

Name of Journal: *World Journal of Clinical Cases*

Manuscript NO: 54817

Manuscript Type: CASE REPORT

Epidermolytic Acanthoma: Case Report and Review of the Literature

Ginsberg A, Rajagopalan A, and Terlizzi J. Epidermolytic Acanthoma

Dear Dr. Jin-Lei Wang,

We would like to sincerely thank you for considering our manuscript and also thank the reviewers for their expertise and thoughtful comments. Below we outline our response to the reviewers' comments and indicate the revisions we have made.

In response to Reviewer 1's comments:

"The authors in this paper describe a patient who presented with perianal Epidermolytic Acanthoma and review the current literature. The case report is convincing, and the paper is scientifically satisfactory, rigorous and well documented. The bibliography is good. In conclusion, this paper due to its characteristics it can be considered for publication in World Journal of Clinical Cases."

We would like to thank Reviewer 1 for this assessment of and we appreciate their time in commenting.

In response to Reviewer 2's comments:

- *"Very interesting case. An English editing is required and also an adherence to the editorial standards."*

In our revisions, we performed extensive grammar and language revisions and reformatted the entire manuscript to adhere to the BPG editorial guidelines as can be seen in our submitted, revised manuscript.

- *“When describe the histological finding in EA, also cite this work (Cheraghlou S, Atzmony L, Roy SF, McNiff JM, Choate KA. Mutations in KRT10 in epidermolytic acanthoma. J Cutan Pathol. 2020 Feb 11. [PMID: 32045015 DOI: 10.1111/cup.13664]), in which whole-exome sequencing of genomic DNA from lesional tissue revealed KRT10 c.466C > T, p.Arg156Cys mutations in 2/3 samples submitted for examination.”*

We added this important information to the Discussion section of the manuscript in Paragraph 2. It is citation #19.

- *“In regard to the treatment, also cite the use of 0.1% tacrolimus ointment in order to improve pruritus (Tan GF, Tan ES, Tey HL. Anogenital epidermolytic acanthomas: effective treatment of pruritus with 0.1% tacrolimus ointment. Dermatol Ther. 2014 Mar-Apr;27(2):113-6. [PMID: 24703270 DOI: 10.1111/dth.12068]).”*

In the updated discussion section of the manuscript, we included this information to Paragraph 8.

We would also like to thank Reviewer 2 for their assessment of our manuscript and to the valuable references they suggested.

In response to Reviewer 3's comments:

- *“Dear editor and authors, The authors presented a case with the relatively uncommon benign perianal Epidermolytic acanthoma (EA), and reviewed the current literature. However, the following points are recommended to be addressed more clearly: The patient presented was human immunodeficiency virus (HIV)-positive. Is there any association of*

the immunosuppressed condition with EA? Please discuss further this issue and insert suitable references.

In response to this comment, we performed further research into this area and found two relevant publications, Yang et al. (Citation #7) and Chun et al. (Citation #22). In the Discussion section of this manuscript, this point is now addressed in paragraph 4. The relationship with HIV/immunosuppression and EA are discussed. We concluded that there is a paucity of data linking immunosuppression and HIV to EA, and suggest this topic for further investigation.

- *In the manuscript, the authors stated below the subheadings of Case Report: (HIV)-positive below the subheadings of Background and Diagnosis: Many reports have confirmed the absence of human papillomavirus (HPV) in EA... below the subheadings of Treatment: ...“was relieved to learn that her lesions did not represent a sexually transmitted disease and were consistent with agminated epidermolytic acanthomas.” Please clarify if this condition (EA) is sexually transmitted or not?*

We amended the manuscript to explain that EA is not sexually transmitted in Paragraph 1 of the Introduction, referencing citation 12, and in the Discussion section paragraph 10.

- *Grammatical error below the subheadings of Treatment: This treatments...*

This sentence has been edited and all other grammatical errors have been edited and revised throughout the manuscript. In our revisions, we performed extensive grammar and language revisions and reformatted the entire manuscript to adhere to the BPG editorial guidelines as can be seen in our submitted revised manuscript.

- *In Figure 2, please use arrows to label the specific features in the panels and revise the legends, since careful histopathological examination is necessary for an accurate diagnosis."*

Figure 2 left panel: the yellow star is over the compact hyperkeratosis and the green arrow points to acanthosis. Figure 2 right panel: green arrows point to vacuolar degeneration of the spinous cell layer. These revisions can be seen in the submitted revised manuscript.

We would like to thank Reviewer 3 for their assessment of our manuscripts and appreciate their time in commenting.

