

## REVISION LETTER

14<sup>th</sup> of August 2016



**Number ID:** 01220111

**Publication Name:** World Journal of Clinical Cases

**Manuscript Type:** Case Report

**Author:** Cohen, PR

**Title:** Paclitaxel-Associated Reticulate Hyperpigmentation: Report And Review Of Chemotherapy-Induced Reticulate Hyperpigmentation

**Manuscript Type:** Case Report

**ESPS manuscript NO: 28069**

Dear Fang-Fang Ji and Xiu-Xia Song:

I respectfully submit my revised manuscript to be considered for publication in the World Journal of Clinical Cases. I appreciate the constructive criticisms of each of the reviewers. The reviewers conclusion recommendation were very favorable--either accept (3 reviewers) or high priority for publication (1 reviewer) or minor revision (1 reviewer). Only 1 of the 6 reviewers recommended major revision.

I have incorporated the recommendations of the reviewers into the revised paper or addressed their comments below or both.

Reviewer: 00504731

Classification: Grade B: Very good

Language Evaluation: Grade A: Priority publishing

Conclusion: Accept

Comments to Author:

*This manuscript reported a case pigmentation after treatment with paclitaxel. The author also reviewed the literature on this phenotype, and provided some pathological examination of the pigmentation area. The manuscript is well written and is worthy of publication.*

I am pleased that the reviewer found the manuscript to be very good and for it to be considered for priority publishing with an overall conclusion to accept the paper. I appreciate that the reviewer found the manuscript to be “well written and is worthy of publication.”

Reviewer: 00504024

Classification: Grade B: Very good

Language Evaluation: Grade A: Priority publishing

Conclusion: High priority for publication

Comments to Author:

*It is interesting and worthy for publication.*

I am pleased that the reviewer found the manuscript to be very good and for it to be considered for priority publishing with an overall conclusion for high priority for publication of the paper. I appreciate that the reviewer found the manuscript to be “interesting and worthy for publication.”

Reviewer: 00505633

Classification: Grade C: Good

Language Evaluation: Grade B: Minor language polishing

Conclusion: Accept

Comments to Author:

*Nicely written.*

I am pleased that the reviewer found the manuscript to be good and for it to be considered for publishing after minor language polishing with an overall conclusion to accept the paper. I appreciate that the reviewer found the manuscript to be “nicely written.”

Reviewer: 02680711

Classification: Grade D: Fair

Language Evaluation: Grade B: Minor language polishing

Conclusion: Accept

Comments to Author:

*General comments to author and editor-This report chronicles the development of a dermal toxic reaction presumably due to paclitaxel. The reaction and report of such is, in one instance, somewhat unique, yet at the same time, potentially confounding.*

*Specific comments to the author-*

*1.As written, the skin reaction appears to be closely related to paclitaxel. However, in order for the skeptical reader to be convinced, it is important to include Naranjo scoring.*

According to Naranjo et al's adverse drug reaction presentation scale, chemotherapy-associated reticulate hyperpigmentation developing as an adverse drug reaction induced by paclitaxel would be assigned to a definite probability category for the reported patient. This information has been added to the discussion (paragraph 8) and summarized in Table 2. In addition, Naranjo et al's paper is cited in the references section (#10); the papers in the reference section and throughout the manuscript have been appropriately renumbered.

*2.The discussion section is lengthy and could easily be contracted; the conclusion as well.*

The details provided in the discussion section are intended to be comprehensive since this is a world literature review of all previously reported patients with chemotherapy-induced reticulated hyperpigmentation. Similarly, the conclusion section presents a succinct, yet complete, summary of the manuscript.

*3.Lastly, it would be of interest to know if this patient has a history of allergies or allergic reactions.*

The patient had a prior history of an allergic reaction after receiving zoledronic acid – a biphosphonate that is used in patients with metastatic cancer to prevent bone complications. This information has been added to the case report: paragraph 1, sentences 2 and 3.

*In summary, the paper is informative though not necessarily provocative. The incidence of this particular drug-related toxicity is relatively low. While the paper may be of interest to some, I suspect, overall, it will have little impact.*

I am pleased that the reviewer found the manuscript to be fair and for it to be considered for publishing after minor language polishing with an overall conclusion to accept the paper. I appreciate that the reviewer found the manuscript to be “unique, informative, and of interest to some.” Responses to each of the specific comments are provided beneath each comment.

Reviewer: 01560575

Classification: Grade C: Good

Language Evaluation: Grade A: Priority publishing

Conclusion: Minor revision

Comments to Author:

*Major comments-Cohen PR reported a case with paclitaxel-associated reticulated hyperpigmentation and reviewed ten cases of a same kind. English writing is excellent and this case report may be acceptable for publication in World Journal of Case Reports if some minor comments listed below are addressed.*

*Minor comments-*

*1. Provide page number in the manuscript.*

Page numbers are provided in the manuscript.

*2. Page 8, lines 4. ...[D]uring...her fourth cycle...she was...should be: During her fourth cycle, she.*

This has been corrected: “During her fourth cycle, she...” (discussion section, paragraph 5 sentence 4).

*3. Page 11, lines 16. “the hyperpigmentation partially or completely resolved in 83%” should be “The hyperpigmentation partially or completely resolved in 83%.”*

This has been corrected: “The hyperpigmentation partially or completely resolved in 83%” is now a separate sentence instead of following the colon (discussion section, last paragraph, sentence 3).

*4. Provide figures of biopsy specimen histology of normal skin for comparison against reticulate hyperpigmentation.*

Figures of the biopsy specimen histology of normal skin for comparison against reticulate hyperpigmentation are provided (Figures 7 and 8). The figures are cited in the case report

and included in the legends section.

