Author's response to reviews

Title: Oral manifestations of Hereditary Nonpolyposis Colorectal Cancer Syndrome: a family case series

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Author's response to reviews: see over
Dear Prof.
Editor-in-Chief
Journal of Medical Case Reports

We have revised our paper "Oral manifestations of Hereditary Nonpolyposis Colorectal Cancer Syndrome: a family case series" in consideration of all reviewers suggestions. And we are sending the revised manuscript to the reviewers for further comment.

List of responses to the editor and reviewers' comments:

Editor:

1. Please include all the co-authors' email addresses in the Title page.
   Authors: The email addresses of all the co-authors were included, as suggested.

2. Please restructure the Abstract section on page 2. The abstract must not exceed 350 words. Please do not use abbreviations or references in the abstract. The abstract should be structured into three sections and should make clear how the case report adds to the medical literature:

   Introduction - An introduction about why this case is important and needs to be reported.

   Please include information on whether this is the first report of this kind in the literature.

   Case presentation - Brief details of what the patient(s) presented with, including the patient's age, sex and ethnic background. If the Case reported is of multiple patients,
please enumerate them accordingly.

Conclusion - A brief conclusion of what the reader should learn from the case report and what the clinical impact will be. Is it an original case report of interest to a particular clinical speciality of medicine or will it have a broader clinical impact across medicine?

Please include information on how it will significantly advance our knowledge of a particular disease etiology or drug mechanism.

Authors: The abstract and the case presentation sections were rewritten in order to follow the aforementioned editor’s comments.

3. Please remove the name of the hospital where the patient was confined, as this may jeopardize the anonymity of the patient.

Authors: As requested, we removed the name of the hospital where the patients were evaluated.

4. Please enumerate the cases in the Case presentation section accordingly (e.g. Case 1 patient...Case 2 patient...)

Authors: We modified the text in order to enumerate the cases diagnosed with HNPCC as suggested (case 1…case 2…). Although we have evaluated a Brazilian family with 20 members, HNPCC was diagnosed in four individuals. All of them presented Fordyce granules and one of them had significant dento-osseous anomalies.

5. Please include an acknowledgement section at the end of the manuscript before the reference list. Please acknowledge anyone who contributed towards the
study by making substantial contributions to conception, design, acquisition of data, or analysis and interpretation of data, or who was involved in drafting the manuscript or revising it critically for important intellectual content, but who does not meet the criteria for authorship. Please also include the source(s) of funding for all authors. Authors should obtain permission to acknowledge from all those mentioned in the Acknowledgements.

Authors: The acknowledgement section was included, as suggested by the editor.

1. Reviewer Yehuda Zadik

There is a need for extensive editing by an English scientific editor (including the Tables). Abbreviations should be spelled-out at first appearance (e.g. FAP).

Authors: We have revised the manuscript, according to the reviewer’s suggestion.

2. Abstract: the number of the studied family members should be mentioned.

Authors: In our study, twenty family members were evaluated. We have included this information in the abstract section.

"In the present family study was observed an association between Fordyce granules and Hereditary Nonpolyposis Colorectal Cancer individuals" – not true; an association may be observed only by statistical analysis (P<0.05) – This is also true for the Conclusion.

Authors: We agree with the reviewer’s comment. Therefore, we have modified the text, as follows:

“Our familial study verified the presence of Fordyce granules in all
individuals diagnosed with Hereditary Nonpolyposis Colorectal Cancer, and the presence of significant dento-osseous anomalies in one case. However, the relationship between oral manifestations and Hereditary Nonpolyposis Colorectal Cancer should be further investigated.”

3. Case presentation: You should describe how did you recruit the participants? (was the family known to suffer from the condition?)

**Authors:** We have modified the text in order to better describe how the participants were recruited. Initially, the diagnosis of the case index was established. The other 19 members of the family were then examined by the Coloproctology Division of our hospital, in order to determine whether individuals presented HNPCC according to the Amsterdam Criteria I and II. Afterwards, all the twenty family members were referred to our Oral Care Center for Inherited Diseases, so that intraoral examinations might be performed and the presence of Fordyce granules and DPRS alterations verified.

Please explain the criteria according which you radiologically differentiated between dense bone islands, hazy sclerosis, osteomas, odontomes, supernumerary teeth and unerupted teeth.

**Authors:** We have used the same criteria previously proposed by Thakker et al., 1995. We have included this information in the text.

4. Discussion: you should present the prevalence of DPRS in general population (as you did for FG).

**Authors:** We have included in the discussion section that the lack of data in the
literature regarding the prevalence of these dento-osseous anomalies precluded a
direct comparison with our results.

5. Because "25% of the unaffected family members also presented FGs" (and
50% of the adults) which is/are much higher than the prevalence in the general
population – FG cannot be considered as pathognomonic feature.

Authors: We have modified the text in order to clarify that FG cannot be
considered a pathognomonic feature. Moreover, the association between FG and
HNPCC should be further investigated.

We listed all responses to the reviewers’ comments, and we hope that the revised
manuscript could be considered for publication.

Yours sincerely,

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