In response to Reviewer 4's comments:

- *Comment: The author want to clarify the diagnosis and treatment choice for the rare benign lesion Epidermolytic acanthoma, I have several questions and comments:*
- *Epidermolytic acanthoma is a benign and small lesion in skin especially in the genital area, it's different from the epidermolytic ichthyosis, although both have EHK, they are easy to distinguish and to diagnosis, why the author compare the two disease here.*

We first mentioned EI due to its also having the feature of EHK. We updated the manuscript to now compare the two diseases.

- *The patient had HIV positive, is there any relationship between the EA and HIV.*

In response to this comment, we performed further research into this area and added that we did not find any publications showing a relationship between EA and HIV. We not discuss two other cases of immunosuppression associated with EA. We conclude that there is insufficient evidence to implicate the patient's HIV status to the

development of EA. This is discussed in the Discussion section of the Manuscript Paragraph 4.

- *The author mentioned that we will treat the patient if the patient desire it. I wonder is there any optimal option suggestion of the sequence for treatment.*

In response to this comment, the we added a new section to the Discussion section to review treatment options. This is found in Paragraphs 7, 8, 9, and 10. Our recommendation is to biopsy or excise the lesion to obtain an accurate diagnosis. For clinicians who then have patients that are definitively diagnosed with EA, we recommend to first explain why treatment is not medically necessary. If the patient then desires removal of the papules for aesthetic, psychological, or other reasons, medical providers should explain possible treatment options as well as their associated risks and benefits to ensure patient makes an informed decision. In general, if the patient has only one or two EA lesions, we recommend excision of lesions and if the patient has more widespread EA, we then recommend using a topical therapy patient.

- *The picture in the right panel which is something like small lesion in the mucosa of rectum.*

The right panel of Figure 1 shows the same lesion as the left panel, just at a higher magnification. It is not rectal mucosa, but perianal skin with lubricating gel. The photo was taken through a clear anoscope that was used to flatten out the perianal skin folds. This clarification has also been updated in the legend for Figure 1 in the revised manuscript.

We would like to thank Reviewer 4 for their assessment of our manuscripts and appreciate their thoroughness.

In response to the Science Editor's comments:

- *Scientific quality: The manuscript describes a case report of epidermolytic acanthoma. The topic is within the scope of the WJCC. (1) Classification: Grade C, Grade C, Grade C and Grade D;*

We have addressed these concerns as seen above in our response to the reviewers.

- *Summary of the Peer-Review Report: The reviewer# 03507996 thinks the case report is convincing, and the paper is scientifically satisfactory, rigorous and well documented. The bibliography is good. The reviewer# 00070162 thinks an adherence to the editorial standards is required. The reviewer# 03072151 suggests the authors should discuss further about the association of the immunosuppressed condition with EA and insert suitable references. The reviewer#02916651 thinks the authors should mention the relationship between the EA and HIV. And is there any optimal option suggestion of the sequence for treatment?*

We have addressed these concerns as seen above in our response to the reviewers.

- *Format: There are 2 figures. A total of 21 references are cited, including 6 references published in the last 3 years. There is no self-citation.*
- *Language evaluation: Classification: Grade B, Grade B, Grade B and Grade B. The author is a native speaker of English.*

We have addressed these concerns as seen above in our response to the reviewers.

- *Academic norms and rules: The authors provided the Signed Informed Consent Form and the CARE Checklist–2016. The authors signed the Conflict-of-Interest Disclosure Form*

and the Copyright License Agreement. No academic misconduct was found in the CrossCheck detection and Bing search.

- *Supplementary comments: This is an unsolicited manuscript. The study was without financial support. The topic has not previously been published in the WJCC.*
- *Issues Raised: The “Author Contributions” section is missing. Please provide the author contributions;*

On the first page of the manuscript the Author Contributions section has been added.

- *PMID and DOI numbers are missing in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout.*

The authors have reformatted the Reference List to show all PubMed and DOI numbers and to show all authors of references. See References in submitted revised manuscript.

- *Please add the “CASE PRESENTATION”, “FINAL DIAGNOSIS”, and “OUTCOME AND FOLLOW-UP” sections to the main text according to the Guidelines and Requirements for Manuscript Revision.*

Following the Introduction section of the manuscript, the section “Case Presentation” has been added, followed directly by “Final Diagnosis” and “Outcomes and Follow Up” as can be seen in the submitted revised manuscript.

- *Re-review: Required.*
- *Recommendation: Conditional acceptance (Han Zhang)*

We would like to thank the Dr. Jin-Lei Wang for his assessment of our manuscripts and appreciate the very valuable comments.

We hope we have made the necessary revisions for this case report to be worthy of publication. Epidermolytic Acanthoma can be a very challenging diagnosis and misdiagnosis confers undue physical, psychological and financial strains on the patient. Ensuring a proper diagnosis of EA will be beneficial to the readers' patients.

Thank you.

Sincerely,

Ariana Ginsberg, Archeta Rajagopalan, and Joseph Terlizzi