I am pleased that the reviewer found the manuscript to be good and for it to be considered for priority publishing with an overall conclusion that this case report may be acceptable for publication in World Journal of Case Reports after minor revision. I appreciate that the reviewer found that the “English writing is excellent.” Responses to each of the minor comments are provided beneath each specific comment.

Reviewer: 01559576

Classification: Grade C: Good

Language Evaluation: Grade B: Minor language polishing

Conclusion: Major revision

Comments to Author:

*Major-*

*The patient experienced malar hyperpigmentation by the preceding capecitabine and reticulated hyperpigmentation by paclitaxel. Do the authors think these two hyperpigmentation occurred by the same mechanism? If no, how was the each mechanism?*

The case report has been expanded and additional history has been provided. The patient’s malar hyperpigmentation is considered to be postinflammatory following erythema on the sun-exposed areas of her face after she began capecitabine. This information is added: case report section, paragraph 4, sentence 3.

*Discussion is too long, and redundant description should be avoided. Table 1 expresses most part of discussions. For example, paragraphs 1 to 6 of the discussion section could be omitted because they are provided in table 1.*

The first six paragraphs of the discussion provide additional clarity for the reader; they not only present, but also summarize, the features of those individuals with chemotherapy-induced reticulate hyperpigmentation. Table 1 provides a succinct composite of these features.

*In discussion, the putative or plausible mechanisms why reticulated hyperpigmentation could occur should be described.*

The pathogenesis of chemotherapy-induced reticulate hyperpigmentation remains to be

established. It has been hypothesized that the hyperpigmentation results from a secondary increase in melanogenesis caused by a direct toxic effect of the chemotherapy on the melanocytes. In addition, local changes in blood flow may partially account for the lesions being located in areas of contact, such as the back and buttocks. This information has been added to the discussion section, second to last paragraph.

*Minor-*

*The regimes of paclitaxel should be provided.*

The regime of paclitaxel--80 mg/m<sup>2</sup> intravenous weekly therapy--is provided: case report, paragraph 5, sentence 1.

*Did the patient receive premedication to prevent hypersensitivity reactions?*

Yes, the patient was premedicated prior to each treatment with paclitaxel to prevent hypersensitivity reactions. She received intravenous dexamethasone (10 mg) and famotidine (20 mg) and intramuscular diphenhydramine (25 mg). This information is added to the case report: paragraph 5, sentences 2 and 3.

*The photos of interface dermatitis should be provided and discuss the difference from reticular hyperpigmentation.*

Clinical images of paclitaxel-induced interface dermatitis are added (Figures 9a, 9b, 9c and 10). They are cited in the case report and discussion of the clinical presentation is included in the legends section.

*Did the reticular hyperpigmentation occur by faslodex and palbociclib?*

No. Chemotherapy-induced reticulate hyperpigmentation did not occur after the patient received faslodex and palbociclib. This information is added to the case report: final paragraph, final sentence.

*What is (6/7, X%)?*

The text has been corrected and reads: (6/7, 86%) (discussion section, paragraph 10, sentence 1).

*For the review of the literature, the key words for electronic search and Database should be described in the Methods.*

Case reports in the Journal do not have a Methods section. However, I concur with the reviewer that the key words for electronic search and Database should be included for the review of the literature. This information has been added to the discussion section:

paragraph 2, sentences 1 and 2.

*In discussion, the authors described breast cancer being the most common solid tumor; however, from only 10 case records (table 1), the incidence of malignancies showing reticulate hyperpigmentation could not be concluded.*

I concur with the comment of the reviewer that the incidence of malignancies showing reticulate hyperpigmentation cannot be concluded from only 10 case records. The text (discussion, paragraph 11, sentence 3) has been appropriately revised to described the number of patients with each cancer: breast cancer was the underlying neoplasm in two women; other metastatic solid tumors, each in one patient, were gastrointestinal tract cancer, mucoid epidermoid carcinoma of the parotid gland, and ovarian carcinoma.

I am pleased that the reviewer found the manuscript to be good and for it to be considered for publishing after minor language polishing with an overall conclusion to request major revision. I appreciate that the reviewers thoughtful comments to consider during the revision of the manuscript.

**\*\*\*\*\*IMPORTANT\*\*\*\*\***

**Some of the figures in the pdf of the 'submitted manuscript' are not in the correct order. Please see the correct designation of the manuscript figures; it would be my pleasure to review the pdf once the figures have been correctly ordered:**

**Figure 1 – all images are correctly labeled and in correct order**

**Figure 2:**

**First image should be Figure 2c**

**Second image is correct: Figure 2b**

**Third image should be Figure 2a**

**Figure 3:**

**First image should be Figure 3d**

**Second image should be Figure 3c**

**Third image should be Figure 3b**

**Fourth image should be Figure 3a**

**Last (fifth) image is correct: Figure 3e**

**Figure 4**

**First image should be Figure 4b**

**Second image should be Figure 4a**

**Figures 5 and 6-- all images are correctly labeled and in correct order**

I sincerely hope that my revised manuscript is now in suitable form to be accepted for publication. Please feel welcome to contact me with any additional recommendations.

As requested in my letter of August 14, 2016 and the response of Fang-Fang Ji (The extension is no problems and attached files are the format for the case report paper. if you have other problems, please contact with me.), I appreciate your approving the extension of my submission of the revised paper to October 4, 2016. I am pleased to provide the paper prior to the due date.

Sincerely yours,



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