratoderma (PPK), Acanthosis Nigricans (AN), Tripe palm, and Acquired Ichthyosis are also associated with underlying malignancies<sup>5,6</sup>. PPK presents with a yellow, wax-like hyperkeratosis of the palms and soles. AN, seen in patients with insulin resistance, presents as palmoplantar plaques which can be a sign of internal gastric cancer<sup>6</sup>. Tripe palm, also associated with gastric and lung malignancies, presents with wrinkled velvety hyperkeratosis of the palmoplantar surfaces<sup>7</sup>. Lastly, acquired ichthyosis is a symmetric scaling of the skin, associated with Hodgkins lymphoma<sup>8</sup>.

Since our patient had a temporal relationship between initiation of a new medication and her presentation, it was likely related, if not the cause of her palmoplantar rash. Chemotherapy, such as Capecitabine, is an important cause of palmoplantar skin eruption known as palmoplantar erythrodysesthesia (PPE). It is characterized by pain, swelling and desquamation, which can progress to ulceration and blistering (Figure 1 and Figure 2). In total, 7%

of patients treated with Capecitabine may experience PPE. Other commonly encountered chemotherapy regimens may also cause PPE, such as Cytarabine, Fluorouracil, and Doxorubicin. Treatments include either withdrawal of the chemotherapy or dose reduction, and supportive measures. In our patient's case, we were limited by not being able to completely stop chemotherapy given her limited therapeutic options; however resuming treatment at a lower dose helped to resolve her symptoms as well as provide a longer life-expectancy.

Common diagnoses aside, medication side-effect and malignancy should be considered in the differential diagnosis of palmoplantar skin eruption to guide appropriate therapy.

## Consent

Written informed consent was obtained from the patient for the publication of the patient's clinical details and accompanying images.

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## Competing interests

No competing interests were disclosed.

## Grant information

The authors declare that no grants were involved in supporting this work.

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# Open Peer Review

Current Referee Status:



Version 1

Referee Report 05 March 2018

doi:10.5256/f1000research.14673.r30832



**Regina Fölster-Holst**

Dermatologische Klinik, Universität Kiel, Kiel, Germany

The authors describe a 79-year old woman presented with palmoplantar rash. This was characterized by painful erythema, edema and desquamation. In this case the history led to the right diagnosis: the woman suffered from metastatic colon cancer and underwent chemotherapy with capecitabine.

There are other diagnoses to be considered in patients with these clinical findings. Only some of them are mentioned by the authors. For the readers a table with differential diagnoses and typical clinical and anamnestic criteria would have been helpful to differentiate between these diagnoses.

**Is the background of the case's history and progression described in sufficient detail?**

Yes

**Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?**

Yes

**Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?**

Yes

**Is the case presented with sufficient detail to be useful for other practitioners?**

Yes

**Competing Interests:** No competing interests were disclosed.

**Referee Expertise:** Pediatric dermatologist, dermatologist

**I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

Referee Report 27 February 2018

doi:10.5256/f1000research.14673.r30831



**Mohamed Badawy Abdel-Naser**

Department of Dermatology and Venereology, Ain Shams University Hospital, Cairo, Egypt

The case report is well written.

The title is not addressing the case. Perhaps it can be reformulated to directly refer to the case.

The statement "however resuming treatment at a lower dose helped to resolve her symptoms as well as provide a longer life-expectancy" - how does reduction of the dose provide longer life-expectancy?

The provided figures, particularly Figure 2, are not clear.

Was any local treatment given to the patient?

**Is the background of the case's history and progression described in sufficient detail?**

Yes

**Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?**

Partly

**Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?**

Partly

**Is the case presented with sufficient detail to be useful for other practitioners?**

Yes

**Competing Interests:** No competing interests were disclosed.

**I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.**

Referee Report 21 February 2018

doi:[10.5256/f1000research.14673.r30835](https://doi.org/10.5256/f1000research.14673.r30835)

**Sidharth Sonthalia** 

Department of Dermatology & Dermatosurgery, Skinnocence: The Skin Clinic & Research Center, Gurgaon, India

1. The title could have been better - "Non-infectious causes of palmoplantar rashes, what to consider" would have been more apt in a case where there was diagnostic confusion based on history and/or examination. In this case, the history of malignancy and the ongoing chemotherapy was forthcoming. Emphasizing upon the fact that one MUST investigate for concurrent malignancy and chemotherapy, to consider non-infectious cause of the hand and foot syndrome (HFS) in a patient

who is presenting with the classical clinical features of HFS and history of capecitabine, the most common chemotherapeutic agent responsible for this condition.

2. Although, despite a strong evidence (history of malignancy and capecitabine) of the etiology of palmo-plantar erythrodysesthesia or HFS, the authors mention that they were considering other less likely diagnoses such as contact dermatitis, dyshidrotic eczema and tinea pedis/manuum. But no confirmatory investigations were done to rule them out. A 10% KOH smear and a punch biopsy should have been taken if these conditions were still being suspected.
3. Ideally, the authors should have mentioned about the state of the nails of the patient also, which often become dystrophic alongwith HFS.
4. It would have been better if the authors had also graded the patient's HFS; in view of the three well-established grading systems in place (WHO, NCI, and one system proposed by Nikolaou et al.<sup>1</sup> especially for darker skin types) that have also been documented to guide regarding the therapeutic approach. Similarly, it would have been better if the patient's quality of life (QoL) affected by HFS was quantified using the simple HFS-14 scale. Nikolaou et al have demonstrated that HFS-14 scale may identify differences in QoL impairment between patients with HFS of same clinical grade and may serve as a valuable tool for anticancer treatment management and assessment of clinical efficacy of treatments used for this condition.
5. The authors should have at least made a mention of an important differential of HFS, i.e. HFS reaction (HFSR) that predominantly involves the pressure-prone areas of the soles and typically arises as a reaction to multiple kinase inhibitors (MKI).
6. Since the HFS was not quantified, nor the patient's morbidity due to pain (limitation of instrumental vs self-care activities) has been mentioned, based upon the relatively scarce data on physical examination, the patient seems to qualify for NCI grade 2 HFS. The approach to management in grade 2 has been recommended to stop the chemotherapy for a short duration till the condition improves to grade 1 or 0 (which was done in the current case) followed by resumption at lower doses. However, there are many practical measures and simple drugs/topical applications which if followed could have expedited the improvement such as avoidance of mechanical stress, use of cold compresses, generous moisturization with a urea-containing cream, and potent topical corticosteroids for a short duration. In fact prophylactic oral pyridoxine and celecoxib (COX-2 inhibitor) have also been suggested for a patient with NCI grade 2 HFS.
7. It is true that in this particular patient, as per the authors' description, uneventful remission occurred within 2-3 weeks of 2-day cessation followed by resumption at low doses of capecitabine, the report would have given out a more wholesome message to the readers if the treatment modalities other than the stoppage of the chemotherapeutic agent were at least mentioned.

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## Is the background of the case's history and progression described in sufficient detail?

Partly

**Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?**

Partly

**Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?**

Partly

**Is the case presented with sufficient detail to be useful for other practitioners?**

Partly

**Competing Interests:** No competing interests were disclosed.

**Referee Expertise:** Systemic dermatology, dermoscopy, pigmentary disorders

**I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.**

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